COMPARISON BETWEEN DEXMEDETOMIDINE ALONE AND PROPOFOL WITH FENTANYL COMBINATION FOR FIBEROPTIC GUIDED ENDOTRACHEAL INTUBATION IN NEUROSURGICAL PATIENTS USING BISPECTRAL INDEX GUIDED CONSCIOUS SEDATION. A PROSPECTIVE, RANDOMISED CASE CONTROL STUDY

Thesis submitted for the partial fulfillment for the requirement of the degree of DM (Neuroanaesthesia)

By

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"They alone see truly who see the Lord the same in every creature, who see the deathless in the hearts of all that die. Seeing the same Lord everywhere, they do not harm themselves or others. Thus they attain the supreme goal."

Whatever you do, make it an offering to me – the food you eat, the sacrifices you make, the help you give, even your suffering.

DECLARATION

I hereby declare that this thesis entitled **"Comparison between Dexmedetomidine alone and Propofol with Fentanyl combination for fiberoptic guided endotracheal intubation in neurosurgical patients using Bispectral index guided conscious sedation. A Prospective, randomised Case control Study",** has been prepared by me under the guidance of Dr. Manikandan.S, Additional Professor, Department of Anaesthesiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.

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CERTIFICATE

This is to certify that this thesis entitled **"Comparison between Dexmedetomidine alone and Propofol with Fentanyl combination for fiberoptic guided endotracheal intubation in neurosurgical patients using Bispectral index guided conscious sedation. A Prospective, randomised Case control Study"** is a bonafide work of **Dr. B. Madhusudhana Rao** D.M. - Neuroanaesthesia Resident, and has been done under my guidance and supervision in Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram. He has shown keen interest in preparing this dissertation.

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Comparison between Dexmedetomidine alone and Propofol with Fentanyl combination for fiberoptic guided endotracheal intubation in neurosurgical patients using Bispectral index guided conscious sedation.A Prospective, Randomised Case Control Study.

INTRODUCTION

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The gold standard in the management of patients with a suspected difficult airway is the Awake fibreoptic intubation (AFOI).[1] Thought being a gold standard many serious anesthesia- related complications could result due to improper management of the airway. Patient's may have very unpleasant experiences, in the form of severe gagging, intense coughing or even have unbearable pain during FOB guided awake intubations even with judicious application of local anesthetic's.[2] This can cause complications like postoperative sore throat, dysphagia. Etc.

This is of immense importance in neurosurgical patients as it not only causes unpleasant experience for the patient's but also the excessive coughing during intubation can cause raise in intracranial pressure or cause worsening of the cervical spine compression and thereby causing worsening of the present neurological condition, and this can further worsening and can be very detrimental to the final outcome of the patient.

Conscious sedation a technique, which is desirable not only to make the procedure more tolerable for patient's but due ensure optimal intubating conditions, especially in the presence of abnormal orolaryngopharyngeal anatomy and pathology.

Deeper plain of sedation can result in loss of already compromised airway with serious consequences. The greatest challenge during AFOI is to provide adequate sedation and analgesia while maintaining a patent airway and ensuring spontaneous ventilation. Optimal conditions for AFOI are having a patient who is very comfortable, cooperative, free from oral or pharyngeal secretion and/or any blood, and are able to maintain their airway and have spontaneous ventilation. In order to achieve these conditions, various pharmacologic agents are chosen to provide sedation which should be short acting, which are easily titrable and should provide the adequate amount of sedation and have little or no suppression of spontaneous ventilation.

Controlled sedation and analgesia are most important criteria to AFOI, but deep plain of sedation can result in jeopardizing the deep sedation.[3] Techniques to improve success rate have included nasal over oral intubation (not always possible or not indicated in studies).

An ideal sedative drug for AFOI should provide adequate anxiolysis, amnesia with a low incidence of recall of the procedure. It should have analgesic properties too, to suppress the gag and cough, and be safe and easy to titrate with minimal respiratory and cardiovascular side effects. The drugs belonging to several classes of have been previously described e.g.

sevoflurane, remifentanil and propofol with either as titrated boluses or target controlled infusion.[1, 4-12]

Dexmedetomidine belongs to class of centrally acting, selective alpha-2 agonist. Dexmedetomidine, which has found useful for sedation in critical care units, it has a shorter half-life and eight fold greater selectivity for alpha 2 (α2) over alpha1 (α1) receptors than its counter partner clonidine belonging to the same group of drug.[1]

Due to its ability to produce profound sedation without causing the respiratory depression associated with other anxiolytic-hypnotic drugs and opioids, dexmedotomidine has been enthusiastically used for AFOI. When respiratory compromise can occur as a result of profound over sedation following very large initial bolus doses.[13] Anterograde amnesia occurs with deeper levels of sedation, while a preserved level of cooperation is seen in otherwise very sedated looking patients. The antisialagogue and moderate analgesic properties of dexmedetomidine have been cited as other advantages.[13, 14] More recently, there have been several case reports of dexmedotomidine being used for AFOI.[3, 15-18]

Propofol, a non‑barbiturate anesthetic agent, can produce rapid onset of anesthesia for induction and for maintenance of anesthesia. The mechanism of

action includes facilitation of inhibitory neurotransmission mediated by GABA A receptor binding.

It is also used for various procedures requiring sedations after intravenous administration in proper sub‑hypnotic dose.[19] There are numerous reports of propofol being used for AFOB using both bolus dose, infusion and with the use of target control infusion (TCI) pumps. It can be used either as a sole agent or with other drugs like midazolam, remifentanil, etc.

The main concern with the use of propofol that under dosing (which may be associated with coughing and movement) whereas the over- dosing can causes airway obstruction and thereby the patient can become very restless and thereby losing the patients cooperation. The use of propofol for AFOI is associated with a lower incidence of recall at the expense of an increased risk of over sedation.[1]

Propofol is routinely used for various neurosurgical procedures ranging from those requiring sedation for procedures like AFOB, for to the induction and maintenance of general anesthesia and even in the postoperative period for sedation in the intensive care unit. [1]

Fentanyl used for the induction of general anesthesia to reduce pain and intubation response endotracheal tube passage.[2] Awake fibreoptic intubation can be associated with intense nociceptive stimulation, especially during

passage of the endotracheal tube through the nose and the larynx. While pure sedatives provide anxiolysis and amnesia and may help to smooth the intubation process, but they cannot substitute for inadequate airway topicalization with local anesthetic.

Though remifentanil, is one of the most preferred opioid drugs used in the developed countries these days, but as it is not freely available in many of the developing countries. Due to this many authors still use other opioids like fentanyl in either in the intermittent boluses or as infusion of fentanyl. This is generally supplemented with a benzodiazepine group of drugs.[1, 20-25]

But one of the greatest challenges with these combinations i.e. boluses of opioids with midazolam for sedation, is that this can cause significant hypoxemia (SaO2 <90%), apnea, and even aspiration.[1]

Fentanyl belongs to an opioid group of family, which helps in reducing the pain by acting on the μ type of opioid receptors. Opioids inhibit voltage-gated calcium channels and also activate inwardly rectifying potassium channels.

Lee et al have used fentanyl infusion with other agents as an analgesic for the awake fiberoptic intubation.[26]

Chu et al. Prospective RCT Dexmedetomidine 1.0 μg/ kg infusion over 10 min vs Fentanyl 1.0 μg/ kg infusion over 10 min. DEX group had better

hemodynamic response to intubation, lower recall, with better patient tolerance and satisfaction scores. However in the DEX group, two patients developed bradycardia and one developed hypotension.[27]

Various methods of AFOB have been described, "spray–as–you-go" technique and using airway blocks with local anesthetics.

In "Spray as you go", local anesthetic agent is sprayed along the path of the airway while advancing the FOB. This can be done using an epidural catheter inserted through the side port of the FOB and is attached to the syringe containing local anesthetic drug. As the FOB is advanced the drug is injected through the catheter for local spray of the drug. The drug can also be injected through the suction port of the FOB as the FOB is guided through the airway.[28]

Local blocks can also be used. The nerves blocked are namely glossopharyngeal, superior laryngeal and recurrent laryngeal nerves can be blocked based up on their anatomical location and this will help in anesthetizing the entire upper airway till the carina.

Though these blocks are effective but they can cause intense discomfort for the patients due to multiple needle injection. Besides identifying these nerves might be difficult in few patients due to various reasons like short necks, obesity, thyroid swelling, and contractures. This also requires multiple

needle pricks which can be case discomfort and pain for the patient as compared to spray as you go technique. Etc. these are also contraindicated in patients with coagulopathy or on those patients receiving anticoagulation.

Hence we chose to use the spray as you technique with 4% lignocaine spray along with two groups using two different drugs- dexmedetomidine and propofol with fentanyl groups used for sedation during the procedure.

AIMS AND OBJECTIVES

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A prospective randomized case control study was performed with the following aims:

We hypothesized that there are no differences in the intubation conditions produced with either dexmetomidine infusion alone or a combination of propofol with fentanyl infusion using BIS guided sedation for awake orotracheal fiberoptic intubation using "spray as you go" technique in patients coming for elective neurosurgical procedures with anticipated difficult airway.

AIMS

1) To compare the awake fiberopticorotracheal intubating conditions in patients undergoing elective neurosurgical procedures with either dexmedetomidine infusion alone or combination of propofol with fentanyl infusion under the guidance of BIS monitoring.

2) Our primary outcome was to measure the time to sedation, cough severity and the quality of intubating conditions & time for intubation, total attempts.

Our secondary outcome was to evaluate the total doses of the drugs required, time, hemodynamic changes, BIS values and corresponding changes in OSS/A, comparison between the difficult airway and the intubation conditions.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Management of a difficult airway is one of the most challenging situations faced by the Anesthesiologist. For the elective management of a patient with anticipated difficult airway, Awake Fiber-Optic bronchoscope (AFOB) assisted intubation is a technique of choice and is considered as the gold standard for safely securing the airway.[29]

In 1954, Hopkins HH and Kapany NS first reported the transmission of a visual image through a flexible fiber-optic bundle.[19] It was over a decade later that Peter Murphy performed a nasal intubation using a fiber-optic choledocoscope in a patient with Still's disease.[30]

Ever since its first demonstration, "the use of flexible FOB guided endotracheal intubation has become the gold standard for the management of difficult airway scenario's in both anticipated and unanticipated airways whether in awake, sedated or in the anesthetized patients". [31-34]

The Practice Guidelines for Management of the Difficult Airway given by the American Society of Anesthesiologists task force on management of the difficult airway in 2013 defined a Difficult Airway, "as the clinical situation in which a conventionally trained anesthesiologist experiences difficulty with facemask ventilation of the upper airway, difficulty with tracheal intubation, or both." This represents a complex

interaction between patient factors, the clinical setting, and the skills of the practitioner.[32]

In a review of a total of 1612 patients undergoing neurosurgical procedures, Heidegger T et al reported a 17% incidence of performing fiber-optic intubation, which was only second to those patients undergoing ear, nose and throat surgeries.[33]

Special consideration of the airway is necessary in neurosurgical patients as they offer significant and very unique anesthetic challenges. Neurosurgical patients with anticipated or unanticipated airway require special airway gadgets like the use of flexible fiber-optic bronchoscope.[19]

Difficult intubation has a reported incidence of 10% to 15% in patients with acromegaly, compared to an incidence of around 2% in the general surgical population. [35-38] A review article by Nemergut EC et al in 121 acromegalic patients revealed that 10% were difficult to intubate. Of these, 50 % of the patients had a Mallampati (MMP) score of 1–2. [36]

Pseudo-ankylosis of the TMJ (temporomandibular joint) can cause significant impairment of mouth opening following a temporal craniotomy, thereby causing difficulty in tracheal intubation.[39] Pseudo- ankylosis has extra-articular aetiology compared to true ankylosis in which the joint itself is involved. The ability of forward subluxation of the jaw is generally preserved in pseudoankylosis.[40] Since this is caused by the contracture of the temporalis muscle, either, due to a connective scar tissue formation or a

Volkman's ischaemic process, rather than muscle spasm itself, after the administration of neuromuscular blocking agents, the degree of mouth opening may not improve, hence an awake fibreoptic intubation is indicated in this situation.[40] At the end of the 2nd week and 12th month after surgery, the incidence of pseudo-ankylosis was 33% and 20% respectively as reported by Kawaguchi Met al.[39]

Though this condition is self-remitting over time; in some patients limited mouth opening may persist for several years after the surgery.[38, 41] Similarly, those patients undergoing skull base surgery, especially the trans-temporal surgical approach, may have reduced jaw movement.[41]

Syndromic children can have craniofacial abnormalities which may be responsible for a difficult airway. One of the most commonly performed procedures for which these children present are for calvarial vault remodeling as the corrective surgery for craniosynostosis. Intubation difficulty can be either due to abnormal development in the oral cavity itself (e.g. Pierre–Robin syndrome- but this airway difficulty tends to improve with increasing age as it corresponds to increase in the jaw size) or due to cervical spine pathology, like fusion of cervical vertebrae (commonly seen in Goldenhar, Apert and Crouzon syndromes patients). [38]

Patients, who have sustained facial trauma, present yet another anaesthetic challenge in safely securing the airway. These patients present with a difficult airway due to facial swelling, laryngotracheal injury,

secondary to the accumulation of the blood or vomitus in the airway which can obscure the view of the pharynx and larynx and airway swelling.[42] Two large reviews of patients who presented with facial fractures, indicated that the incidence of the coexisting cervical spine injuries was between 1.8% and 6.7%. [43, 44] Awake intubation is rarely used as a primary approach in trauma;[42] However, it can have unique advantages and has been used in various situations which have been published as case reports where, following trauma, airway has been secured via a transorbital intubating approach,[45] awake fibreoptic intubation etc. following a penetrating facial injury with a crossbow bolt, in situ.[46]

The other concerns in patients presenting for trauma or tumor spine surgery is that these patients might have an unstable spine, where flexion or extension of the neck can cause further deterioration in the neurological status.

The awake fibreoptic approach is a reliable intubation technique in patients with acute and chronic cervical spine lesions.[47] Cervical spine lesions such as osteoarthritis, ankylosing spondylitis, or severe rheumatoid arthritis can result in an immobile and stiff neck. Patients with halo traction offer additional problem for upper airway access. [38]

The prevalence of Rheumatoid arthritis in the USA is 0.3% to 1.5%. Cervical joint involvement is commonly seen in male patients, and the incidence can vary between 15% and 86%.[48] The most frequent

complication seen in these patients is the anterior atlanto-axial subluxation. This is exacerbated by neck flexion and as direct laryngoscopy, causes the C1–C2 extension; it has been advocated as an acceptable technique. [48] Posterior atlanto-axial subluxation is relatively uncommon and vertical atlanto-axial subluxation, is seen in 10% to 20% of patients. These patients require the head to be maintained in a neutral head position. This is an indication for doing an AFOB in these patients.[38]

In about 10% to 20% of these rheumatoid patients, sub-axial subluxation is seen and it most frequently occurs at the C5–C6 level. This can be managed with a similar airway protocol as that which is used in patients who have sustained traumatic cervical spine injuries. This condition can be very dangerous due to the instability of the cervical spine and an AFOB would be prudent.[48]

With the further progression of rheumatoid disease, severe ankylosis of the cervical spine can occur, thereby limiting the neck movement further. This causes the shift of the emphasis from just protecting the unstable cervical spine into a difficult airway where in, there will be technical difficulties encountered during intubating the trachea, due to the presence of a fixed cervical spine.[38] AFOB is strongly indicated in such patients. Wattenmaker I et al conducted a study on 128 patients with rheumatoid arthritis who were undergoing spine surgery. They suggested that these patients have a lower incidence of stridor after extubation if they underwent

AFOB, and they postulated that it was due to a reduction in soft-tissue trauma during intubation. [49]

Cervical spine injury is considered as a difficult airway and difficult airway management is anticipated in these patients. It was Goldberg W who conducted a study on 34,000 patients who presented with blunt trauma. 2.5% of these patients had sustained cervical spine injuries as well.[50] They found that the fractures mostly occurred at C2 (24%) level and C5–C6 and C6–C7 level were associated with dislocations. They also concluded that the vertebral body was the site which was most frequently fractured. [50]

Though the optimal management of the airway in cervical spine trauma is still controversial. Various techniques are recommended in these patients for tracheal intubation. This includes the use of the standard direct laryngoscopy method with manual in-line stabilization (MILI),[51] cricothyroidotomy, [52] use of the ILMA- intubating laryngeal mask,[53, 54] use of gadgets like lighted stylet[55] and use of variations of the standard laryngoscope.[56]

Heath KJ in 1994 conducted a study of 50 patients, in whom the author defined difficult laryngoscopy as a Cormack and Lehane grade 3 or 4. As per this definition difficult laryngoscopy was seen in 22% of patients who required neck stabilization using MILI technique of immobilization and in 64% of patients who were either with a neck collar or who required a tape and sandbag for immobilization of the cervical spine.[57] Though there

is a theoretical advantage of decreased cervical spine movement during FOB guided intubation, it might be difficult to realize its actual benefit clinically. [57]

Most anesthesiologists preferred to use AFOB for intubating patients who had cervical spine disease. In a survey conducted in 452 members belonging to the American Society of Anesthesiology, FOB was the preferred technique for intubating patients with stable cervical spine disease.[58]Jenkins K et al conducted another similar survey on 833 members belonging to the Canadian Anesthesiologists' Society. 67% of them preferred doing an AFOB intubation in patients who presented with a cervical cord compression for discectomy.[59] Similarly, 78% of 472 members belonging to American Society of Anesthesiology preferred conducting an AFOB intubation, in patients who sustained cervical spine injury.[60]

Many small retrospective observational studies conclude that there are varying thresholds for performing AFOB in patients with cervical spine injuries.[61] One of the main high-lighting features of these studies is that, though a variety of choices are available for the airway management, the secondary cervical injury attributable to the intubation procedure has a very small incidence. In another observational study conducted on 327 patients who presented with cervical spine disease, 39% of them were intubated using an AFOB technique.[62] Most anesthesiologists prefer to use this

technique especially if patients presented with unstable or fractured vertebrae, myelopathy or spinal canal stenosis. The authors considered these criteria as an indication for the use of AFOB guided intubation. [38]

Various patient related factors, which indicate a potentially difficult intubation are, a history of previous difficult airway, patients with high risk of aspiration, patients with cardiovascular instability which may be exacerbated during laryngoscopy, any contraindication to short acting depolarizing muscle relaxants like suxamethonium, history of obstructive sleep apnea, obese patients, and syndromic patients. Patients with metabolic disorders such as mucopolysaccharidosis also present with difficult airways, though generally seen in children, it may present in adult patients like Hurler-Scheie, Maroteaux, Hunters or Morquio syndromes. [38]

Patients with various oropharyngeal pathology like restricted mouth opening (small mouth) due to connective tissue disorders, retrognathism which can be present either independently or in association with a syndrome, presence of any oral tumors, any previous history of oral radiotherapy or surgery for TMJ disease, including rheumatoid arthritis, trauma or oropharyngeal abscesses also present difficult airway scenarios.[38]

Neck pathology includes limited mobility of the cervical spine due to sero-negative arthritis, any prior surgery or cervical spine instability like in trauma and AAD.[38]

The greatest advantages of AFOB is that the head can be maintained in a neutral position as the cervical muscle tone is preserved, neurological assessment can be performed post-intubation, the larynx can be visualized in patients with an immobile spine and the patient can also be positioned prior to general anesthesia. [38]

There is always a fear of deterioration of the neurological function following the conventional methods of tracheal intubation after cervical spine injury.[63, 64] However, even in such cases, it has been very difficult to confidently attribute these injuries due to the intubation procedure. Currently there are no published data which can suggest that AFOB intubation improves the final outcome in patients with cervical spine injury, compared to any other intubation techniques. If AFOB is performed by untrained personal that lack the necessary skills, it can even be detrimental. There are reports of even complete airway obstruction, which occurred during the FOB intubation in two awake patients with cervical spine injury.[65]

Various non-neurosurgical patients related reasons for AFOB intubation are often secondary to the technical difficulty which is associated with conventional laryngoscopy. Those patients who are at risk of aspiration of gastric contents, it is advantageous to try and preserve the airway reflexes especially if rapid sequence induction is either not possible or contraindicated. In addition, AFOB intubation can produce less

variability in hemodynamic parameters than any other standard anesthetic induction especially if multiple or prolonged laryngoscopy attempts are anticipated.[19]

Neurosurgical patients with anticipated or unanticipated airway include; traumatic, congenital or degenerative cervical spine lesions, diseases of the pituitary gland associated with acromegaly or Cushing's syndrome, patients undergoing awake craniotomy or patients on stereotactic frames for stereotactic biopsy or craniotomy, congenital craniofacial malformation and all other patients with difficult facial and oropharyngeal anatomy.

Various airway maneuvers used to secure the airway may aggravate intracranial hypertension in patients who have sustained traumatic brain injury and in patients with intracranial space occupying lesions with compromised conscious level. Intracranial dynamics are closely related to ventilation, cerebral blood flow increases with hypercarbia and hypoxia with a resultant raise in ICP (intracranial pressure). Laryngoscopy and intubation too can cause a rapid raise in the ICP and mean arterial pressure (MAP) there by increasing the CBF and thus compromising the intracranial dynamics and increasing the morbidity. Routine intraoperative airway management may be complicated by the complex requirements of positioning and preoperative intracranial hypertension, which also can contribute to worsening of the neurological status.

The ischemic or injured brain can poorly tolerate hypoxia and hypercarbia. This can significantly decrease the favorable outcome in traumatic brain injury. Several factors are related to pathophysiologic alterations in neurosurgical patients. These factors will influence the technique and choice of securing the airway. Techniques include ways of blunting the hemodynamic response and addressing other issues in trauma management and in the management of increased ICP.

Various routinely used gadgets for intubation in the general population may worsen the neurological condition in patients with cervical spinal instability, such as patients with traumatic, congenital or degenerative cervical lesions like, disk prolapse, RA, ankylosing spondylosis, Chiari malformation, DM etc and many other difficult airway scenario conditions like obesity, difficult mouth opening, decreased thyro-mental distance, etc.

Aprahamian C in 1984 reported in an adult cadaveric model with C5-6 ligamentous injury that chin lift and jaw thrust caused a greater than 5 mm increase in the disc space. [66] This widening was not prevented by the presence of Philadelphia collar. The introduction of an oesophageal obturator airway caused a 3-4 mm increase in disc space. Anterior neck pressure to facilitate nasotracheal intubation caused a posterior subluxation of more than 5 mm. Head tilt, and insertion of a nasopharyngeal or an oropharyngeal airway did not cause any significant displacement of the

spinal segments. Cricoid pressure applied during rapid sequence induction for emergency intubation has been generally believed to displace the spine. But a study conducted on the cadaver, by using a lateral cervical spine radiographs showed negligible spine movement with cricoid pressure.[67]

The effect of spinal immobilization on techniques of airway management maneuvers used for spine immobilization may restrict the exposure of larynx during laryngoscopy. Immobilization of the neck with collars, straps and sand bags restricted the mouth opening and hence caused a poor laryngoscopic view (CL grade 3 and 4) in 64% of the patients.[57] Visualization improved with manual inline traction but was still poorer compared to the view in the optimal intubating position. MILI decreases, but does not completely eliminate the cervical spine movement caused during laryngoscopy.[68] Axial traction applied through weights or by an assistant, as it has been advocated earlier, can be deleterious. In patients with unstable cervical spine fractures, axial traction has been shown to cause a mean distraction at the fracture site of 7.75 mm.[69] Therefore, the current emphasis during intubation of a patient with an unstable cervical spine is on manual inline stabilization and not axial traction.

Though there are various techniques of securing the airway in patients who sustained cervical spine injury, direct laryngoscopic oro-tracheal intubation with MILI is the most commonly recommended technique for securing the airway in these patients.

During normal DL and oral intubation, significant extension occurs at the junction between occipital bone and C1 and also between C-1 and C-2.[65, 69] MILI reduces this head extension by 50% in anaesthetized patients.[70] However, in a study conducted on cadavers with C4 injuries, MILI did not prevent the movement at the cervical spine. This happens to be the major limitation factor of this manoeuver[65]. Axial traction on spine can further worsen the spinal cord injury and hence should be avoided during either laryngoscopy or intubation. As previously discussed, if the cervical collar is left in place during intubation, laryngoscopic view can be difficult and a higher grade of CL grade can be encountered.[57]

Gum elastic bougie is an important and commonly available adjunct used during DL for intubation. By using a bougie, less pressure is required by laryngoscopist, thereby avoiding the potential displacement of the fractured spine.[51]

Influence of the type of laryngoscope on cervical movement: The cervical spine movement caused by McIntosh curved blade or Miller's straight blade were not significantly different during DL intubation.[71] In a comparison of McIntosh and McCoy laryngoscopes, McCoy laryngoscope improved visualization of the larynx by at least one grade in 49% of cases.[72] Another study compared Miller and McIntosh blades with the Bullard laryngoscope.[73] Head extension and neck movements were less and laryngeal visualization was better with the use of the Bullard

laryngoscope. However, there were problems associated with Bullard laryngoscope, which included prolonged time for intubation, fogging, and occasional inability to pass the tracheal tube through the glottis. Angulated video intubating laryngoscope significantly improved the laryngeal view compared with direct laryngoscopy with cricoid pressure.[74]

Awake Intubation: Awake intubation is considered safe in a patient with spinal injury as the normal muscle tone provides protection and the neurological status of the patient can be monitored. The various options available for awake intubation are blind oral or nasal intubation and awake fibreoptic oral or nasal intubation. Despite the safety claimed for awake intubation, a number of limitations of these techniques must be appreciated. Awake intubation is slower compared to rapid sequence intubation. Cooperation from the patient is very essential for the success of the procedure. Considerable expertise of the operator is required to accomplish awake intubation. Blind nasal intubation is complicated by epistaxis, laryngospasm and oesophageal intubation.

In cadavers with C-5 and C-6 instability, blind nasal intubation caused least cervical spine movements.[75] In C-1 and C-2 instability both oral and nasal intubations produced similar cervical spine movement.[74] In cadavers with C-3 injury, awake fibre-optic technique produced no movement of unstable segments as assessed by video fluoroscopy.[76]

The gold standard in the management of patients with a suspected difficult airway is the Awake Fibre-Optic Intubation (AFOI[)]. [1] However, patient's may have extremely unpleasant experiences, in the form of severe gagging, intense coughing or even unbearable pain during FOB guided awake intubations although judicious application of local anesthetic is routinely done. [2] This can result in postoperative sore throat and pain. This is of immense importance in neurosurgical patients as it not only contributes to an unpleasant experience for the patient, but also the excessive coughing during intubation can cause raise in intracranial pressure or cause worsening of the cervical spine compression thereby worsening the preexisting neurological status, and hence can be very detrimental in the final outcome of the patient.

Various methods of FOB have been described. It can be where in the patient is awake (AFOB) and spontaneously breathing or after giving general anesthesia under muscle paralysis. AFOB can be done by giving conscious sedation with spray of local anesthetic drug during advancement of the bronchoscope, "Spray As You GO" (SAYGO) technique or by using airway blocks with local anesthetics.

"Spray as you go" technique:

In the "Spray as you go" technique, local anesthetic agent is sprayed along the path of the airway while advancing the FOB. This can be done by using an epidural catheter inserted through the side port of the FOB to

which is attached a syringe containing the local anesthetic drug. As the FOB is advanced the drug is injected through the catheter for local spray of the drug. The drug can also be injected through the suction port of the FOB as the FOB is guided through the airway.[28]

Local blocks can also be used. Blocking the following nerves, namely glossopharyngeal, superior laryngeal and recurrent laryngeal nerves will help in anesthetizing the entire upper airway upto the carina.

Blockade of the Glossopharyngeal Nerve:

Blocking this nerve facilitates the smooth passage of endotracheal tube as this blocks the gag reflex during the AFOB guided intubation. Two techniques are described to block the glossopharyngeal nerve, the intraoral approach and the Peri-styloid block.

In the Intraoral approach – this nerve is blocked by injecting 4- 5 ml of local anesthetic drug sub-mucosally using a 22-gauge needle at the base of the posterior tonsillar pillar, as it is here, where it crosses the palatoglossal arch.

In the Peri-styloid approach, with the patient in supine position, a line is drawn between the mastoid process and the angle of the mandible. The styloid process is palpated by applying deep pressure along this line drawn, posterior to the angle of the jaw. A short, small-gauge needle is inserted, once the styloid process is felt, the needle is then withdrawn slightly and directed posteriorly off the styloid process. Once this bony

contact is lost, 5 to 7 mL of local anesthetic agent is injected after careful aspiration for blood. Both the procedures are contraindicated in patients with coagulopathies or on anticoagulation.

Internal branch of Superior laryngeal nerve:

This nerve originates from the superior laryngeal nerve lateral to the greater cornu of the hyoid bone. [77-79] The nerve generally passes 2 to 4 mm inferior to the greater cornu of the hyoid bone, here it passes under the mucosa in the pyriform recess after piercing the thyrohyoid membrane. This nerve supplies the base of the tongue, aryepiglottic fold, arytenoids and the posterior surface of the epiglottis.[19]

Direct infiltration is accomplished by using a 25G needle. At the level of the thyrohyoid membrane, and inferior to the cornu of the hyoid bone, the needle is inserted to make contact with the cornu, after which the needle is minimally retracted and 2mL of 2% lidocaine is injected after negative aspiration. This is performed with the neck in extended position. [19, 80]

Recurrent Laryngeal nerve (RLN):

RLN provides sensory innervation to the trachea and vocal folds. Blockade of this nerve helps in the easy and comfortable passage of the endotracheal tube into the trachea. Trans-laryngeal block of the recurrent laryngeal nerve is done at the level of the cricothyroid membrane. A 10-mL

syringe with a 22or 20 gauge needle is advanced through this membrane until air is aspirated into the syringe. Then 4ml of 4%lidocaine is injected after asking the patient to take deep breath and hold it. This spray of the drug induces coughing that helps in dispersing the LA into the tracheobroncheal tree.

The other method of blocking the RLN is by spraying the LA via the injection port of the fiber-optic bronchoscope.

Though these blocks are effective, they can cause intense discomfort for the patients due to multiple needle injections. Besides identifying these nerves might be difficult in few patients due to various reasons like a short neck, obesity, presence of a thyroid swelling, contractures etc. These airway blocks are also contraindicated in patients with coagulopathy and in those patients receiving anticoagulation.

One of the disadvantages of the individual nerve blocks are that they require multiple injections, which cause discomfort and pain for the patient as compared to the SAYGO technique. This experience may also prove to be very unpleasant due to the severe gagging; intense coughing and the pain which may be quite unbearable during FOB guided awake intubations even with judicious application of local anesthetics. [2] This can cause postoperative sore throat, severe throat pain.

This is of immense importance in neurosurgical patients as it not only results in an unpleasant experience for the patient, but the excessive cough

during intubation can cause a raise in intracranial pressure or can cause worsening of the cervical spine compression and thereby worsen the clinical status.

One of the ways to overcome this discomfort faced by the patients, is either by administering drugs which allow conscious sedation or by giving complete General Anaesthesia (GA). This is characterized by the absence of purposeful response to any stimulus, loss of airway reflexes, depression of respiration and disturbance of circulatory reflexes.

The disadvantage of giving GA is that, the airway can be lost due to loss of the tone of the neck musculature and can result in airway loss in an already anticipated difficult airway leading to a catastrophe.

Optimal conditions for AFOI demand that a patient be comfortable, cooperative, free of oropharyngeal secretions/blood and are able to maintain their airway.

Conscious sedation is a form of sedation where in, drugs are administered to cause depression of consciousness during which time, patients are able to respond spontaneously to verbal commands or light tactile stimulation. During this type of sedation, patients are able to keep his/her airway patent maintaining spontaneous ventilation. Conscious sedation may be achieved by a wide variety of drugs, most commonly, Propofol. This technique is desirable not only to make the procedure more tolerable for patient, but also ensures optimal intubating conditions,

especially in the presence of abnormal orolaryngopharyngeal and cervical anatomy and pathology.

In deeper sedation, there is a further decrease in the level of the consciousness which can progress to a complete loss of consciousness wherein patients tend to respond only to a painful stimulus. It is associated with loss of the patient's ability to maintain their airway, inadequate spontaneous ventilation with or without compromised cardiovascular function, and has risks similar to general anaesthesia, hence requiring an equivalent level of care.

Providing analgesia is also an integral part of AFOB technique. This could be achieved, either by reducing or eliminating pain perception, by using locally active drugs or generally by depressing the pain perception in the central nervous system.

In order to achieve these conditions, various pharmacologic agents are chosen to provide sedation. These drugs ideally should be short acting, easily titratable, provide the adequate amount of sedation and have little or no suppression of spontaneous ventilation. The ideal sedative for AFOI should also provide adequate anxiolysis and amnesia with a low incidence of recall of the procedure. It should also have analgesic properties, to suppress the gag and cough, with minimal respiratory and cardiovascular side effects.

The greatest challenge during AFOI is to provide adequate sedation and analgesia while maintaining a patent airway and ensuring spontaneous ventilation. Optimal conditions for AFOI include that a patient be comfortable, cooperative, free of oropharyngeal secretion and blood, and are able to maintain their airway and have spontaneous ventilation. In order to achieve these conditions, various pharmacologic agent are chosen to provide sedation which should be short acting, easily titratable, provide the adequate amount of sedation and have little or no suppression of spontaneous ventilation.

Controlled sedation with analgesia are most important criteria to AFOI, but deep sedation can result in loss of the airway with serious consequences.[3]

Techniques to improve success rates have included nasal over oral intubation (not always possible or not indicated in studies) and usage of various techniques of intubation and various different drugs used for sedation (sevoflurane, remifentanil and propofol either as titrated boluses or target controlled infusion) [4-12]

Sedation requires proper monitoring of the patient. Most commonly practiced methods for monitoring the depth of sedation are (e.g., visual analogue scale), observer based (e.g., observer's assessment of awareness/sedation (OAA/S) score) and machine based (e.g., Bi-spectral index score (BIS)).[15, 81, 82]

The disadvantage of OAA/S score is that it requires frequent patient stimulation, which may there by alter the actual level of sedation. However, the BIS score offers an advantage over OAA/S is that it gives a continuous and objective assessment with no stimulation of the patient. BIS monitor which indicates the level of sedation is based up on the electroencephalogram (EEG) i.e., a cerebral activity based monitor. This uses a complex algorithm which depicts the results as a single whole number between '0' to '100' where '0' is total burst suppression and '100' is fully awake. But the score of this monitor cannot be expected to follow the progression of sedation linearly.[83]

Arbour R had reported that a BIS reading of 70-80 corresponds with a clinical state where the patient is "able to respond to loud verbal, limited tactile stimulation" and BIS score of 60-70 corresponds with a state where patient is "responsive to loud verbal and intense tactile stimulation."[84] In OAA/S score of 3 the patient "responds only after the name is called loudly/or repeatedly."[85]For this reason, in the present study, the OAA/S score 3 has been considered as conscious sedation on clinical observation and a BIS score 70 has been taken as a adequate state of conscious sedation when monitored instrumentally.

Hence, the time required to reach a BIS score of 70 and the time to achieve OAA/S score 3 was noted. The assessment of OAA/S score was done according to the 5-point scale routinely used.

Chisholm et al did not find a good correlation in the EEG-based monitor of sedation, namely, between 61 and 80 scores when one would like to measure light to moderate sedation, [86]although EEG-based monitor of sedation demonstrated a correlation with the clinical assessment of sedation scores and responsiveness at the extremes of sedation. Though the use of BIS based monitoring of sedation is very appealing, the conventional methods of clinical assessment of sedation are extremely important as patient contact is always maintained. Dipanjan Bagchi et al had suggested that the BIS monitoring should be used as an adjunct to clinical assessment rather than as the primary monitor. Kasuya Y advised the combination of both these methods of monitoring sedation as they act complementary in ensuring a better understanding of the patient's response to sedation than when using either of the method alone. [63R] By simply targeting sedation by using the EEG based monitor and there by ignoring the other clinical signs of over sedation will not be prudent and can cause over-sedation and its severe consequence's especially in a patient with anticipated difficult airway resulting in the loss of the airway. Therefore, we in our study, chose to use both BIS guidance to titrate the sedation along with the OAA/S.

The ideal sedative for AFOI should provide both anxiolysis and amnesia adequately with a low incidence of having a recall for the procedure. It would be ideal if this drug can have analgesia propertiestoo

and hence it would suppress the gag and cough. It should also be safe and very easy to titrate with a very minimal effect on the cardiorespiratory system. The use of several classes of drugs have been described.[85]

Dexmedetomidine belongs to the class of centrally acting, selective alpha-2 agonists. Dexmedetomidine, which has been found useful for sedation in critical care units, has a shorter half-life and has an eightfold greater selectivity for alpha 2 over alpha1 receptors than its counter partner clonidine belonging to the same group. 1I It acts on the Locus Ceruleus alpha2 receptors which mediate sedative properties, while the spinal alpha2 receptors mediate its analgesic effects.[87, 88] The presynaptic alpha2 receptors in the peripheral nervous system and the post-synaptic alpha 2 receptors which are present in the central nervous system, mediate the cardiovascular effects of a2 agonists. Inhibition of noradrenaline release causes bradycardia, and thus a reduction in the cardiac output leading to hypotension. But, a2 receptors located directly on vascular tissue cause vasoconstriction, which can result in hypertension, secondary to the administration of large bolus doses of a2 agonists.[89]

Due to its ability to produce profound sedation, without any respiratory depression which is an adverse effect generally associated with other anxiolytic-hypnotic drugs and opioids, dexmedotomidine has been enthusiastically used for AFOI. Respiratory compromise has been reported as a result of profound sedation following very large initial bolus doses.[13]

In one study, healthy volunteers were sedated till they were became unresponsive to shaking and shouting, but they were still able to maintain spontaneous respiration with a patent airway.[88] Anterograde amnesia occurs with deeper levels of sedation, while a preserved level of co-operation is seen in otherwise very sedated looking patients. It also has anti-sialagogue and moderate analgesic properties which prove to be a major advantage.[13, 14]More recently, there have been several studies and case reports of dexmedetomidine being used for AFOI.[3, 15-18]

It is generally infused at 1 μg/kg over 10-20 min to avoid peak-dose hypertension, which may exacerbate a bradycardia thereby causing secondary fall in cardiac output. The initial bolus is followed by an infusion at a rate of usually of 0.1-0.7 μg /kg/hr.[27, 90]

Propofol, is a non‑barbiturate anesthetic agent, can produce rapid onset of anesthesia, and is used for induction and maintenance of the same. The mechanism of action includes facilitation of inhibitory neurotransmission mediated by GABA A receptor binding. This allosterically increases binding affinity of GABA for the GABA A receptor coupled with a chloride channel, causing activation of the receptor, leading to hyperpolarization of the nerve membrane. Propofol (like most general anesthetics) binds multiple ion channels and receptors.

It is also used for various procedures requiring sedation after intravenous administration in the proper sub‑hypnotic dose.[83] There are

numerous reports of propofol being used for AFOB using both bolus dose, infusion and with the use of target control infusion pumps. It can be used either as a sole agent or with other drugs like midazolam, remifentanyl, etc.

The main concern with the use of propofol is the difficulty in balancing between under dosing (which may be associated with coughing and movement) and over-dosing which can cause airway obstruction and loss of cooperation. This balance may be being able to be difficult to achieve. The use of propofol for AFOI is associated with a lower incidence of recall at the expense of an increased risk of over sedation.[1]

Propofol is routinely used for various neurosurgical procedures ranging from those requiring sedation for procedures like AFOB to induction and maintenance of general anesthesia and even in the postoperative period for sedation in the intensive care unit.[1]

Fentanyl is an opioid used for the induction of general anesthesia to reduce pain and intubation response to endotracheal tube passage.[2] Awake fibre-optic intubation can be associated with intense nociceptive receptors stimulation, especially during passage of the endotracheal tube through the nose and the larynx. While pure sedatives provide anxiolysis and amnesia and may help to smoothen the intubation process, they cannot substitute for inadequate airway topicalization with a local anesthetic. Opioids are strong analgesics agents which have some hypnotic effect and can help attenuate

the coughing and hemodynamic changes caused due to airway instrumentation.

Though remifentanil is one of the most preferred opioids in use today, it is not freely available in many developing countries, and hence many authors still report using either incremental boluses or infusion of fentanyl, generally in combination with a benzodiazepine, like diazepam or midazolam. [1, 22] But one of the greatest challenges with this combination i.e. boluses of opioids with midazolam for sedation can be the threat of causing significant hypoxemia (SaO2 <90%), apnea, and even aspiration [1]

Fentanyl belongs to the opioid group of drugs, which help in reducing the pain by acting on the μ type of opioid receptors. These drugs bind to specific receptors located throughout the central nervous system and other tissues.

There are four major types of opioid receptors which are: mu (μ, with subtypes μ 1 and μ 2), kappa (κ), delta (δ), and sigma (σ). All these receptors couple to the G proteins and binding of an agonist to the receptor causes hyperpolarization of the membrane. The effects of acute opioid intake are mediated by inhibition of cAMP (adenylyl cyclase) causing reductions in intracellular cyclic AMP concentrations and there by leading to the activation of phospholipase C. Opioids also inhibit voltage- gated calcium channels and also activate inwardly rectifying potassium channels.

Lee et al had used fentanyl infusions with other agents as an analgesic for awake fiber-optic intubation.[26]

Chu et al. did a prospective RCT in which Dexmedetomidine 1.0 μg/ kg infusion was given over a period of 10 min vs Fentanyl 1.0 μg/ kg infusion over 10 min. Compared to the Fentanyl group, patients belonging to the Dexmedetomidine group had better hemodynamic responses to intubation, lower recall, with better patient tolerance and better satisfaction scores. However, in the Dexmedetomidine group, two patients developed bradycardia and one developed hypotension. [27]

Thirty patients were randomized by Lee et al. They either received propofol (1 mg/kg bolus followed by an infusion of 1 mg/kg/hr.) or a combination of midazolam (0.05 mg/ kg) and fentanyl (1 μg/kg bolus).[26] They reported that the patients in the propofol group were more sedated though there was no significant difference between the two groups in the time taken for the procedure, incidence coughing during the procedure or the intubating conditions. Neidhart et al. combined propofol with remifentanil and infused it at a fixed rate of 2 mg/kg/hr. and 0.05 μg/kg/min respectively. They reported that 35 of the 40 patients had ‘‘good to very good’’ sedation in whose tracheas were all intubated successfully. No patient became hypoxic, and the heart rate and blood pressure remained within the limits of 30% from the baseline in all but one.[91]

In 2007, Huitink et al. published a case series in which 40 patients were given propofol at a fixed rate of 150 mg/hr. and local anesthetic spray was used by the standard SAYGO technique. They found there were ‘‘no complications’’ associated with the technique; however, they did not report any respiratory observations. [92]

Various articles, few RCTs, [17, 27, 90, 93] few case reports and case series [16-18, 55, 94-97]describe the use of dexmedetomidine for sedating patients undergoing AFOI, usually as the sole agent but occasionally in combination with midazolam [90] or ketamine. [15] A TCI system for dexmedetomidine has also been described for AFOB.[94]

Tsai et al. in 2010 conducted a prospective randomized trial in 40 patients needing AFOI to either dexmedetomidine (1.0 μg/ kg) or propofol TCI (effect-site concentration 3.6 μg /mL). [93] Intubating conditions were satisfactory in both the drugs groups; however, patients in the dexmedetomidine group had less discomfort, heart rate changes, and episodes of airway obstruction.[93]

Hagberg et al. randomized 30 patients with ‘‘expected difficult airways’’ into two groups. One group received dexmedetomidine bolus of 0.4 μg/ kg followed by an infusion at a rate of 0.7 μg/ kg/hr and the other group received remifentanil bolus 0.75 μg/ kg followed by an infusion at a rate of 0.075 μg/ kg/min. The authors concluded that there were no

differences in the recall, hemodynamic stability, patient tolerance or satisfaction scores between the two groups; however, the dexmedetomidine group required more attempts during intubation with a first attempt success rate of 38% in the dexmedetomidine group as compared to 76% in the remifentanil group. But the mean oxygen saturation levels were found to be lower in the remifentanil group. Interestingly, the sedation scores were lower in the dexmedetomidine group, which may suggest that the smaller initial bolus of Dexmedetomidine used in this study may have lacked efficacy in comparison with the doses used in other studies. This may be a contributing factor to the higher number of attempts at intubation in the DEX group.[33]

Bergese et al in 2008, randomized 105 patients requiring AFOI to either a Dexmedetomidine bolus of 1 μg/kg over 10 minutes followed by an infusion at 0.7 μg/kg/hr or a ‘‘placebo’’ with midazolam and fentanyl as the rescue drug to achieve a Ramsay sedation score of 2, prior to attempts at either oral or nasal intubation. They found that a mean bolus dose of 1.07 mg and 2.85 mg of midazolam was used as a rescue drug in the dexmedetomidine and ‘‘placebo’’ groups, respectively. In the placebo group, 28% of patients developed significant hypertension and 24% developed significant tachycardia, as compared to the Dexmedetomidine group in which 27% of patients became hypotensive with significant decreases in the heart rates as well.

Chu et al. randomized 30 oral cancer patients with limited mouth opening, either into dexmedetomidine group or fentanyl group. Patients belonging to both the groups received the respective drugs at 1 μg/kg. In the dexmedetomidine group, patients had better intubating conditions and tolerance of the procedure with less hemodynamic fluctuations in response to intubation with minimal adverse effects.[27] Again, it is not surprising that this study was in favor of the hemodynamic outcomes of dexmedetomidine when the dose of fentanyl used in the other group was lesser than that used by Ovassapian et al. (1 μg/kg vs.1.56 μg/kg) who had used it in combination with midazolam at a dose 0.12 mg/ kg. They reported increases of ≥20 mmHg in mean arterial pressure and ≥20 beats/minin heart rate in 30% of their patients.[93]

It could be argued that the relatively long loading time of the loading dose of dexmedetomidine may one of its disadvantages; however, the main and most important side effects reported with its use are bradycardia and hypotension.[16, 89] But the bradycardia generally doesn't appear to be a significant problem, which can be explained due to the concurrent use of glycopyrrolate in most of the studies, but hypotension is of greater concern, especially if it is subsequently followed by the induction of general anesthesia. [1]

Another concern with the use of dexmedetomidine is its effect on the

respiratory patter. There are few reports describing its use in patients with raised intracranial pressure. In this subset of patients if there is a risk of hypoventilation there is a concern that this may further increase the Intra Cranial Pressure (ICP).[97]

In 1997, Parkes et alnebulized patients with 6 mg/kg of 10% lignocaine solution through a nebulizer mask prior to instrumentation of the airway with a FOB. [85] The serum lignocaine levels were measured and the authors found that it always remained below the standard accepted threshold limit of 5 mg/l. The highest levels obtained in the study were 0.45 mg/l, which was much less than threshold value. In a similar study, conducted by Langmack et alon 51 asthmatic volunteers who underwent FOB, the authors measured the serum lignocaine levels achieved with topical lignocaine. The average total dose used was 8.2 mg/kg (600 mg). They concluded that this was safe in all patients as assessed by serum lignocaine concentrations.[110]. However, in 1993, Wu et al reported seizures in a patient who received a total dose of 300 mg of topical lignocaine during FOB. [111] The serum lignocaine concentrations were found to be well above the acceptable toxic limits. Hence, a constant vigilance for any early signs and symptoms of lignocaine toxicity is mandatory especially while using large doses.

K. A. Williams, combined the method of nebulization and direct

application of lidocaine to the airway in 25 un-sedated subjects undergoing AFOB intubations. It produced good conditions for fibre-optic intubation. In their series, a maximum calculated dose of 9 mg/kg lignocaine produced one peak plasma lidocaine concentration of 4.5 mg/L but none greater than 5 mg/L. They concluded that when both these methods are combined i.e. nebulization and topical anesthesia, the maximum dose of calculated lidocaine administration should not exceed 9 mg/ kg. [98]

In a randomized, double-blinded, clinical study on patients with clinical predictors or history of difficult intubation requiring awake fiberoptic orotracheal intubation, Fu S. Xue et al, compared the safety and efficacy of 2% and 4% lidocaine during airway topical anesthesia with the SAYGO technique via the FOB. They concluded that both 2% and 4% lidocaine administered topically by a SAYGO technique could provide clinically acceptable intubating conditions for AFOI in sedated patients with difficult airway. Compared with 4% lidocaine, however, 2% lidocaine requires a much smaller dosage and thereby results in lower plasma concentrations. [99]

M. Bonnin et al in 2007 assessed an objective intubation score after intubation. This intubation score was based upon the anaesthesia quality; vocal cords relaxation and immediate tracheal tube tolerance. They gave different scores for each of these variables, which were assessed during the

FOB naso-tracheal intubation with a lowest score of less than 3 and highest score of 8.[100]

Anesthesia quality graded as asleep or deep sedation then two points was given and if the patient showed slight resistance then a score of zero was given.

Vocal cords were viewed just prior to the passing of FOB into the trachea before intubation and were classified as closed; in mid position or relaxed and open and a score of 0,1 and 2 were given respectively.[100]

Immediate tracheal tube tolerance was assessed as Bad, disturbing cough with swallowing; Middle; coughing or swallowing not disturbing the procedure and Good, no coughing or swallowing. Each of these were scored as 0, 2 and 4 respectively.[100]

Then total Intubation score (anaesthesia quality, vocal cords relaxation, immediate tracheal tube tolerance) was calculated. It was interpreted based up on the total score. If the total score was less than 3, it was considered as a difficult or impossible fibre-optic intubation. If the total score was more than three but less than 7 it was considered as a disturbed procedure for fibre-optic intubation but still, there were chances of successfully intubating the tracheal. However, if the total score was more than [7], it was considered as an easy and successful fibre-optic tracheal intubation.[100]

MATERIALS AND METHODS

MATERIAL AND METHODS

This study is a prospective, randomized case control study. After the Technical Advisory Committee and Institutional Ethics Committee approval (Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum {Tertiary referral center, University level hospital}) and with written informed consent (In English and Malayalam- regional language), 40 adult patients with anticipated difficult airway undergoing elective neurosurgical procedure's, requiring awake fiberoptic orotracheal intubation were enrolled for this study. Data was collected from June 2014 to June 2015. Blinding of the study could not be done due to the easy identification of the milky white color of propofol.

Rationale for having that number or sample size:

Based up on the previous studies the minimum number of patients required to get a statistically significant numbers was 17 or more, hence we decided to recruit 20 patients in both the groups considering we might encounter some drop outs. [3, 93, 101]

Sampling method:

Consecutive patients satisfying inclusion criteria were included in the study till the sample size is reached.

The following were the inclusion criteria for both the groups.

Age: 19-60 years.

Patients coming for elective neurosurgical procedure with anticipated difficult airway.

Patients categorized as American society of Anesthesiology (ASA) class I and II

Preoperative Glasgow coma scale (GCS) 15.

No features of raised intracranial pressure or herniation syndromes.

Criteria for difficult airway was taken as:

A. Patients with history of difficult intubation,
B. Modified Mallampati (MMP) class 2 or more,
C. Patient's with a history of obstructive sleep apnea and severe snoring on sleeping in the supine position
D. Thyromental distance less than 60 mm (corresponding to an average distance of 3 finger breadths)
E. Limited mouth opening with interincisor distance less than 30 mm and
F. Head and neck movement less than 80°.

Exclusion criteria were:

1. Patient refusal for the consent

2. ASA class III and above

3. Age less than 18 years and more than 60 years

4. GCS <15

5. Coagulation Abnormalities

History of TIA or Stroke

Cerebral aneurysm

Emergency surgery

Known allergy to drugs like lignocaine, Dexmedetomidine, Fentanyl or propofol

Patients posted for redosurgery

Preoperative heart rate <50 bpm, presence of Heart block

Systemic hypertension stage III & above or those patients on antihypertensive medication with α-methyldopa, Clonidine or beta blockers

Presence of Coronary artery disease, Left ventricular dysfunction

Pregnant or Nursing woman

Participation in another drug study during the preceding1month period.

Abnormal coagulation profile

Pregnant women, pediatric or geriatric age group patients, person's incompetent to give informed consent or prisoners were not be recruited for this study.

The patients enrolled in the study were divided into two groups (Group D- dexmedetomidine & Group PF- propofol with fentanyl) with 20 patients in each group, based up on a computer generated randomization program.

1) **Group D**- BIS guided sedation with Dexmedetomidine infusion along with spray as you go technique was used while undergoing awake fiberoptic orotracheal intubation.
2) **Group PF** –BIS guided sedation with propofol and Fentanyl infusion along with spray as you go technique was used while undergoing awake fiberoptic orotracheal intubation.

Patients who met the inclusion criteria were explained about the study drug and study protocol. Informed written consent was obtained from patients who were willing to participate in this study.

Patients were kept fasting for 8 hours before the proposed study time based up on the NPO guidelines. All the patients were premedicated with 0.2mg of glycopyrrolate, 30 minutes intramuscular injection prior to shifting to operation theatre for its antisialogogue effect.

The study was performed in a quiet Neurosurgery operating theatre before any surgical intervention, with the following personnel present: one consultant neuroanaesthesiologist (principal investigator 2; PI-2), one senior resident in Neuroanesthesia (principal investigator 1; PI-1) and one anaesthesia technician for assistance during the procedure. The first principal investigators performed all the intubations under the guidance of 2nd principal investigator.

After shifting the patients to the operation room they were all placed in a semi-recumbent position. All the ASA standard monitoring was applied which included ECG, pulse-oximeter and a non-invasive blood pressure cuff (NIBP) {PHILIPS intellivue MX700}. 2-3mL lidocaine 4% was administered via metered-atomization-device (MAD) catheter through the oral cavity and pharynx to reduce gag reflex. A bispectral index (BIS) brain monitoring was also attached on the forehead, after through cleaning the surface with spirit, and the baseline BIS value will be noted.

Total maximum dose of lignocaine will be calculated based on body weight, not to exceed 7 mg/kg. Under Lignocaine (2%) skin infiltration, I.V access was secured on the dorsal aspect of the hand and base line intra venous infusion of 0.9% saline was initiated at a rate of 5–10 ml/kg during the loading phase of the drug.

Oxygen was provided through out the procedure with a fame mask at 6L/min till the intubation was either completed or abandoned.

In all patients, the posterior pharynx was anesthetized with 5 intraoral sprays using 10% lidocaine each depression of the release button delivered 0.1 mL (10 mg).

Once the patient's airway was anesthetized by using lignocaine nebulization and spray, patient was placed supine on the operation table with head in neutral position. After this all the patients were sedated based on the groups they were randomized into. All measures were taken to keep the head in the neutral position through out the procedure till the intubation was either completed or abandoned and the patients was positioned for the surgery by the surgeon.

In the dexmedetomidine (group D) [DEXEM: Themis Chemicals, Haridhwar] a loading dose of drug at 1 mcg/kg over 10 minutes by using an infusion pumps, followed by 0.5mcg/kg/hr infusiontill target BIS value reached up to 70.

In propofol with fentanyl group (group PF) [NEOROF: Neon laboratories, Mumbai, TROFENTYL: Troikaa Pharmaceuticals Ltd. Gujarat], propofol was initiated at 1 mg/kg /hr with fentanyl 1mcg/kg bolus over 10 minutes loaded in separate syringes, followed by 1mg/kg/ hr of propofol and

1mcg/kg of fentanyl infusion with using a infusion pump till target BIS value reached up to 70.

All baseline values were obtained, heart rate using ECG, pulse oximeter (SpO2), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MAP), level of sedation using the bispectral monitor (BIS) and OAA/S. Blood pressures was monitored at base line (0 minute), then at one minute followed by every three minutes until intubation and then every 5 minutes thereafter.

Incidents of hypertension, hypotension, tachycardia, or bradycardia were also recorded and were treated accordingly. Episodes of apnea >60 seconds or a drop in O2 saturation <95% were treated by decreasing the infusion rate to 0.05 mL/kg/hr and bag mask ventilation with 100% oxygen, as necessary.

For episodes of apnea longer than 2 minutes, infusion was discontinued and bag mask ventilation was commence until the patient began to breath spontaneously.

An oral airway was inserted into the oropharynx and the jaw lift maneuver was performed by an assistant if the patient desaturated < SpO_2 95% or had any airway obstruction.

Once the target BIS of 70 was achieved then a bite block was inserted into the oral cavity to avoid biting the FOB and hence damaging it. Airway topical anesthesia was achieved with the spray-as-you-go technique using 4% lignocaine in a 10 ml syringe attached to the drug port of the FOB and an eloquent of 2 -3 ml was sprayed while advancing the FOB through the entire airway passage. [32] The FOB was inserted through the oral airway into the hypopharynx and its tip was first positioned at the epiglottic vallecula and then in the vicinity of the piriform recess.

The FOB was then advanced into the trachea and its tip was positioned 4cm below the vocal cords. During inspiration, 3 mL of the 4% lignocaine was sprayed into the trachea. Carinal stimulation was avoided by advancing the tip of the FOB a maximum of 4 cm below the glottis.

After the topical instillation of local anesthetics, patient was again given oxygen at 6L/min for 5 minutes for the onset of the action of the drug. Then an appropriate sized cuffed polyvinyl chloride endotracheal tube (ETT) that was preselected for the patient was threaded over the FOB. FOB was again inserted into the trachea and after confirming the carina through it the ETT was railroaded over the FOB into the trachea and was secured 3–4 cm above the carina.

After the intubation the position of ETT was again confirmed by using chest auscultation and capnography by connecting on to the ventilator. Patients were asked to obey simple commands.After confirmation of the ETT it was secured using a plaster. The study ended at this point. General anesthesia was induced with titrated doses of intravenous propofol, fentanyl and vecuronium for muscle relaxation. Anesthesia was maintained with IV fentanyl, 0.5-1.5 MAC sevoflurane with air: oxygen mixture in oxygen and vecuronium top ups based on the Train of Four count during the surgery. Then allthe patients were positioned according the need for the surgery and the surgery was conducted as planned.

The intraoperative management of the patient was at the discretion of the attending anesthesiologist. Patient's neuromuscular blockade was reversed with Inj. Glycopyrolate 0.01 mg/kg with Inj. Neostigmine 0.05mg/kg. Trachea was extubated once the patient met all the required criteria for extubation and was shifted to neurosurgical intensive care unit for observation. Those patients who did not meet the extubation criteria were also shifted to the neurosurgical intensive care unit for elective mechanical ventilation based up the neurological status of the patient at the end of the procedure as decided by the consultant neuroanesthesiologist and neurosurgeon per established institutional protocols.

Postoperatively patients were reassessed for any discomfort post intubation or any recall of the event after the patient was extubated and was conscious and oriented on the 1st postoperative day.

The following parameters were noted during the entire procedure were - heart rate (HR), SpO_2 , SBP, MBP,DBP with BIS value and OSS/A at baseline i.e. "0" min, then at one minute and after that every three minutes till 30 minutes using a stop watch. The cough severity and the intubation score (Annexure 1 &2) were also recorded. The time of starting the infusion and the ending time was notes. Total dose of the drugs used in each group (Gp-D and Gp-PF) with the total dose of lignocaine, time taken to achieve BIS – 70; total time for intubation; total intubation attempts; and any additional maneuver's required.

Intubation time was defined as the placement of FOB in the oral cavity (after the initial period of anesthetizing the airway) till the confirmation of the correct position of the ETT.

Procedure was considered as failed intubation if patients refused for awake FOB intubation any time during the study or had severe cough with an intubation score of less than 3 with or with out severe resistance for either FOB or intubation or had severe hemodynamic fluctuation like bradycardia less than 50 not responding to inj. Atropine or glycopyrolate with or with out

hypertension (more than 20% from baseline blood pressure recordings) or severe hypotension (less than 20 % from the base line blood pressure recording) or had desaturations (less than 90%) or any inability to do the FOB guided intubation or failure to achieve a BIS value of 70 with adequate sedation. Any attempt of more than three times for AFOB guided intubation was also considered as intubation failure. In these situation the study was considered as a failure and AFOB was abandoned and patients was intubated with FOB under general anesthesia using fentanyl, propofol for induction and vecuronium for muscle relaxation. After the intubation the ETT position was reconfirmed using capnography and five point auscultation methods and the surgery was preceded as per the plan with no change in the anesthesia techniques. These patients were again assessed in the postoperative period for any intraoperative awareness for the AFOB and the severe of any discomfort in the throat or oral cavity was assessed.

STATISTICS

STATISTICS

Statistical software, namely SPSS 17.0(Chicago, SPSS inc.) were used for the analysis of the data, and Microsoft word and Excel were used to generate graphs, tables, etc. Based up on the previous studies the proposed number of patients required for the study was 40 (a sample size of 20 patients per group), which was required to produce a statistical power of 80% (0.80) and a type I error of 0.05. All the data are expressed as mean ± Standard Deviation (SD) for quantitative data and number (%) for the categorical data type. Statistical analysis was done with Chi-square test or Fischer's exact test for descriptive and nominal data. Mann-Whitney U test was used to compare non-continuous data and non-normally distributed data. Data was also expressed as interquartile range and median in the Mann- Whitney U test. Which includes Heart Rate (HR), SBP, MBP, DBP, BIS, OAA/S. For correlation the Spearman Rank Correlation Between BIS & OAA/S. The level of significance was 5% ($P < 0.05$) and a "p" value less than 0.01 as highly significant.

The correlation between the sedation scales i.e. BIS and OAA/s was tested using the Spearman's rank-order correlation test. This test is the nonparametric version of the Pearson product-moment correlation. Spearman's

correlation coefficient, (ρ also signified by r_s) measures the strength of association between two ranked variables.

Positive values reveal positive linear correlation and Negative values demonstrate negative linear correlation. “0” denotes no linear correlation and closer the value is towards 1 or –1, the stronger and more significant the correlation will be. Spearman's correlation coefficient of more than 0.8 is considered as strong correlation and 0.5 to 0.8 is considered as good correlation.

RESULTS

RESULTS

Based up previous studies the sample size was chosen to be 40 as max of 17 per group would account for the power of study more than 80%.A total of 40 patients were enrolled into the study. Based up on a computer generated random number they were divided into the two groups i.e. Gp D (Dexmedetomidine group) and Gp PF (Propofol with fentanyl group).

One patient from the Group: D was excluded as he did not cooperate for the AFOB and had a failed AFOB. Hence the patient was intubated under general anesthesia. Due to this, the sample size were 19 patients in Gp D and 20 patients in Gp PF. [GP.D- (n= 19), Gp.PF- (n= 20)]

Table 1 shows the demographic comparison between the groups.The average age of the patients in GP D and Gp PF was 41.89± 11.04 and 39.15 ± 7.62 respectively. The BMI in both the groups was comparable and was not statistically significant. Though the average weight and height of the patients in Gp- D was more compared to the other group and was statistical significant,($p<0.05$) BMI was comparable in both the groups. Fifteen patient's in both the groups were American society of anesthesiologist risk score (ASA) I and four patient's in GP D and five patients in the Gp- PF belonged to ASA II with a P value of 1.00 which is not statistically significant.

Table 1- Shows the comparison of the Demographic Data of the patients.

	GP. D (n= 19)	**GP. PF** (n= 20)	**"p" value**
AGE (yr's)	41.89± 11.04	39.15 ± 7.62	0.375#
WT (Kg)	70.37±11.97	63.05±9.81	**0.043***
HT (cm's)	165.11±7.88	158.05±6.83	**0.005***
BMI (Kg/M^2)	25.65±3.12	25.35±3.12	0.769#
SEX (M/F)	14/5 (73.7/26.3)	12/8 (60/40%)	0.501#
ASA (I/II)	15/ 4 (78.9/21.1)	15/5 (75.0/25.0)	1.000#

- Data expressed as Mean ± SD and Mean (%)
- *= p value < 0.05 and is considered significant
- # = p value > 0.05 and is not statistically significant.

Preoperative airway examination results:

A) Mouth opening: The mouth opening was around 3 cm in 15 of the total 19 patients in Gp. D and sixteen in GP PF. One patient in both the groups had mouth opening of 2 cm and three patients had mouth opening of 2.5 cm in both the groups as shown in Table 2.

Table 2: Shows the MOUTH OPENING of the two groups

Groups	**Mouth Opening**		
	2 cm	**2.5 cm**	**3cm**
Gp.D	1 (5.3%)	3 (15.8%)	15 (78.8%)
Gp. PF	1 (5.0%)	3(15%)	16 (80%)

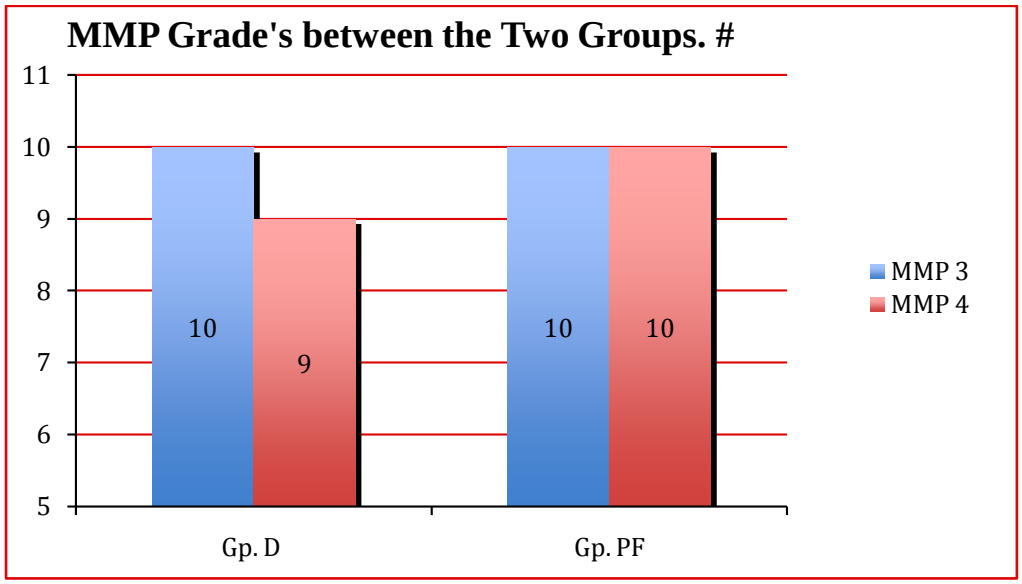
B) **Modified Mallampatti Score (MMP):** Ten patients in both the groups had a MMP score of 3. MMP 4 was present in 9 patients in GP D and in 10 patients in Gp. PF (Table 3 & Fig. 1)

Table 3:Shows Modified Mallampatti Score (MMP) between the groups

	MMP 3 n (%)	**MMP 4 n (%)**	**Fisher Exact test**
GP D (19)	10 (52.6)	9 (47.4)	p =1.000
GP- PF (20)	10 (50.0)	10(50.0)	

#- **p value > 0.05,** hence considered not statistically significant.

Fig. 1:Comparison of the MMP between groups



 # - p value > 0.05, hence considered not statistically significant.

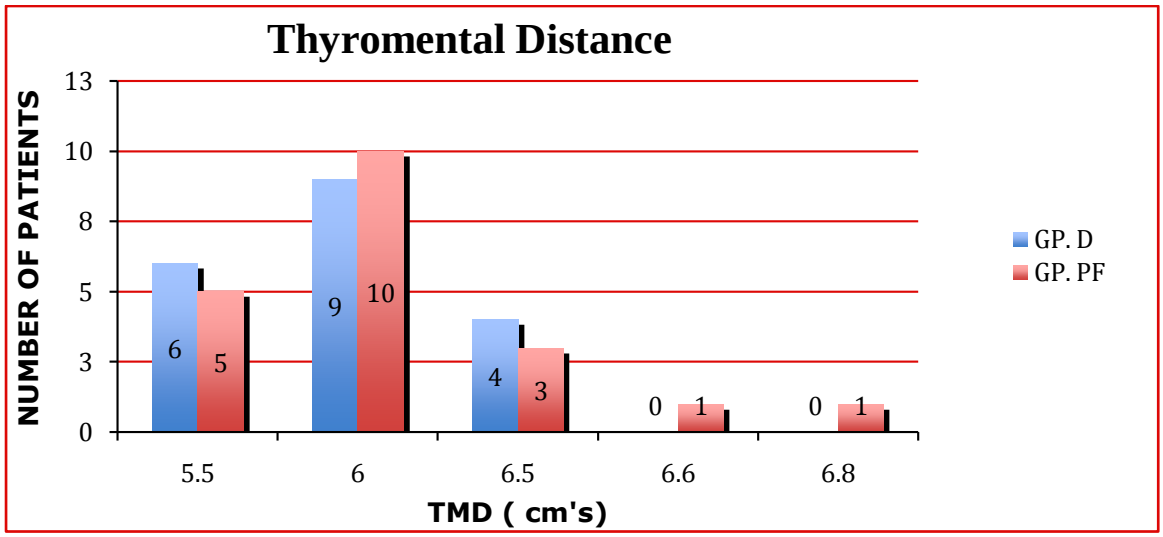
C) **Thyromental Distance.**

The normal thyromental distance isapproximately 6.5cm. A total of 15 patients in both the groups had TMD less than 6.5 cm of which six patients in Gp. D and five patients in Gp PF had 5.5cm and nine in Gp D and 10 in Gp PF had around 6cm. A total of four and five patients in Gp D and Gp. PF had above 6.5cm. (Table 4 & Fig 2.)

Table 4: Shows the comparison of the Thyromental Distance (TMD) between the groups

TMD (cm)	GP. D	Gp.PF	Total
5.5	6 (31.6 %)	5 (25%)	11(28.2)
6	9 (47.4%)	10 (50%)	19 (48.7)
6.5	4(21.1%)	3 (15%)	7 (17.9%)
6.6	0 (0%)	1(5.0%)	1(2.6%)
6.8	0 (0%)	1 (5%)	1(2.6%)
Total	19 (100%)	20 (100%)	**39 (100%)**

Fig. 2: Comparison of the Thyromental Distance (TMD) between the groups



D) **Neck movements:** Cervical neck extension was restricted in around 84.2% (16) and 80% (16) of the patients in Gp D and Gp. PF respectively. Three patients in Gp. D and four patients in Gp .PF had a normal neck extension respectively. Neck extension between both the two

groups was not statistically significant as done by using Fisher's exact t test. (Table 5)

Table 5: Shows the comparison of the Neck extension<80^{o} between the groups

Neck extension<80^{o}	Gp. D	Gp. PF	Fisher's Exact Test
Yes	16 (84.2%)	16 (80%)	p-value= 1.000$^{\#}$
NO	3 (15.8%)	4(20%)	
Total	**19**	**20**	

= Statistical not significant as p value > 0.05.

E) Cervical Spine Disease: Six in Gp D and seven patients in Gp-PF had cervical spine disease, the remaining thirteen patients in both the groups had normal cervical spine. The "p "value using the Fisher Exact Test was 1.000 (> 0.05%), which was not statistically significant for both MMP class and cervical spine disease. (Table 6)

Table 6: Shows the comparison of the Cervical Spine Disease between the groups

	Present N (%)	Absent N (%)	Fisher Exact Test
GP D (19)	6 (31.6)	13 (68.4)	p =1.000$^{\#}$
GP- PF (20)	7 (35)	13 (65.0)	

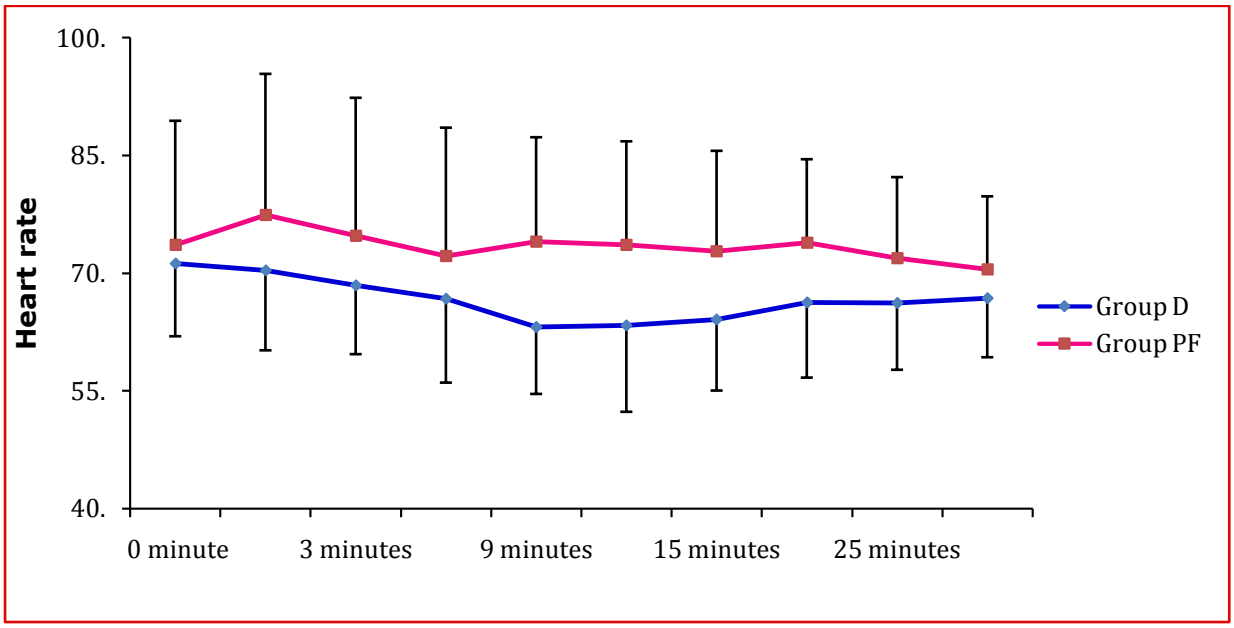
#- **p value > 0.05,** hence considered not statistically significant.

Table 7: Table comparing the Heart Rate (HR) between the 2 groups:

HR	Group D			Group PF			Mann-Whitney U test	
	Median	Inter quartile range (percentile)		Median	Inter quartile range (percentile)			
		25th	75th		25th	75th	Z	p
0 min	75.0	64.0	78.0	68.0	61.5	89.0	.098	.922
1 min	68.0	62.0	78.0	68.5	65.3	97.0	1.04	.298
3 min	66.0	62.0	74.0	67.0	62.0	86.0	.87	.382
6 min	68.0	60.0	72.0	65.0	60.5	77.0	.619	.536
9 min	60.0	58.0	70.0	70.5	64.0	81.3	2.65	**.008***
12 min	65.0	52.0	72.0	72.0	65.3	79.0	2.26	**.023***
15 min	65.0	55.0	70.0	69.5	61.8	86.8	1.92	.054
20 min	65.0	60.0	70.0	69.0	66.0	84.0	2.00	**.045***
25 min	65.0	60.0	72.0	69.0	64.0	80.0	1.59	.111
30 min	65.0	60.0	72.0	69.0	62.5	80.0	1.11	.265

- = $p<0.05$, considered as statistically significant.

Fig. 3: Heart Rate comparing the two groups.



This is a table 7 & Fig 3, comparing the heart rates between the two groups at different time interval initially at 0, 1 and every 3 minutes till 15 min and after that every 5 minutes till 30 mins. Mann-Whitney U Test at nine, twelve and twenty minutes the heart rate was significantly different and was lower in the Gp D as compared to the Gp. PF. The heart rate at all other time intervals were non-significant in both the groups. The heart rate values were lower in the Gp.D compared to the Gp.Pf. The lower heart rate trend in the Gp.D can be explained by the inherent ability of the Dexmedetomidine to cause decrease the heart rate. Since the average duration of the drugs infusion was 12.11± 2.28 in the Gp. D as compared to the 10.65 ± 2.52 minutes in the Gp. PF. This can explain the significant difference in the heart rate at the 9^{th} and the 12^{th} minute of starting the drug compared to the other group. However the heart rate at 20^{th} minute can

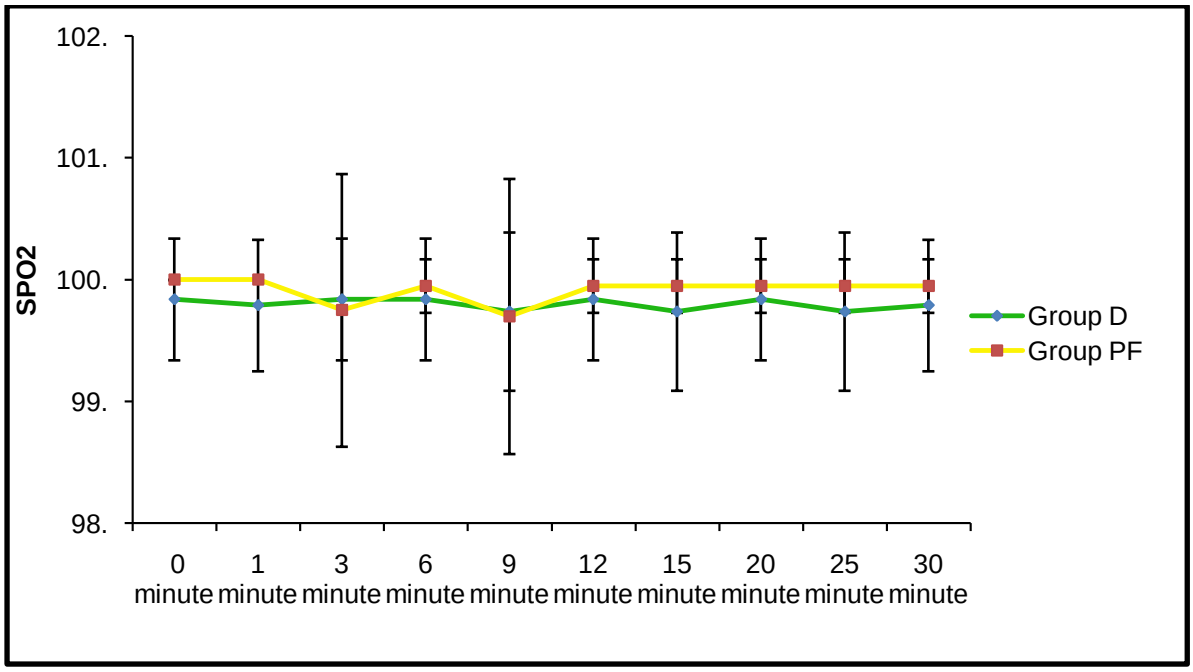
probably be explained as by this time the intubation response might have subsided hence the heart rate would have stabilized to lower limit due to the residual effect of the Dexmedetomidine unlike the drugs in the other group i.e. Gp.PF cause less change in the heart rate.

Table 8: Comparison Of SpO_2 Between The Two Groups.

SpO_2	Group D			Group PF			Mann-Whitney U test	
	Median	Inter quartile range (percentile)		Median	Inter quartile range (percentile)			
		25th	75th		25th	75th	Z	P#
0 minute	100.0	100.0	100.0	100.0	100.0	100.0	1.470	0.142
1 minute	100.0	100.0	100.0	100.0	100.0	100.0	1.824	0.068
3 minute	100.0	100.0	100.0	100.0	100.0	100.0	0.578	0.564
6 minute	100.0	100.0	100.0	100.0	100.0	100.0	0.669	0.504
9 minute	100.0	100.0	100.0	100.0	100.0	100.0	0.508	0.611
12 minute	100.0	100.0	100.0	100.0	100.0	100.0	0.669	0.504
15 minute	100.0	100.0	100.0	100.0	100.0	100.0	1.148	0.251
20 minute	100.0	100.0	100.0	100.0	100.0	100.0	0.669	0.504
25 minute	100.0	100.0	100.0	100.0	100.0	100.0	1.148	0.251
30 minute	100.0	100.0	100.0	100.0	100.0	100.0	1.121	0.262

= test not significant as p> 0.05.

Fig. 4: Comparison of SpO2 betweenthe Two Groups.



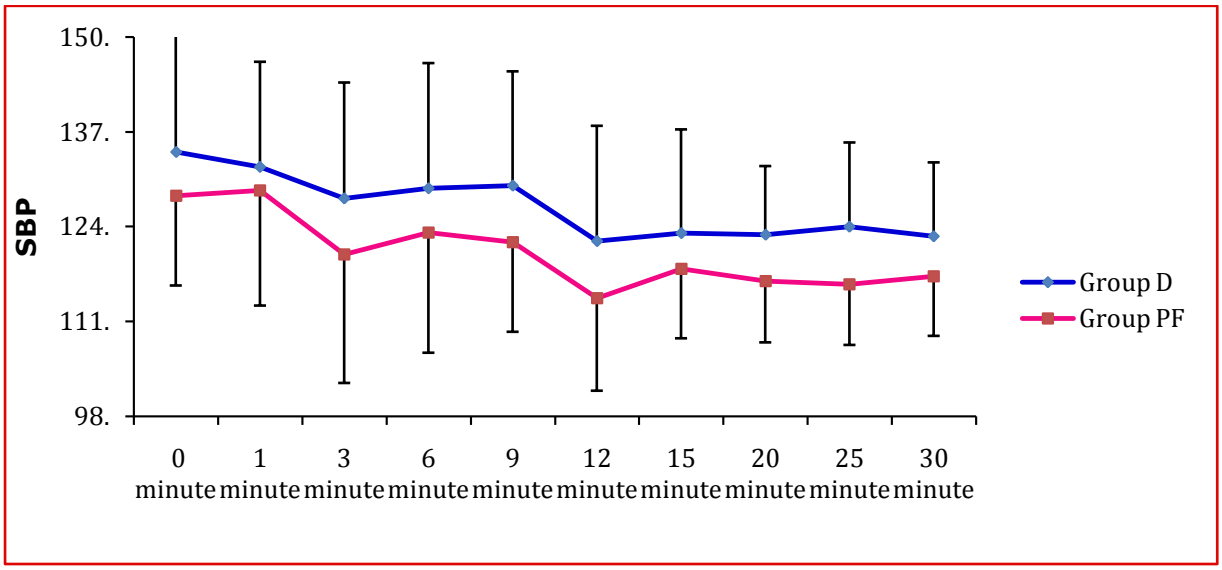
Based up on the data from the table and the SpO_2 graph there was no difference in the oxygen saturation in both the groups at all the time intervals. The "p" value at all the time intervals was > 0.05 and hence was considered as non-significant. (Table 8 & Fig.4)

Table 9: Comparison Of SBP Between The Two Groups

SBP	Group D			Group PF			Mann Whitney U test	
	Median	Inter quartile range (percentile)		Median	Inter quartile range (percentile)			
		25th	75th		25th	75th	Z	p
0 minute	133.0	127.0	145.0	130.0	118.5	134.5	1.411	0.158
1 minute	130.0	122.0	148.0	127.5	122.0	138.5	0.690	0.490
3 minute	124.0	118.0	135.0	119.0	107.8	132.0	1.591	0.112
6 minute	136.0	116.0	143.0	122.0	117.8	134.0	1.196	0.232
9 minute	130.0	115.0	141.0	123.5	115.0	129.8	1.549	0.121
12 minute	122.0	110.0	136.0	114.0	102.0	123.3	1.649	0.099
15 minute	124.0	112.0	134.0	116.0	110.5	125.0	0.929	0.353
20 minute	124.0	116.0	130.0	116.0	110.0	123.3	2.159	**0.031***
25 minute	122.0	116.0	135.0	116.0	110.5	122.0	1.949	0.051
30 minute	122.0	116.0	130.0	120.0	110.5	122.0	1.625	0.104

* = $p < 0.05$: And is considered as statistically significant.

Fig. 5: Comparison of SBP betweenthe Two Groups.



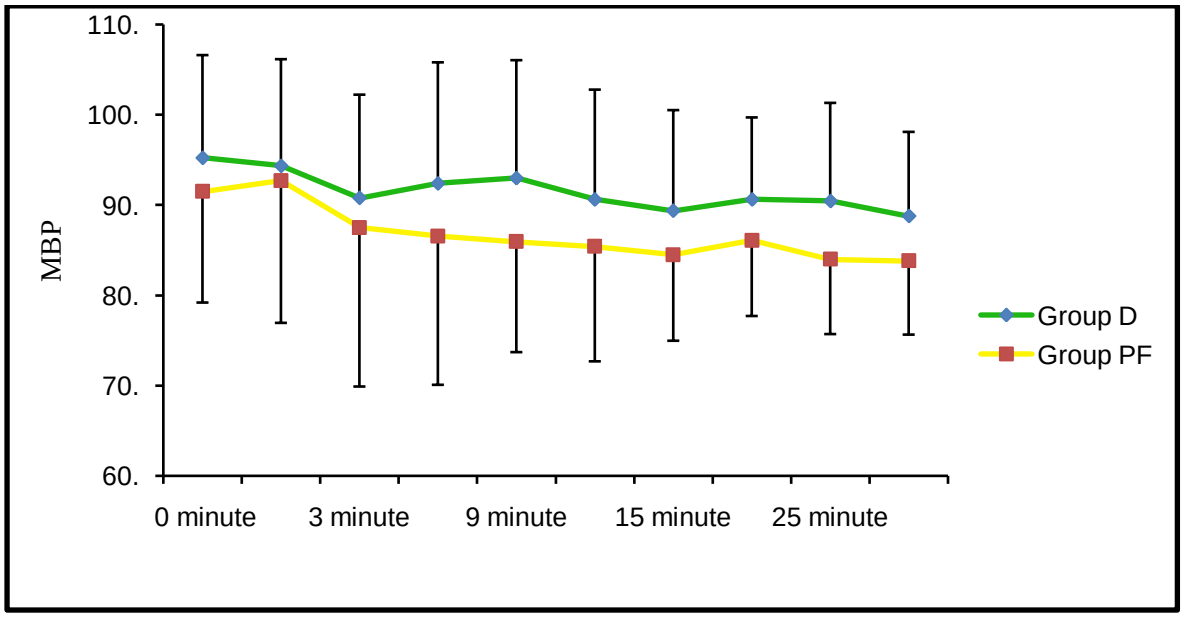
In the graphical representation of the SBP it can be seen that the SBP was lower in the Gp.PF as compared to the Gp.D at all the time interval.The effect on the hemodynamic caused by the dexmedetomidine can also be the reason for the lower values of the SBP, MBP and DBP in the GP.D as compared to the Gp. PF. Though there was no statistically significant difference between the MAP and DBP statistically at all the time interval compared to the Gp. PF. However, the changes in the SBP were significant difference at the 20^{th} minute time interval (p=0.031*) between the two groups. This could be probably be hypothesized due to the hemodynamic effect of the dexmedetomidine. Though as by the end of 20^{th} minute the intubation response due to FOB might have subsided along with the added hemodynamic changes brought about by inducing general anesthesia once the ETT position was confirmed and patient's neurological status was assessed. (Table 9 & Fig 5)

Table 10: Comparison Of MBP Between The Two Groups

MBP	Group D			Group PF			Mann-Whitney U test	
	Median	Inter quartile range (percentile)		Median	Inter quartile range (percentile)			
		25th	75th		25th	75th	Z	P#
0 minute	96.0	89.0	103.0	92.0	89.0	100.5	1.341	0.180
1 minute	92.0	86.0	102.0	92.5	84.8	100.0	0.197	0.844
3 minute	89.0	83.0	98.0	85.5	81.3	97.3	0.648	0.517
6 minute	96.0	84.0	104.0	87.5	78.0	96.8	1.408	0.159
9 minute	94.0	83.0	102.0	87.5	76.0	94.8	1.646	0.100
12 minute	90.0	81.0	98.0	84.0	78.8	93.3	1.245	0.213
15 minute	90.0	78.0	99.0	81.5	78.0	93.8	1.440	0.150
20 minute	92.0	82.0	97.0	85.0	78.5	93.5	1.521	0.128
25 minute	92.0	78.0	99.0	82.5	78.0	91.3	1.916	0.055
30 minute	90.0	78.0	97.0	83.5	78.0	84.0	1.719	0.086

= p> 0.05 hence non-significant.

Fig. 6: Comparison of MBP between the Two Groups.



The two groups were comparable in regards to the mean blood pressure though the MAP in the Gp. PF was less at all the time interval than Gp. D. (Table 10)

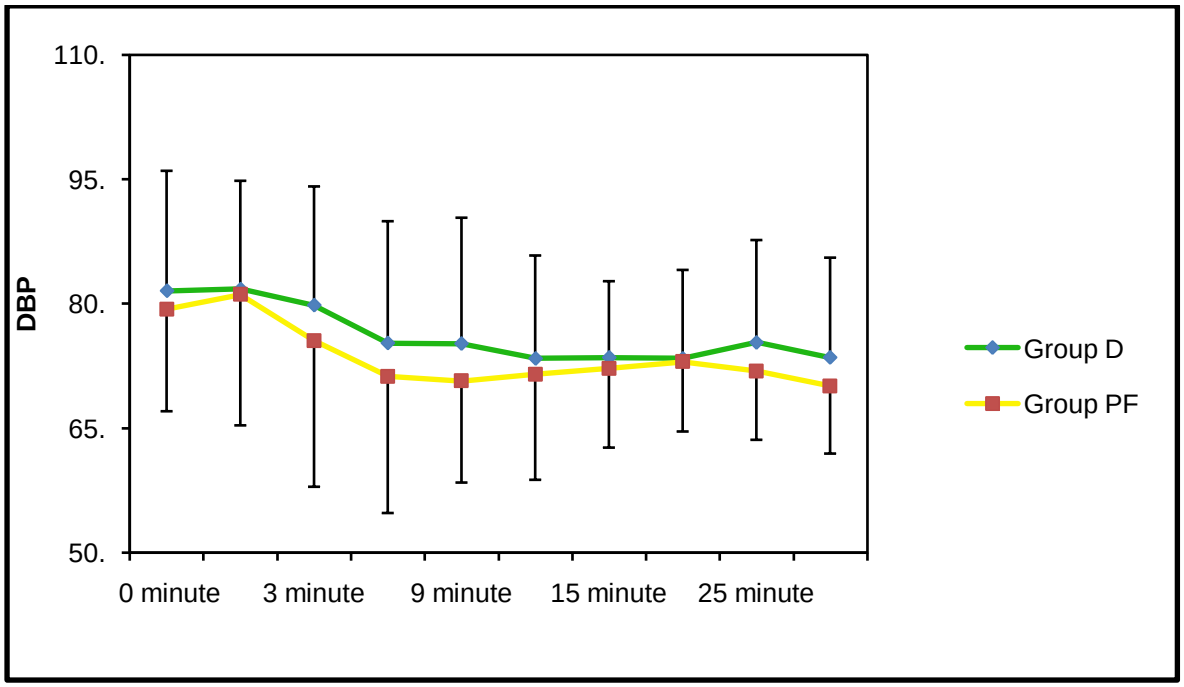
In the graph the upper limit of the SD is represented in Gp. D as compared to the lower limit of SD in Gp. PF. (Fig 6)

Table 11: Comparison of DBP between the Two Groups.

DBP	Group D			Group PF			Mann Whitney U test	
	Median	Inter quartile range(percentile)		Median	Inter quartile range(percentile)			
		25th	75th		25th	75th	Z	P[#]
0 minute	80.0	72.0	89.0	79.0	70.0	86.0	0.662	0.508
1 minute	82.0	75.0	89.0	81.0	71.5	90.0	0.014	0.989
3 minute	80.0	71.0	88.0	72.0	68.8	87.0	0.831	0.406
6 minute	80.0	63.0	84.0	68.5	56.8	84.0	0.578	0.563
9 minute	79.0	63.0	84.0	73.5	54.0	79.8	0.999	0.318
12 minute	72.0	63.0	83.0	69.0	55.5	86.5	0.650	0.516
15 minute	73.0	65.0	82.0	74.0	64.3	78.0	0.494	0.621
20 minute	76.0	64.0	80.0	76.0	65.0	78.8	0.141	0.888
25 minute	76.0	64.0	82.0	72.5	64.0	78.3	1.042	0.297
30 minute	74.0	63.0	82.0	68.5	64.0	74.0	0.888	0.375

[#] = p> 0.05 hence non-significant.

Fig. 7: Comparison of DBP between the Two Groups.



As seen the Diastolic Blood Pressure was lower in the Gp. PF as compared to the Gp.D, but was not statistically significant. (Table 11 & Fig.7)

But at all other time interval the SBP, DBP and MBP were comparable between the two groups.

Table 12: Comparison of BIS between the Two Groups.

BIS	Group D			Group PF			Mann Whitney U test	
	Median	Inter quartile range (percentile)		Median	Inter quartile range (percentile)			
		25th	75th		25th	75th	Z	p
0 minute	98.0	98.0	100.0	98.0	98.0	100.0	0.166	0.868
1 minute	97.0	96.0	98.0	97.0	96.0	98.0	0.235	0.814
3 minute	93.0	90.0	97.0	92.0	90.0	94.0	1.278	0.201
6 minute	84.0	84.0	89.0	85.0	80.0	86.0	0.899	0.369
9 minute	78.0	74.0	82.0	73.0	70.0	77.5	2.363	**0.018***
12 minute	70.0	70.0	74.0	70.0	68.0	70.0	1.971	**0.049***
15 minute	70.0	60.0	70.0	60.0	58.0	70.0	1.108	0.268
20 minute	58.0	55.0	60.0	55.0	52.0	58.0	1.686	0.092
25 minute	54.0	51.0	55.0	54.0	51.0	55.0	0.470	0.638
30 minute	52.0	50.0	55.0	52.0	50.0	53.0	0.727	0.467

*= $p < 0.05$, and is statistically significant.

Fig. 8: Comparison of BIS between the Two Groups.

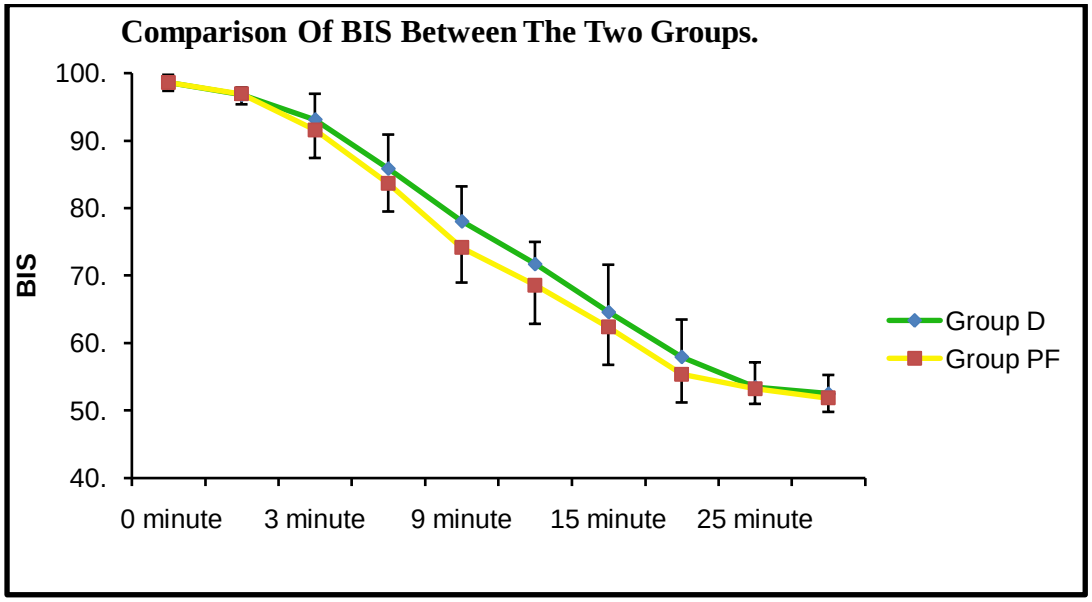


Table 13: Time to Achieve BIS < 70.

Groups	N	TIME TO ACHIEVE BIS <70		t	p
		Mean	sd		
Group D	19	11.89	2.49	2.533	0.016*
Group PF	20	10.00	2.18		

* = p< 0.05, and is statistically significant.

The BIS value was significantly different only at 9 and 12 minutes, with a p value of 0.018* & 0.049* respectively using the Mann Whitney U test. But it was comparable at all other time interval. Though time taken to achieve BIS of less than 70 was earlier in the Gp. PF as compared to the Gp. D of 10.0 and 11.89 minutes respectively. This was statistically significant with a p value of 0.016 (<0.05).

The slope of the curve (BIS graph), Gp. PF starts dropping earlier than that of the other group almost after 3 minutes of start of the infusion of the drugs and equal almost after 15 minutes, though at these times interval BIS values are not statistically significant. (Table 12, 13 & Fig 8)

Table 14: OAAA/S score comparing the two group.

OAA/S	Group D			Group PF			Mann-Whitney U test	
	Median	Inter quartile range(percentile)		Median	Inter quartile range9 percentile)			
		25th	75th		25th	75th	Z	P#
0 minute	5.0	5.0	5.0	5.0	5.0	5.0	0.000	1.000
1 minute	5.0	5.0	5.0	5.0	5.0	5.0	0.548	0.584
3 minute	4.0	4.0	5.0	4.0	4.0	4.8	1.233	0.218
6 minute	3.0	3.0	4.0	3.0	3.0	4.0	0.832	0.406
9 minute	3.0	2.0	3.0	2.5	2.0	3.0	0.910	0.363
12 minute	2.0	2.0	2.0	2.0	1.0	2.8	0.956	0.339
15 minute	1.0	1.0	2.0	1.0	1.0	2.0	0.681	0.496
20 minute	1.0	1.0	1.0	1.0	1.0	1.0	1.826	0.068
25 minute	1.0	1.0	1.0	1.0	1.0	1.0	0.000	1.000
30 minute	1.0	1.0	1.0	1.0	1.0	1.0	0.000	1.000

= p> 0.05 hence non-significant.

OAA/S is a score where in the max score is 5 and minimum is 1. At the "0" min as all the patients were conscious obeying the OAA/S score was 5. Once the sedation was started the rate of change in the sedation score was the same in both the groups. A score of 3 was taken adequate for doing FOB. The p values between the two groups at different time interval was more than 0.05 and hence was considered as non-significant. (Table 14)

Fig. 9: Box Plot Graph- OAA/S In Gp.D

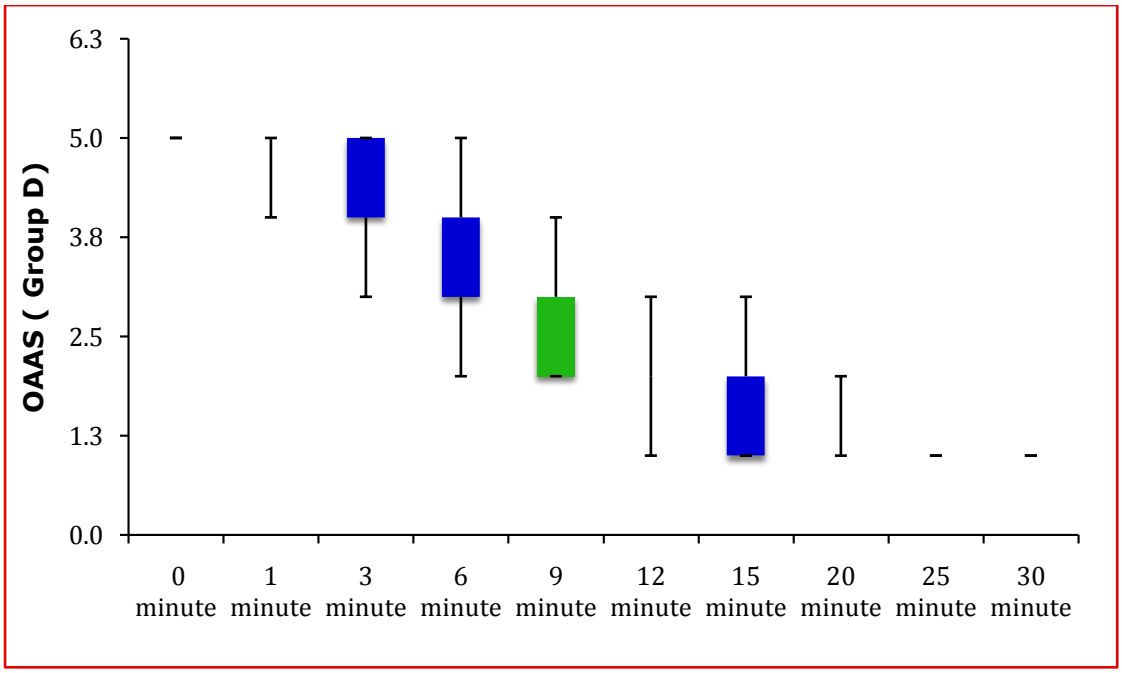
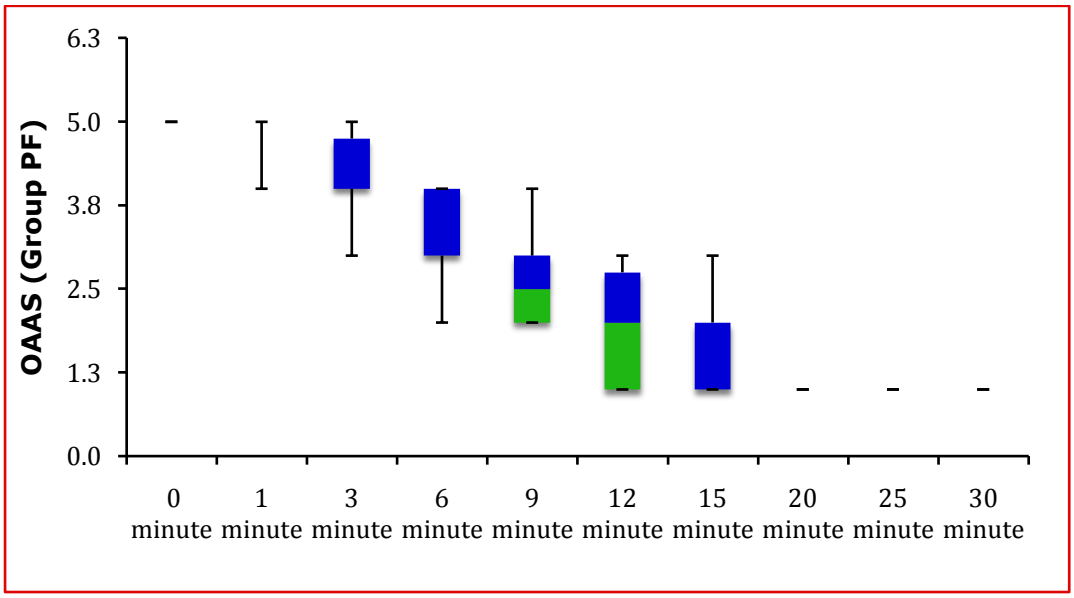


Fig. 10: Box Plot Graph- OAA/S In Gp.PF



By plotting a Box and plot graph comparing the two groups with OAA/s on the y axis and time interval on the X axis, we can assess that there is no statistically significance difference between the two groups. (Fig. 9& 10)

Spearman Rank Correlation between BIS & OAA/S

We also wanted to know if there was any correlation between the two sedation scores i.e. one by using the BIS and other by doing a clinical assessment i.e. OAA/s scale. We used Spearman rank correlation to look for any correlation between the each groups.

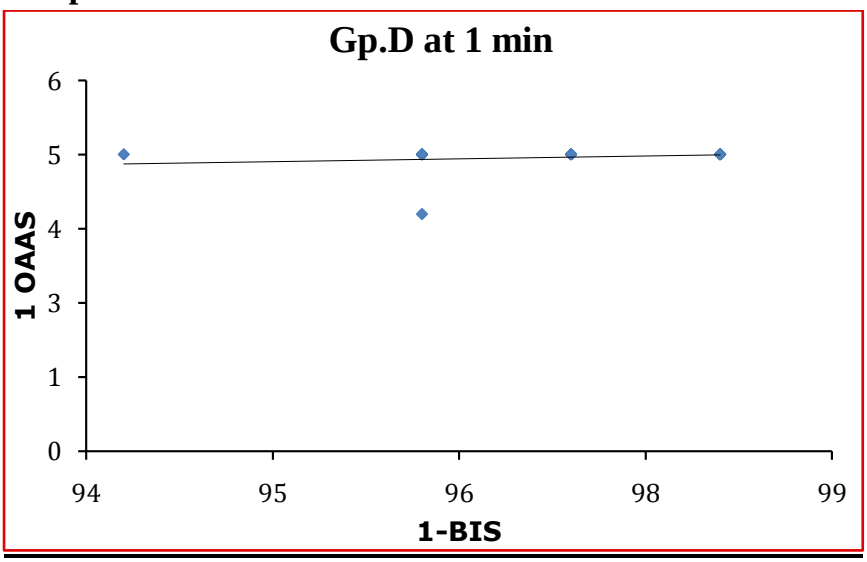
In the Gp. D, there was significantly correlation between the BIS and OAA/S at 3, 6, 9, 12, 15 and at 20 minute time intervals as given in the chart below. But there was no correlation at 0, 25 and 30 minute's interval after starting the drug.

Table 15: Spearman Rank Correlation Between The Two Groups.

Correlation between the BIS & OAA/S (Spearman rank correlation) : Group D	Spearman's rho - ρ	p
0 minute	-	-
1 minute	0.226	0.351
3 minute	0.881	<0.001*
6 minute	0.557	0.013*
9 minute	0.667	0.002*
12 minute	0.610	0.006*
15 minute	0.846	<0.001*
20 minute	0.570	0.011*
25 minute	-	-
30 minute	-	-

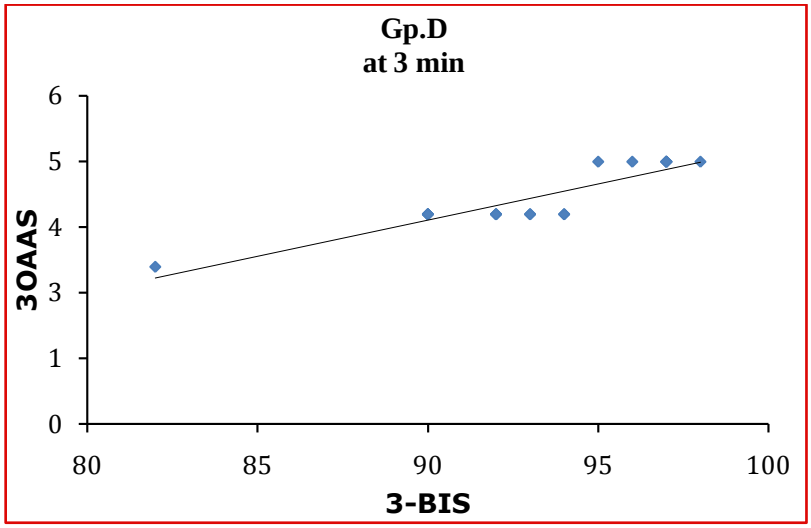
* p< 0.05 = considered statistically significant

Fig. 11A: Spearman Rank Correlation between BIS & OAA/S at 1min in Gp.D



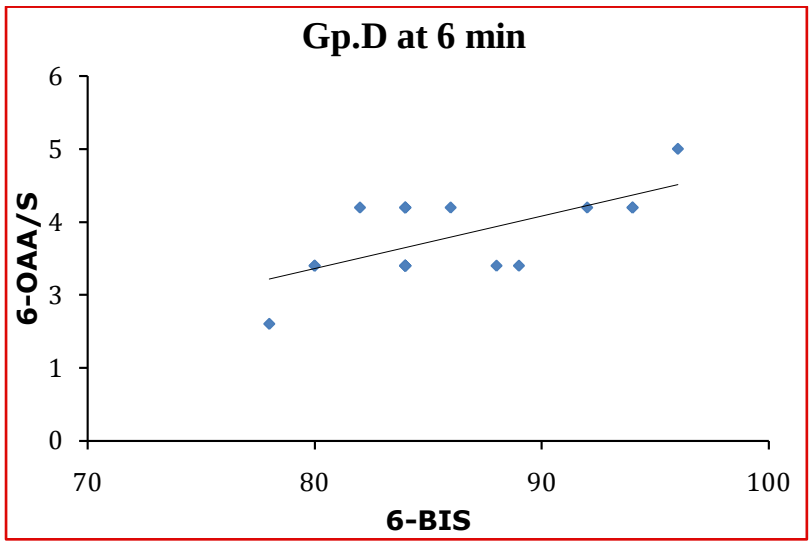
p=0.351. (> 0.05) hence non significant

Fig. 11B: Spearman Rank Correlation between BIS & OAA/S at 3min in Gp.D



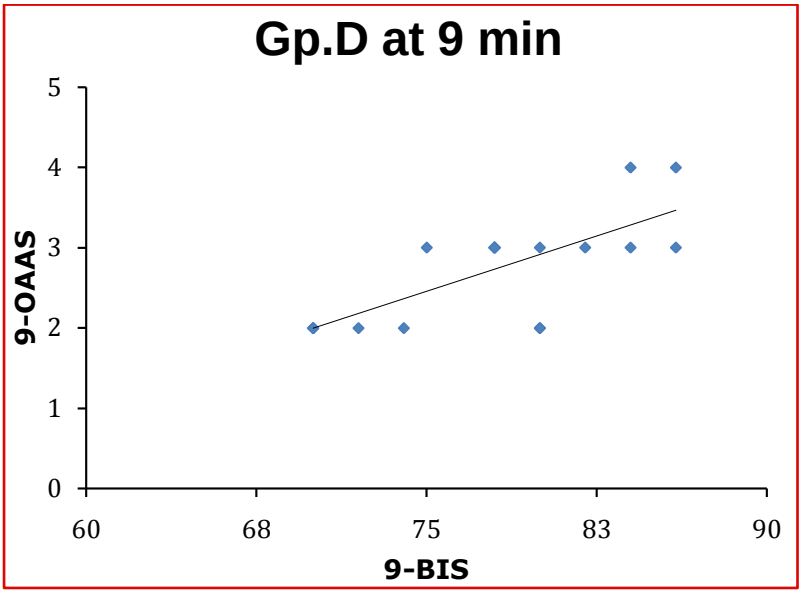
p = <0.001, data is statistically significant.

Fig. 11C: Spearman Rank Correlation between BIS & OAA/S at 6min in Gp.D



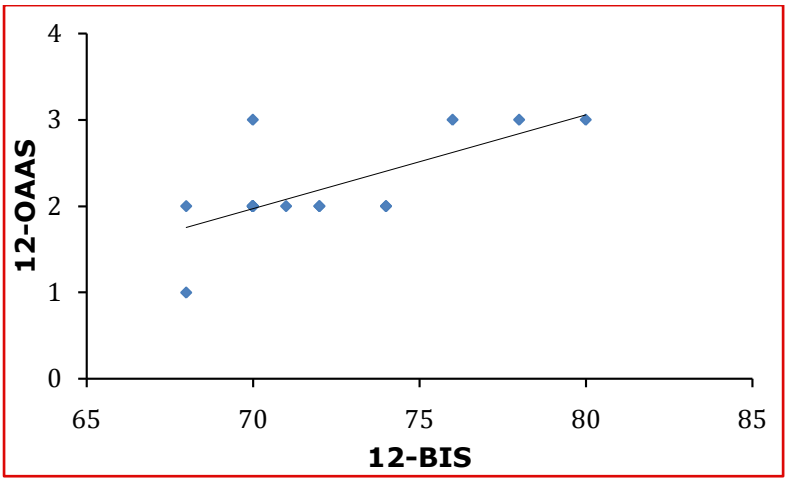
p= 0.013, data is statistically significant.

Fig. 11D: Spearman Rank Correlation between BIS & OAA/S at 9min in Gp.D



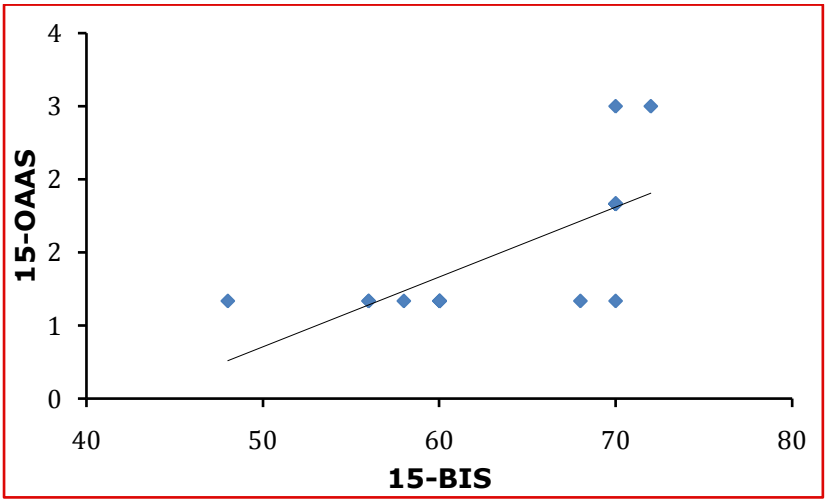
p=0.002, data is statistically significant.

Fig. 11E: Spearman Rank Correlation between BIS & OAA/S at 12min in Gp.D



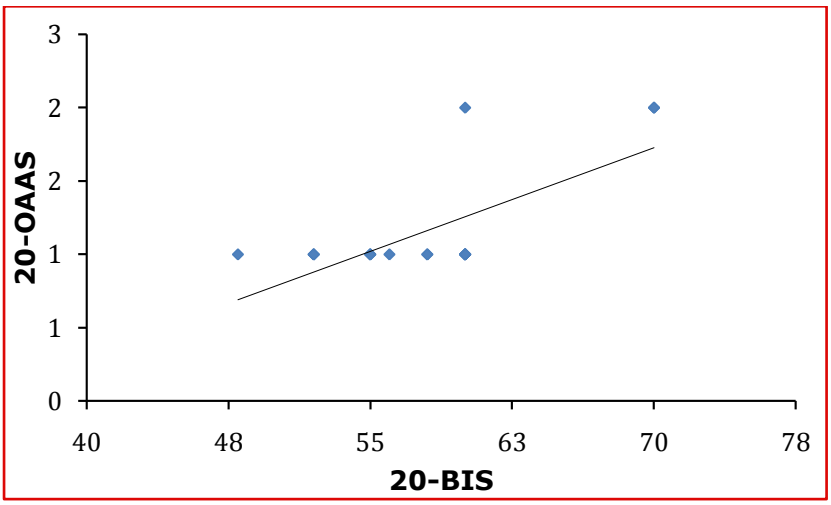
p=0.006, data is statistically significant

Fig. 11F: Spearman Rank Correlation between BIS & OAA/S at 15min in Gp.D



p=<0.001, data is statistically significant.

Fig. 11G: Spearman Rank Correlation between BIS & OAA/S at 20min in Gp.D



p=0.011, data is statistically significant.

Based up on the graphs it can be concluded that there is a strong correlation between the BIS score and the OAA/S scale at these time intervals. (Table 15 & Fig 11A-G)

Table 16: Spearman Rank Correlation Between BIS & OAA/S In the Gp. PF.

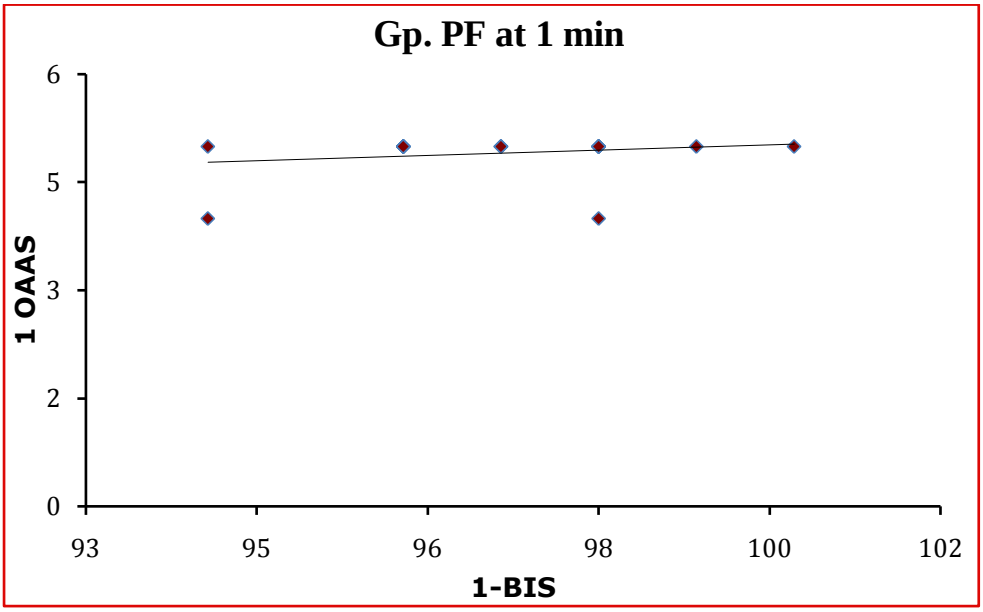
Correlation between the BIS and OAA/S (Spearman rank correlation): Group PF	Spearman's rho - ρ	p
0 minute	-	-
1 minute	0.120	0.614
3 minute	0.749	**<0.001***
6 minute	0.437	0.054
9 minute	0.900	**<0.001***
12 minute	0.777	**<0.001***
15 minute	0.815	**<0.001***
20 minute	-	-
25 minute	-	-
30 minute	-	-

*= p<0.05: hence is statistically significant

By using the Spearman rank correlation test in the GP. PF it can be commented that there is a strong correlation between the two scales at 3 minute, 9, 12 and 15 minutes only as compared to the other group.

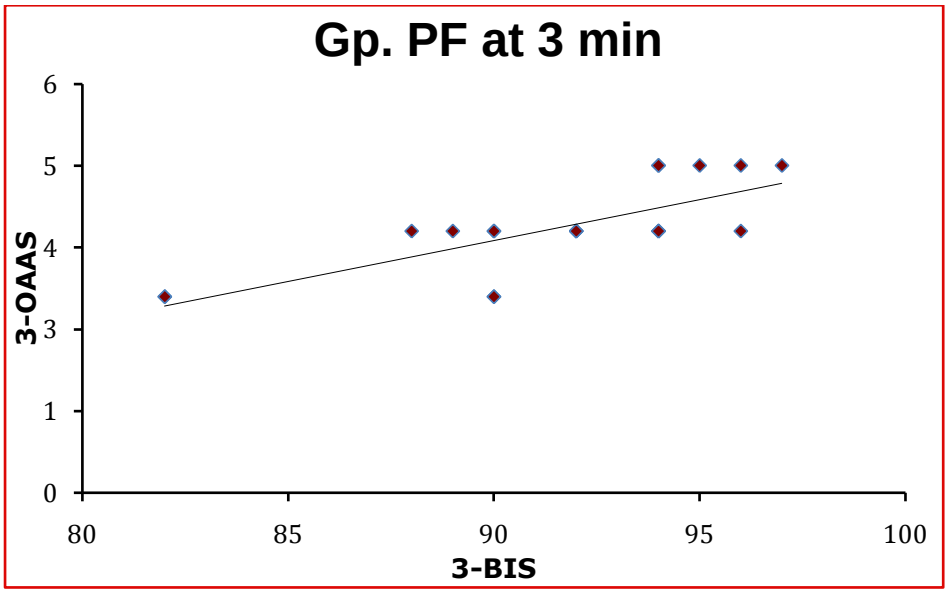
This can also be seen with the graphs based up on the slopes of the line. There is a positive correlation between the BIS and OAA/S in the GP. PF at the 3, 9, 12, 15 minutes time intervals. (Table 16 & Fig.12 A-F)

Fig. 12A: Spearman Rank Correlation between BIS & OAA/S at 1min in Gp.PF



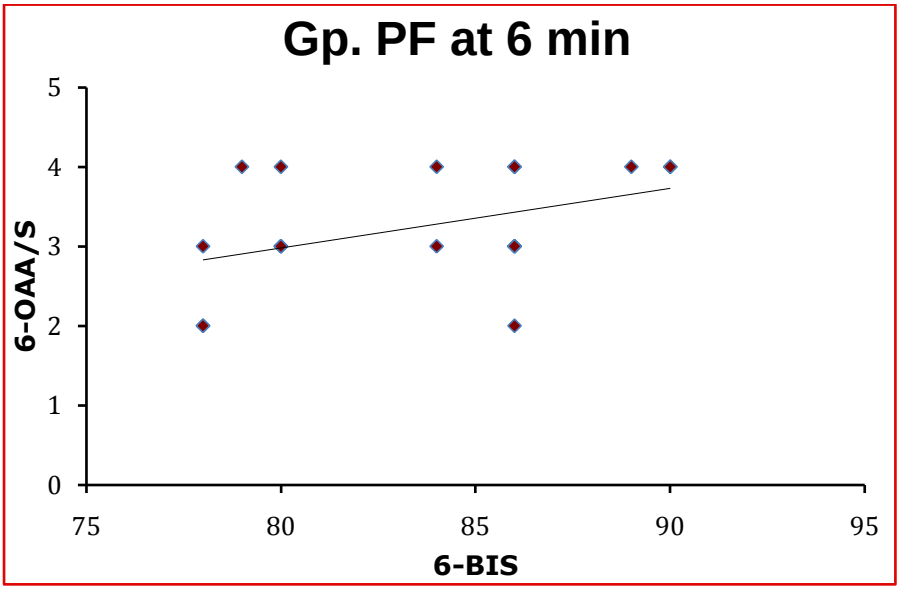
p = 0.614 (> 0.05) hence non significant

Fig. 12B: Spearman Rank Correlation between BIS & OAA/S at 3min in Gp.PF



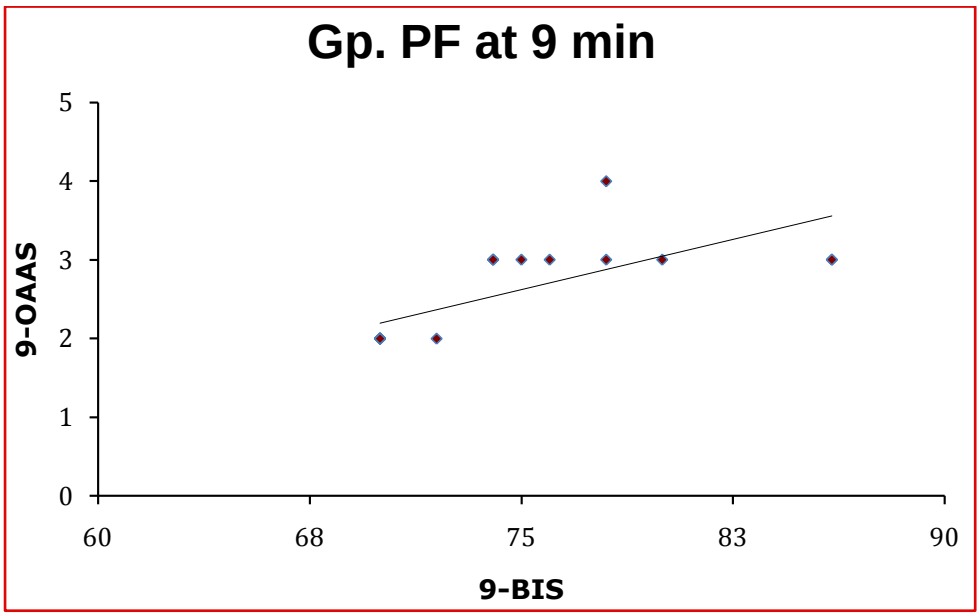
p= <0.001, data is statistically significant.

Fig. 12C: Spearman Rank Correlation between BIS & OAA/S at 6min in Gp.PF



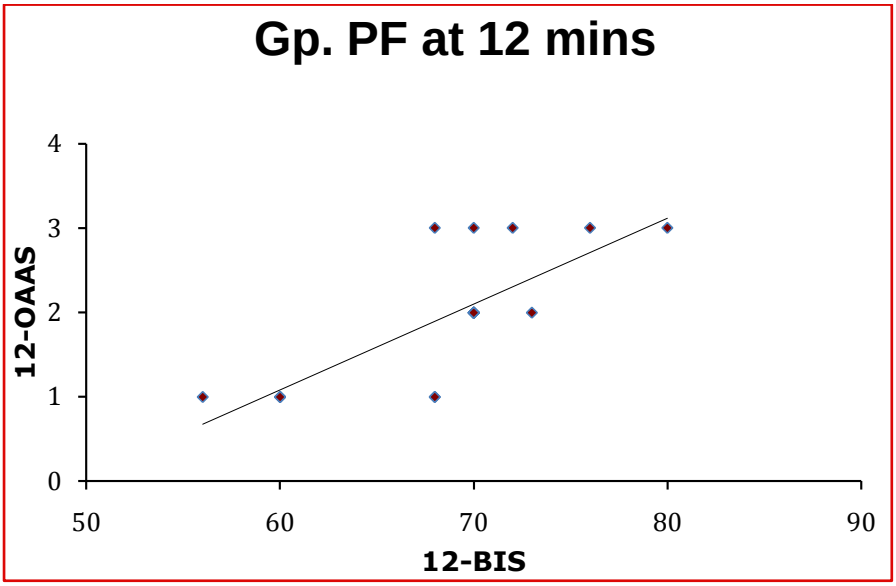
p=0.054, data is not statistically significant

Fig. 12D: Spearman Rank Correlation between BIS & OAA/S at 9min in Gp.PF



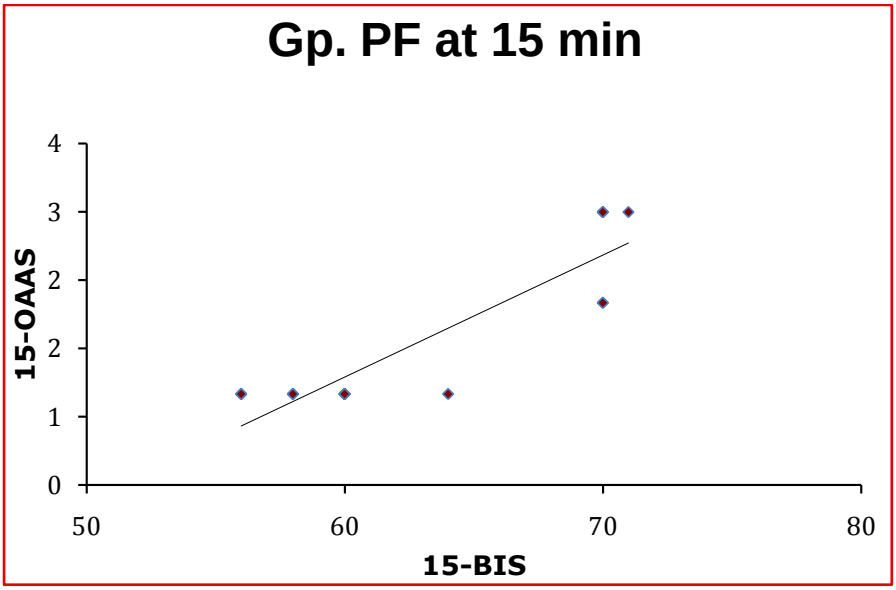
p=<0.001, data is statistically significant

Fig. 12E: Spearman Rank Correlation between BIS & OAA/S at 12min in Gp.PF



p=<0.001, data is not statistically significant.

Fig. 12F: Spearman Rank Correlation between BIS & OAA/S at 15 min in Gp.PF



p=<0.001, data is not statistically significant.

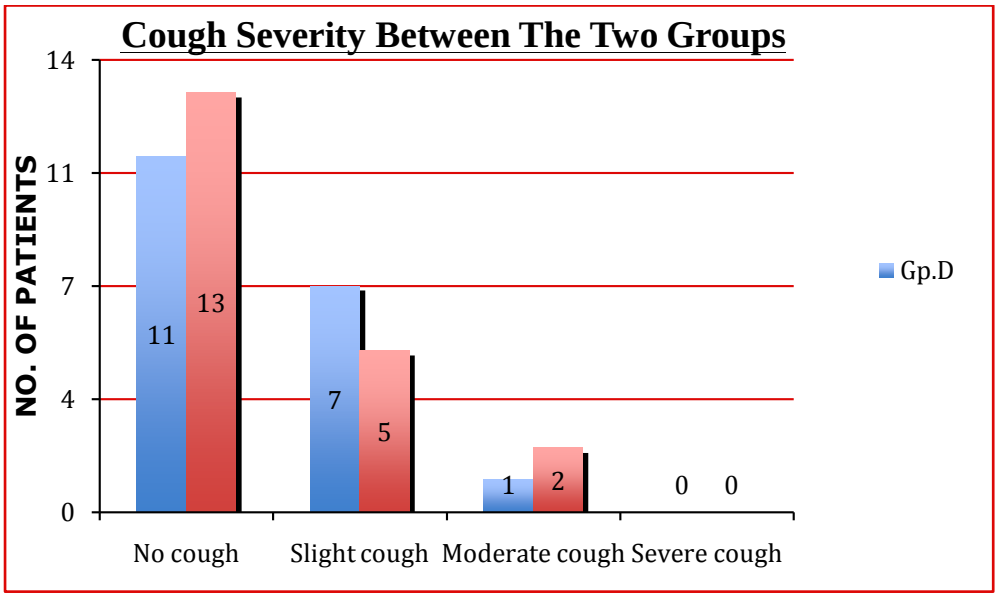
Table 17: Cough severity scale.

	No cough	Slight cough	Moderate cough	Severe cough	Total No.	Pearson Chi-Square
Gp.D	11(57.9)	7(36.8)	1(5.3)	0	19 (100)	0.668#
Gp. PF	13 (65.0)	5(25.0)	2(10.0)	0	20(100.0)	
Total	24 (61.5)	12(30.8)	3 (7.7)	0	39 (100)	

statistically not significant as 'p' value > 0.05%.

χ^2 =0.808 ; df = 1 Data expressed as N(%)

Fig. 13: Cough Severity between the Two Groups



Cough severity was graded as no Cough, slight cough, mod cough and severe cough. Twenty four (61.5%) patients in the total population i.e. 57.9 % in Gp. D and 65% of the patients in Gp. PF had a "no cough" during the AFOB. Around 36.8% of the patients in Gp D had slight cough as

compared to only 25% (5 patients) in Gp. PF. Moderate cough was noticed in 5.3% and 10% of the population in Gp. D and Gp. PF respectively. Though, there was some difference between the groups in cough severity but this difference was not statistically significant as the p value was > 0.05% done by using Pearson Chi-Square test. (Table 17 & Fig.13)

Table 19: Intubation score

Criteria	Evaluation	Score	Gp. D N(%)	Gp. PF N(%)	P value	Mann-Whitney U test / P-value
Anesthesia Quality	Asleep, deep sedation	2	19 (100)	20 (100)	1.000	136.000/ **p= 0.039***
	Slight, resistance	0	0	0		
Vocal Cords Relaxation	No	0	0	0	0.064	
	In part, middle	1	3 (15.8)	0 (0)		
	Relaxed, open	2	16 (84.2)	20 (100)		
Endotracheal tube Tolerance	Bad, disturbing: cough, swallowing	0	0	0	**0.047***	
	Middle; coughing or swallowing not disturbing the procedure	2	7 (36.8)	2 (10)		
	Good, no coughing or swallowing	4	12 (63.2)	18 (90)		

- * = Data is statistically significant as p<0.05
- # = Data not statistically significant as p>0.05

Table 20:Comparison Of Total Intubation Score Between The Two Groups

	N	TOTAL INTUBATION SCORE		t	p
		Mean	sd		
Group D	19	7.11	1.24	2.230	**0.032***
Group PF	20	7.80	0.62		

- *=P<.05: statistically significant.

Intubation score was assessed on the three headings: anesthesia quality, vocal cords relaxation and the ETT tolerance.

The anesthesia quality in both the groups were comparable with a p value >0.05, and 19 patients in Gp. D and 20 patients in the Gp. PF were, “asleep, deep sedation” and had a score of 2. (Table 18 & 19)

VC Relaxation:

3 patients (15.8%) in the GP .D had a score of 1 i.e. the vocal cords were, “in part, middle” as compared to none in the Gp. PF.

Vocal cords were found as, “Relaxed, open” in all the 20 patients (100%) in Gp.PF and 16 (84.2%) patients in the Gp. D with a p value of 0.064 (>0.05) and was considered as not significant.

ETT Tolerence:

A score of 2 was given if the patient had ETT tolerance -Middle; coughing or swallowing not disturbing the procedure. 7 (36.8%) patients in the Gp.D had a score of 2 as compared to only 2 (10%) patients in the Gp.PF.

In contrast 18 (90%) patients in the Gp.PF had a score of 4 i.e. "Good, no coughing or swallowing" during the ETT passing through the intubation as compared to the only 12 (63.2%) patients in the GP.D. This test was statistically significant with a p value of 0.047 (<0.05).

By using Mann-Whitney U test / P-value test on the intubation score it was found to be statistically significant between the two groups with a p value of 0.039 (<0.05). e total intubation score in the Gp. D was 7.11 as compared to the 7.8 in the GP. PF. Hence it can be concluded that the total intubation score was better in the Gp. PF than Gp. D.

Table 20: Intubation Time

	N	INTUBATION TIME		t	p
		Mean	sd		
Group D	19	27.79	21.18	2.181	0.036*
Group PF	20	16.10	10.95		

*= p<0.05: data is statistically significant

Gp. PF required a significantly lesser time to intubate as compared to Gp.D with a p value of 0.036 (<0.05). The time in Gp PF was 16.10 ± 10.95 seconds as compared to 27.79±21.18 seconds in the Gp.D. (Table 20.)

Table 21: Total Intubation Attempts

Total Intubation Attempts.	Category				Total		P value
	Group D		Group PF				
	N	%	N	%	N	%	
1.0	18	94.7	19	95.0	37	94.9	p=0.970 #
2.0	1	5.3	1	5.0	2	5.1	
Total	19	100.0	20	100.0	39	100.0	

χ^2 =0.001 df = 1 p=0.970

= p> 0.05, hence considered as not significant.

Around 94.7% in Gp D and 95% of the patients in the group PF were intubated on the first attempt. One patient in both the groups required the 2nd attempt of intubation. The test was comparable between the two groups and the p value was > 0.05 (*0.970*) and hence there was no statistically difference between the two groups with respect to the intubation attempts. (Table 21)

Table 22: Total dose of Lignocaine:

	N	TOTAL LIGNO DOSE		t	p
		Mean	SD		
Group D	19	331.58	107.56	1.931	0.061
Group PF	20	275.00	72.95		

= p> 0.05, hence considered as not significant.

The total lignocaine in Gp D was 333.58 ± 107.56 mg, which was more than that used in the Gp.PF of 275.00 ± 72.95 mg. But this was not statistical significant with a p value of 0.061 (>0.05). The average lignocaine /kg was 4.75± 1.40 as compared to 4.42± 1.24 mg/kg in Gp.PF with p value of 0.442. (Table 22, 23 & Fig. 14)

Fig. 14. Total dose of Lignocaine per Kg

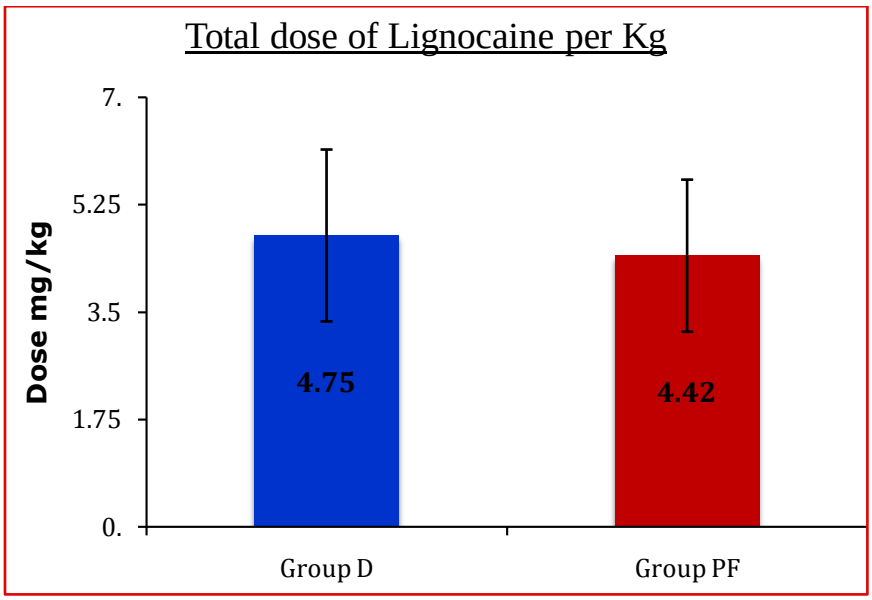


Table 23: Total dose of Lignocaine per Kg

	N	Total dose of Lignocaine per Kg		t	p
		Mean	sd		
Group D	19	4.75	1.40	0.776	0.442#
Group PF	20	4.42	1.24		

= Data not statistically significant

The average dose Propofol required was 85.50 ± 21.64 mg and Fentanyl was 76.50 ± 13.29 μg in the Gp. PF. The total dose of Dexmedetomidine used in the 83.68 ± 17.55 μg.

Table 24: Additional Maneuver's Required

Additional Maneuvers Required	**GROUP D (No. / %)**	**GROUP PF (No. / %)**	**Chi Square Test**
Required	2 (10.5)	3 (15.0)	*p =0.676*[#]
Not Required	17 (89.5)	17 (85)	
Total	19(100%)	20 (100%)	

χ^2 *=0.174 df = 1;* # = Data not statistically significant.

Few patients in both the group's required additional maneuvers like jaw lift to keep the patency of the airway. Two patients in the Gp.D (10.5%) and three (15.0%) patients in Gp.PF had desaturation due to tongue fall. Oxygen saturation transiently decreased to ≤95%. It improved instantaneously after jaw lift with oxygen in one patient in Gp. PF (PF6) and in both the patients belonging to the Gp. D. However the two patients in the Gp. PF (SpO_2 decreased to 93% & 92% in PF 8 & PF 14 respectively) required bag and mask ventilation as per the protocol. Only those patients who had desaturated to < 95% were considered as having airway complication as given in the table below.

Remaining patients in both the groups did not require any additional maneuvers i.e. 89% and 85% of patients in Gp. D and Gp. PF. There was no statistically difference between the two groups in terms of use of additional maneuvers with a "p" value of 0.676 (> 0.05). (Table 24)

Table 25: Complication in both the groups.

Complications		Category		P value
		Group D N(%)	Group PF N(%)	
No		17(89.5)	18 (90.0)	p=0.957#
Yes	Bradycardia	2 (10.5)	-	
	Desaturation (< 95%)	-	2(10.0)	
Total		19 (100.0)	20 (100.0)	

χ^2 =0.003; df = 1; # = Data not statistically significant

Table 26: Treatment for the complication

Complications		Category		Treatment given	Fisher's Exact Test (p)
		Group D N(%)	Group PF N(%)		
No		18 (94.7)	18 (90.0	-	1.000#
Yes	Significant Bradycardia	1 (5.3)	-	Inj. Glycopyrrolate	
	Desaturation (< 95%)	-	2(10.0)	Jaw lift with Bag & mask ventilation	
Total		19 (100.0)	20 (100.0)	-	

= Data not statistically significant

Only those incidences that required some form of intervention were considered as having complications. A total of 17 patients in the GP.D and 18 patients in the Gp. PF did not have any complication.

The two patients belonging to the Gp -D had developed bradycardia (D 7^{th} patient at 12^{th} minute of starting the drug with heart rate -45bmp and another patient D 13^{th} developed bradycardia at the 6^{th} minute with heart rate falling up to 43bmp). D 7^{th} patient's heart rate improved spontaneously once the infusion of the drug was stopped transiently without the need for any treatment however the D 13^{th} patient required intravenous Inj. Glycopyrrolate 0.2µg, following which patient's heart rate improved to 68 bpm. Though two patients in the Gp D required jaw lift but their SpO_2 level did not decrease below 95%. It improved immediately after doing the maneuver hence this was not considered as a complication.

In contrast to the Gp-PF where none of the patients had developed bradycardia but three patients (PF 6, PF 8 & PF 14) required additional airway maneuvers to improve the airway obstruction. Two out the three required bag and mask ventilation as per the protocol (SpO_2 decreased to 93% & 92% in PF 8 & PF 14 respectively). After the bag and masks ventilation their SpO_2 improved and the procedure of AFOB was conducted as per the plan. The third patient (PF6) who had developed airway obstruction and had a lowest SpO_2 value of 96% but it improved with jaw

lift maneuver only thereby this was not considered as a complication. Table 25& 26)

The incidence of complication, treatment required and jaw lift maneuvers were not statistically significant between the two groups as given in the above tables.

Table 27: Post-Operative Discomfort

Post Op Discomfort	**Category**		**Total N (%)**	**P value**
	Group D N (%)	**Group PF N (%)**		
Yes	2 (10.5)	0 (0.0)	2 (5.1)	0.136
No	17 (89.5)	20 (100.0)	37 (94.9)	
Total	19 (100.0)	20 (100.0)	39(100)	

χ^2 =2.219 df = 1 :p=0.136= p> 0.05, hence considered as not significant.

In the postoperative period two patients in the Gp-D complained about having some sore throat (D1 and D11 patients) and required to occasionally clear their throat for the same. Both D1 & D11 patients had slight cough during the procedure and had an intubation score of 5 each. D1 was intubated on the 2nd attempt as compared to D11 who was successfully intubated in the first attempt only. This sore throat had recovered on the 2nd

postoperative day after 3% saline nebulization. On the contrary none of the patients in the Gp-PF complained about it. (Table 27)

Table 28: Postoperative recall of the intubation:

Post Op Recall	**Category**		**Total**
	Group D	**Group PF**	
	N (%)	**N (%)**	**N (%)**
Yes	0(0.0)	0 (0.0)	0 (0.0)
No	19 (100.0)	20 (100.0)	39 (100)
Total N (%)	19 (100.0)	20 (100.0)	39(100)

None of the patients in either of the groups had any recall of the events during the AFOB procedure. (Table 28)

DISCUSSION

DISCUSSION

This study was conducted to compare the awake fiberoptic bronchoscopic (AFOB) orotracheal intubating conditions in patients with anticipated difficult airway using the Spray as You Go technique who was undergoing elective neurosurgical procedures with either Dexmedetomidine infusion alone or combination of Propofol with Fentanyl infusion under the guidance of BIS and OAA/S. The primary outcome was to measure the time to sedation, cough severity and the quality of intubating conditions & time for intubation, total attempts. And the secondary outcome were to evaluate the total doses of the lignocaine drugs required, intubation time, hemodynamic changes, BIS values and corresponding changes in OSS/A, comparison between the difficult airway and the intubation conditions, hemodynamics, intubation conditions, and patient comfort in the postoperative period.

The current study showed that both Dexmedetomidine alone (Gp. D) and combination of Propofol with Fentanyl (Gp. PF) were effective in conscious sedating patients undergoing AFOB guided orotracheal intubation using the SAYGO technique using Sedation scales (BIS and OAA/S) guided targeted therapy. This study also showed that the combination of Propofol with fentanyl could be safely used for AFOB with

intubation score and postoperative recovery profile better than that compared to patients who received Inj. Dexmedetomidine for conscious sedation.

In our study both the groups (Gp. D and Gp. PF) were comparable based up on their demographic data (Age, BMI, Sex, ASA grade, MMP, cervical spine disease and Neck extension<80^{o}).

The heart rate was comparable between the two groups except at 9, 12 and 20 minutes with the p value of 0.008, 0.023 and 0.023 respectively where it was statistically significant. The heart rate was lower in the Gp.D compared to the Gp.Pf. The lower heart rate trend in the Gp.D can be explained by the inherent ability of the Dexmedetomidine to cause decrease the heart rate. Since the average duration of the drugs infusion was 12.11± 2.28 in the Gp. D as compared to the 10.65 ± 2.52 minutes in the Gp. PF. This can explain the significant difference in the heart rate at the 9^{th} and the 12^{th} minute of starting the drug compared to the other group. However the heart rate at 20^{th} minute can probably be explained as by this time the intubation response might have subsided hence the heart rate would have stabilized to lower limit due to the residual effect of the Dexmedetomidine unlike the drugs in the other group i.e. Gp.PF cause less change in the heart rate. The hemodynamic effects of dexmedetomidine results from a decrease in noradrenaline release diminished centrally mediated sympathetic tone

and increased vagal activity.[102]

It is well documented that Dexmedetomidine infusion can cause bradycardia, atrial fibrillation, hypotension or hypertension especially at higher dose.[103] However, there are also few reports of unaltered hemodynamics even with higher doses of dexmedetomidine infusion.[104] Yavascaoglu *et al*. reported that when compared to esmolol, dexmedetomidine had more effectively prevented the hemodynamic response to tracheal intubation.[105] There are various reports have been mentioned in the literature regarding the attenuation of intubation response in patients who were posted for coronary artery bypass graft surgery[106, 107].

Peden *et al*. had reported bradycardia and sinus arrest in young volunteers who received a bolus of dexmedetomidine followed by the infusion. The author had recommended to prophylactic administer glycopyrrolate prior to dexmedetomidine.[5] In our study we had administered 0.2µgm of injection glycopyrrolate intramuscular thirty minutes prior to shifting the patient to the operation theater for its antisialogogue effect before performing a AFOB procedure, which can also help in the preventing such side- effects. In spite of premedicating all the patients with Inj. Glycopyrrolate, two patients in the Gp.D had bradycardia of which one patient required rescue therapy with intravenous administration of 0.2µgm of injection glycopyrrolate. However the other

patient in the same group did not require injection glycopyrrolate as the heart rate had improved spontaneously. There were no similar incidences of bradycardia observed in the Gp. PF.

This hemodynamic effect of dexmedetomidine can also be the reason for the lower values of the SBP, MBP and DBP in the GP. D compared to the Gp. PF. Though there was no statistically significant difference between the MAP and DBP statistically at all the time interval compared to the Gp. PF. However, the changes in the SBP were significant difference at the 20^{th} minute time interval (p=0.031*) between the two groups. This could be probably be hypothesized due to the hemodynamic effect of the dexmedetomidine. Though as by the end of 20^{th} minute the intubation response due to FOB might have subsided along with the added hemodynamic changes brought about by inducing general anesthesia once the ETT position was confirmed and patient's neurological status was assessed.

The oxygen saturation (SpO_2) in both the groups was comparable and was statistically non significant. Though few patients in both the group's required additional maneuvers like jaw lift to keep the patency of the airway. Two patients in the Gp.D (10.5%) and three (15.0%) patients in Gp.PF had desaturation due to tongue fall. Oxygen saturation transiently decreased to ≤95%. It improved instantaneously after jaw lift with oxygen

in one patient in Gp. PF (PF6) and in both the patients belonging to the Gp. D. However the two patients in the Gp. PF (SpO_2 decreased to 93% & 92% in PF 8 & PF 14 respectively) required bag and mask ventilation as per the protocol. Only those patients who had desaturated to < 95% were considered as having airway complication as given in the table below.

Remaining patients in both the groups did not require any additional maneuvers i.e. 89% and 85% of patients in Gp. D and Gp. PF. There was no statistically difference between the two groups in terms of use of additional maneuvers with a "p" value of 0.676 (> 0.05). (Table 24)

The desaturation in the Gp.PF could probably be explained due to synergistic effect of propofol and fentanyl together suppressing the respiratory center and decrease in the muscle tone of the pharynx.[102] besides fentanyl can also produces chest wall rigidity hence there is a risk of hypoxia and desaturation due to this. The unique property of dexmedetomidine, that it maintains spontaneous respiration in a deeply sedated patient, without causing any airway obstruction or respiratory depression minimal desaturation has been reported at higher doses of the drug. Mondal S et al in their study observed that the incidence of desaturation was less in the group (four patients) who had received dexmedetomidine 1 mcg/kg than other group-received fentanyl 2 mcg/kg over 10 minutes (4 vs 25 patients respectively) with a p < 0.0001, which

was highly significant. The authors managed the desaturation episodes with the administration of oxygen through the port of the bronchoscope.

Various other studies have used dexmedetomidine for AFOB as it proved that it causes very little respiratory depression and desaturation.[88, 101]. Hall et al had concluded that dexmedetomidine may provide a better field for fiberoptic endoscopy.[14, 108]

Dexmedetomidine belongs to class of centrally acting, selective alpha-2 agonist. This has found useful for sedation in critical care units, it has a shorter half-life and eight times greater selectivity for alpha 2 over alpha1 receptors than its counter partner clonidine belonging to the same group of drug.[1] It acts on the Locus ceruleus α2 receptors mediate sedative properties, and the spinal α2 receptors mediate its analgesic effects.[87, 88] The presynaptic alpha2 receptors in peripheral nervous system, Post-synaptic alpha 2 receptors which are present in the central nervous system, which mediate the cardiovascular effects of a2 agonists. Inhibition of noradrenaline release causes bradycardia, and reduced cardiac output. This leads to hypotension; however, a2 receptors located directly on vascular tissue cause vasoconstriction, which can result in hypertension, secondary to the administration of large bolus doses of a2 agonists.[89]

Dexmedetomidine has also been proved as an effective drug used for AFOI in certain difficult airway scenarios[18,81,82] Propofol, a

non‑barbiturate anaesthetic agent, it produces rapid onset of anesthesia for induction and for maintenance of anesthesia. The mechanism of action includes facilitation of inhibitory neurotransmission mediated by GABA A receptor binding. This allosterically increases binding affinity of GABA for the GABA A receptor coupled with a chloride channel, causing activation of the receptor leads to hyperpolarization of the nerve membrane. Propofol (like most general anesthetics) binds multiple ion channels and receptors. It is also used for various procedures requiring sedations after intravenous administration in proper sub‑hypnotic dose. There are numerous reports of propofol being used for AFOB using both bolus dose, infusion and with the use of target control infusion pumps. It can be used either as a sole agent or with other drugs like midazolam, ramifentanyl, etc.

Fentanyl used for the induction of general anesthesia to reduce pain and intubation response endotracheal tube passage.[2] Awake fibreoptic intubation can be associated with intense nociceptive stimulation, especially during negotiating the ETT through the nose and the larynx. While pure sedatives provide anxiolysis and amnesia and may help to smooth the intubation process, but they cannot substitute for inadequate airway topicalization with local anesthetic. Opioids are strong analgesics agents, which has some hypnotic effect and can help attenuate the coughing and hemodynamic changes due to the airway instrumentation.

The "Time To Achieve BIS <70" was significantly less with a p value of 0.016 ($p< 0.05$) in the Gp. PF (10 ± 2.18 minutes) as compared to the Gp. D (11.89 ± 2.49 minutes).

In our study we used dexmedetomidine alone in one group (Gp. D), which was infused at 1μg/kg bolus over 10 minutes by using an infusion pumps, followed by 0.5mcg/kg/hr infusion till target BIS value reached up to 70. This was chosen as it does not cause any respiratory depression and it is believed that it has analgesic property also and is hence is commonly used for AFOB. In the other group of patients who received propofol with fentanyl combination (Gp. PF), the bolus dose of propofol (1 mg/kg/hr) and fentanyl (1mcg/kg) was given over 10 minutes followed by 1mg/kg/ hr of propofol and 1mcg/kg of fentanyl infusion. They used two separate infusion pump's, till target BIS value reached up to 70. We decided to use this combination of agents, as propofol will provide the hypnosis and fentanyl will supplement the analgesia for easy passage of the endotracheal tube through the trachea during AFOB. Similarly Lee et al have used fentanyl infusion with other agents as an analgesic for the awake fiberoptic intubation.[26]

The BIS values were significantly different only at 9 and 12 minutes, with a p value of 0.018 & 0.049 ($p< 0.05$) respectively. The slope of the curve (BIS graph), Gp. PF starts dropping earlier than that of the other group almost after 3 minutes of start of the infusion of the drugs and equal

almost after 15 minutes, though at these times interval BIS values are not statistically significant.

Though the level of sedation was early detected by using the BIS monitor as against the use of clinical scale of OAA/S where in there was no significant difference between the two groups with respect to the drop of the OAA/S score and time to achieve a score of 3 which has been proven to be adequate for AFOB. When correlation was done between the two sedation scales, it was found that in Gp .PF there was a strong correlation between the BIS & OAA/S scales at 3, 9, 12,15 minutes with p value of <0.001, <0.001, <0.001, &<0.001 respectively. In contrast to this the two sedation scales had strong correlation at 3, 6, 9, 12, 15, and at 20 minutes of starting the dexmedetomidine infusion in Gp. D, with a p value of <0.001, 0.013, 0.002, 0.006 , <0.001 and 0.011 respectively.

In a study conducted by the Bagchi, *et al*. had concluded that a divergence exists between the time to achieve a BIS score 70 and time to achieve OAA/S score 3 using midazolam, compared with the propofol, during onset of the sedation. Monitoring sedation scores with the help of BIS and OAA/S score demonstrates poor correlation during onset of sedation while using midazolam. They found that a better correlation was found while using the propofol. They had also commented that since clinical sedation the main target, relying only on an EEG based monitor to

which displays a dimensionless whole number on the screen may not be wise enough as this might end in an inadequate level of sedation with loss of airway control. In contrary to their study, we found that BIS and OAA/S had a strong correlation between the both the groups. Bagchi, *et al* also commented that the use of BIS to monitor sedation is appealing. However, the conventional clinical methods of assessing the sedation scores are also equally important as patient contact is always maintained. Monitoring system like the BIS should always be employed along with the clinical assessment rather than just as the primary monitor. Besides by combining different methods (clinical assessment and by using EEG based method like BIS monitor) of can provide complementary information with better understanding regarding the pattern of sedation in which each patient responds which could be overlooked or missed using a single technique of monitoring.[83]Simply looking at an EEG based monitor and ignoring the clinical signs of over sedation or vise versa might not be prudent can cause significant over or under dosing of the drug.

In an another study performed by Hall et al. who had assessed the patient's alertness every 10 minutes, as opposed to 1-minute intervals. In the Remifentanil group the RSS score of 3 was achieved almost immediately after the loading dose unlike in the Dexmedetomidine group achieved an RSS score of 3 at a slower rate than remifentanil, but it always achieved enough sedation to begin AFOI, therefore, attempts at AFOI were

begun earlier the Ramifentanyl group than when dexmedetomidine was used. Nearly half the REM patients had a BIS score of < 80 after 5 minutes, while it was not until 13 minutes that fifty percent of the DEX patients had BIS < 80. This does not necessarily explain why even at an RSS score of 3, still more attempts needed to successfully intubate a patient in the DEX group. Due to this delay in attaining the appropriate sedation score allowed the patients in the DEX group to remain at awake levels longer, leading to further stimulation of the patients due to the RSS assessments done every minute, while the REM group did not continuously undergo RSS assessments as almost all patients in this group had achieved RSS scores of 3 or greater almost immediately post loading dose.[14]

Due to these discrepancies between the different clinical score and BIS of <80%, we chose to use both BIS and OAA/S scales for assessing the sedation scores and it was performed at much shorter interval of as compared to the above study. We however did not perform the sedation scale assessment as constant stimulation of the patient every minute might hamper in sedation of the patient and patients might tend to awaken from their sedation can there by get aggressive or uncooperative. However BIS could be monitored every minute but we measured both the sedation score at constant time interval along with the other parameters to keep uniformity.

The intubation score for AFOB was better in the Gp.PF as compared to the Gp. D with a p value of 0.039 ($p< 0.05$).

Bergese *et al*concluded that dexmedetomidine at 1 mcg/kg bolus was safe technique and also beneficial for those patients undergoing AFOB guided intubation even without airway block or any topical anesthesia.[90] This is similar to our study where the bolus dose of dexmedetomidine was infused at 1μg/kg over 10 minutes

Chu et al. Prospective RCT Dexmedetomidine 1.0 μg/ kg infusion over 10 min vs Fentanyl 1.0 μg/ kg infusion over 10 min. DEX group had better hemodynamic response to intubation, lower recall, with better patient tolerance and satisfaction scores. However in the DEX group, two patients had bradycardia and one had developed hypotension. [27]

Mondal. S et al conducted a similar study on 60 patients who were scheduled for elective laparotomies. Group A received dexmedetomidine 1 mcg/kg and Group B received fentanyl 2 mcg/kg over 10 minutes. The authors had concluded that Dexmedetomidine was more effective than fentanyl in providing better intubation conditions, sedation, hemodynamic stability and less desaturation during AFOI.[102] But unlike their study we in our study had used fentanyl at 1 mcg/kg along with propofol which was initiated at 1 mg/kg /hr over 10 minutes.

These results are similar to the study conducted by the Lallo A et al who had compared the efficacy and ease of titration of propofol (P) and remifentanil (R) using the help of target-controlled infusions (TCI) during

FOB. Here the authors found that the cough severity was 13/7/7/2 vs 18/6/3/2 with no statistical difference between the two groups.[109]

Bonnin M et al in their study compared between the TCI infusions of propofol with 4% sevoflurane in patients with anticipated difficult airway. They concluded that the intubation score was also comparable between the two groups (P = 0.24); this score was based up on the easy practice of FOB and thereby successful intubation. The number of patient's with a cough was eight in the propofol group and five in the sevoflurane group. Vocal cord relaxation was also comparable (P = 0.67). The satisfaction score was also comparable in the groups (P 1⁄4 0.31), with a score related to good to very good satisfaction. [100]

In our study the intubation score was 7.11 ± 1.24 vs 7.80±0.62 with a p value of 0.032, in Gp .D and Gp.PF respectively. Though there was no difference in the anesthesia quality and vocal cord relaxation between the groups but the endotracheal tube tolerance was better in the Gp.PF as compared to the GP. D, with a p value of 0.047 (<0.05) and was considered significant.

The time required for intubation was significantly lesser in the Gp. PF as compared to Gp.D with a p value of 0.036 (<0.05). The time required for intubating the trachea was 16.10 ± 10.95 seconds in the Gp PF was as compared to 27.79±21.18 seconds in the Gp.D. The intubation time

required in our study was less than that required by the Rong Hu et al which was 30.9± 8.8 sec vs 33.3±6.5 sec in the dexmedetomidine group and the Remifentanil group respectively with a p value of 0.31 which was not significant.[101]

This in comparison to the study conducted by the Davide Cattano et al on 34 patients comparing remifentanil and dexmedetomidine for AFOB guided intubation. The intubating attempts (1^{st} /2^{nd}/ 3^{rd}) in the Remifentanil group was 13/3/1 as compared to 5/4/4.[3] In our study the total intubation attempts i.e. (1^{st}/ 2^{nd} /3^{rd}) were 18/1/0 and 19/1/0 in Gp D and Gp. PF. The test was comparable between the two groups and the p value was > 0.05 (*0.970*) and hence there was no statistically difference between the two groups with respect to the intubation attempts. Hence in our study the total intubating attempts were much lesser compared to the previous study as majority of the patients were able to be intubated in the first attempt itself.

Parkes et al.nebulized patients with 6 mg/kg of 10% lignocaine solution through a nebulizer mask prior to instrumentation of the airway with a FOB. The serum lignocaine levels were measured and the authors found that it always remained below the standard accepted threshold limit of 5 mg/l. The highest levels obtained in the study were 0.45 mg/l, which was much less than threshold value.[85]

In a similar study, conducted by Langmack et al.on 51 asthmatic volunteers who underwent FOB, the authors measured the serum lignocaine levels achieved with topical lignocaine. The average total dose used in their study was 8.2 mg/kg (600 mg). They concluded that this was safe in all patients based on their serum lignocaine concentrations.[110] However, Wu et al. reported seizures in a patient who received a total dose of 300 mg of topical lignocaine during FOB. The serum lignocaine concentrations were found to be well above the acceptable toxic limits. Hence, the authors recommend for a constant vigilance for any early signs and symptoms of lignocaine toxicity is mandatory especially while using large doses.[111]

K. A. Williams, combined the method of nebulization and direct application of lidocaine to the airway in 25 unsedated subjects undergoing AFOB intubations. It produced good conditions for fibreoptic intubation. In their series, a maximum calculated dose of 9 mg/kg lignocaine produced one peak plasma lidocaine concentration of 4.5 mg/L but none greater than 5 mg/L. They concluded that when both these methods are combined i.e. nebulization and topical anesthesia, the maximum dose of calculated lidocaine administration should not exceed 9 mg/ kg. [98]

In an another study conducted by Fu S. Xue et al, where the authors had compared the safety and efficacy of 2% and 4% lidocaine during airway topical anesthesia with the SAYGO technique via the FOB. They

concluded that either 2% or 4% lidocaine administered topically by a SAYGO technique could provide clinically acceptable intubating conditions for AFOI in sedated patients with difficult airway. Compared with 4% lidocaine, however, 2% lidocaine requires a much smaller dosage and thereby results in lower plasma concentrations. [99]

In our study the total lignocaine required to anesthetized the airway in Gp D was 333.58 ± 107.56 mg, which was more than that used in the Gp.PF of 275.00 ± 72.95 mg. But this was not statistical significant, as the p value of 0.061 (>0.05). Though the total lignocaine dose required to anesthetize the airway was more in the Gp.D as compared to the Gp. PF but the average lignocaine /kg body weight was 4.75 ± 1.40 in the Gp. D, as compared to 4.42 ± 1.24 mg/kg in Gp.PF with p value of 0.442 and was not significant. Unlike Wu et al's study none of the patients in the either of the groups had any neurological or cardiac adverse events.

Rong Hu et al had found that the incidence of postoperative sore throat and hoarseness was 5 and 2 in the Dexmedetomidine group as compared to the 5 and 3 in the Remifentanil group.[101] In our study, the incidence of postoperative period two patients in the Gp-D complained about having sore throat and required to occasionally clear their throat for the same. Both the patients had slight cough during the procedure and had an intubation score of 5 each. D1st patient was intubated on the 2nd attempt as compared to D11th who was successfully intubated in the first attempt

only. This sore throat had recovered on the 2nd postoperative day after 3% saline nebulization. On the contrary none of the patients in the Gp-PF complained about it. None of the patients in either of the group had hoarseness in the postoperative period.

Hu R et al also assessed the incidence of recall of endoscopy and intubation. They found that 8/6 and 14/13 patients in the Dexmedetomidine group and Remifentanil group respectively, with a p value of 0.057 (>0.05) and 0.027 (<0.05). [101] Lallo A et al in their study found that the 14 patients out of 29 in propofol group and 26 out of 29 patients in the remifentanil group had recall to the procedure with a p value of 0.0001 (<0.05), which is highly significant. [109] Compared to the previous studies in our study none of our patients had any recall of AFOB intubation. The possible explanation for this discrepancy in the postoperative recall for endoscopy and intubation could be due to the nasotracheal intubation procedure chosen by both Rong Hu et al and Lallo A et al as compared to orotracheal intubation done in our study. [101,109]

LIMITATION OF THIS STUDY

There are few limitations of the study:

1. One of the major limitation of this study is that due to the color of the propofol blinding could not be done hence this could allow some degree of bias. Besides the investigators were only involved in assessing the observation rather than an investigator who was blinded for the study protocol. This also could have caused some bias by the investigators.

1. Though the sample size was calculated based up on previous studies and was limited to 20 in each group. Results obtained from our study could be taken with caution and a larger randomized control trial is probably required.

3.We had chosen all patients with anticipated difficult airway undergoing elective neurosurgical procedure hence probably these results could not be validated in patients coming for emergency surgeries with anticipated difficult airway. Besides the benefits of this study could be different in different subgroup of neurosurgical patients.

4. Though the lignocaine dose was calculated based up on the body weight which is not a reliable method, the ideal method would be to

measure the serum lignocaine levels. This was not measured due to unavailability of this facility at our center.

Perhaps a future study with a larger sample size and adequate power, randomized double blinded prospective study comparing various drugs in the neurosurgical patients with different airway difficulties is warranted.

CONCLUSION

CONCLUSION

Our study shows that either Dexmedetomidine alone or Propofol with fentanyl combination can be successfully used for awake fiber optic intubation under monitoring for sedation, in patients posted for neurosurgical procedures with anticipated difficult airway.

We found that combination of Propofol with Fentanyl provided better intubating condition compared to dexmedetomidine infusion with shorter intubating time, better intubation score, decreased coughing, decreased Lignocaine dose per kg body weight and better postoperative profile during the AFOB if supplemented with Lignocaine using “Spray As You Go technique”

Both BIS and OAA/S are reliable indicators of sedation with good correlation with each other.

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ANNEXURES

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान
तिरुवनन्तपुरम - 695 011, केरल, भारत
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY
THIRUVANANTHAPURAM - 695 011, INDIA
(An Institute of National importance under Govt. of India)

Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013)

SCT/IEC/ 626/JUNE -2014 17-06-2014

Dr. B. Madhusudhana Rao
Senior Resident
Department of Anesthesiology
SCTIMST.

Dear Dr. Madhusudhana Rao,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "COMPARISON BETWEEN DEXMEDETOMIDINE ALONE AND PROPOFOL WITH FENTANYL COMBINATION FOR FIBEROPTIC GUIDED INTUBATION IN NEUROSURGICAL PATIENTS WITH ANTICIPATED DIFFICULT AIRWAY USING BISPECTRAL INDEX GUIDED CONSCIOUS SEDATION- A PROSPECTIVE, RANDOMISED CASE CONTROL STUDY" (IEC/626) on 7th June, 2014.

The following documents were reviewed:

1. *Covering letter addressed to the Chairman, dated 28.05.2014.*
2. *IEC Application form, Proforma, Consent form (English and Malayalam)*
3. *Proposal for study, Short CVs of PI and Co-PI's*
4. *TAC Approval Letter.*

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IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC

CONSENT FORM

Title of the study:

Comparison between Dexmedetomidine alone and Propofol with fentanyl combination for fiberoptic guided intubation in neurosurgical patients with anticipated difficult airway using Bispectral index guided conscious sedation. A Prospective, Randomised Case Control Study.

Name of the Investigators:

Dr. B. Madhusudhana Rao, Dr. Manikandan.S, Prof. Dr. Suresh Nair.

You are being requested to participate in this study, which compares between dexmedetomidine alone and Propofol with Fentanyl combined infusion for fiberoptic guided (FOB) orotracheal intubation in neurosurgical patient's with anticipated difficult airway using Bispectral index (BIS) guided conscious sedation. Both these tools (FOB & BIS) are used routinely as part of Anaesthesia in this institute and worldwide. We have planned to include about 40 people from this hospital in this study.

What does Dexmedetomidine do when given to you?

Dexmedetomidine is a sedative/ anaesthetic drug given before the surgery through blood vessel to produce sleep and unconsciousness. It also decreases pain and nervousness. This drug has been used in patients all over the world in neurosurgical patients and found to be safe.

What does Fentanyl do when given to you?

Fentanyl is an opioid drug used routinely in anaesthesia given for the purpose of analgesia during surgery. It reduces pain and anxiety and reduces the dose of anaesthetic gases required. This drug is widely used all

over the world as part of anaesthesia protocol.

What does Propofol do when given to you?

Propofol is a sedative/ anaesthetic drug given before the surgery through blood vessel to produce sleep and unconsciousness. This also prevents the vomiting after the surgery. This drug is widely used all over the world as part of anaesthesia protocol.

What is conscious sedation?

This is a form of anaesthesia where patient is sedated with the use of anaesthetics drugs but will fully respond for the oral commands. However patient will be totally pain free and comfortable. This is a standard form of anesthesia and has been used all over the world in neurosurgical patients and found to be safe, comfortable and pain free.

What is Fiber Optic Bronchoscope (FOB)?

Intubation is a process of inserting an endotracheal tube into the tracheal for providing continuous oxygen through the surgery provided with the help of a ventilator, as patient cannot breath spontaneously during general anesthesia. Various gadgets are available for intubation. FOB is the gold standard for intubation especially in an anticipated difficult airway. FOB is an instrument with light source, which is used for intubation the tracheal under direct vision. This tool has been used all over the world in neurosurgical patient's for intubation with anticipated difficult airway for and is found to be safe.

What is Bispectral Index (BIS)?

BIS is an instrument whereelectrodes are placed over the forehead of the patient and connected to the monitor. This will assess the depth of unconsciousness. However this is totally pain free, and is a standard of care for patients undergoing neurosurgical procedures.

If you take part what will you have to do?

On the day of surgery you will be nebulized with lignocaine for 10minutes to anesthetize the airway. Then you will be taken inside the Operation Theatre. Monitors to check your heart beats, blood pressure and oxygen saturation level will be attached. A small venous line will be inserted under local anesthesia in the hand for fluid and drug administration. Based on a computer generated random number patients will be allotted into one of the two groups. There is equal chance that you can fall into either of the two groups. The throat will be sprayed with local anaesthetic drug following which you will not have discomfort in your throat as it is now anaesthetised. Based on the groups in which you will be included you will be sedated either with Dexmedetomidine alone or propofol with fentanyl combinations in a dose according to their body weight. Once the BIS score and sedation level is appropriate, FOB will be inserted orally into the tracheal and under vision an endotracheal tube will be inserted into the trachea. After the intubation, general anaesthesia will be induced and maintained as per the routine anesthesia practice in the hospital. During the intubation process all the parameters to be studied will be recorded. After recording the parameters, the surgery will continue as planned by the neurosurgical team. At the end of surgery endotracheal tube will be removed once the patient is fit for extubation, and patient will be shifted to neurosurgical intensive care unit for monitoring and / or ventilation.

Does Dexmedetomidine have any side effects?

The majority of people have not had any side effects. Some people have experienced some side effects such as decrease in blood pressure, decrease in heart beat, dry mouth. These side effects are usually mild and temporary and easily correctable with appropriate medicines. In the event of such incidences, the appropriate treatment will be instituted immediately and if needed, the administration of the study drug will be stopped as per

the discretion of the anaesthesiologist.

Does Fentanyl have any side effects?

The majority of people have not had side effects. Some people experience muscle rigidity and nausea. These side effects are usually mild and temporary and easily treated. If any such event occurs appropriate treatment will be instituted immediately.

Does Propofol have any side effect?

The majority of people have not had side effects. Some people experience pain while injecting the drug. Other side effects are allergic reaction, hypotension, tachycardia or bradycardia. These side effects are usually mild and temporary and easily treated. If any such event occurs appropriate treatment will be instituted immediately.

Does FOB use have any side effects?

The majority of people have not had any side effects. The reported side effects are coughing, sore throat and transient numbness of throat due to the use of local anaesthetic agents but as patient will be sedated these side effects will be less. Other reported complications are very rare and include oral bleeding due to minor trauma to the gums or oral cavity. Intubation can induce vagal and sympathetic reflexes such as hypertension or hypotension, tachyarrhythmias or bradycardia, bronchospasm, laryngospasm, cyanosis, or in very rare cases cardiopulmonary arrest.Thesecomplications are very rare as patients will be adequately sedated prior to intubation as sedation and local anaesthetic spray will mostly blunts the hemodynamic effects of FOB. Furthermore the patients with risk of getting injured are excluded by the exclusion criteria.

What are the different methods of intubation?

During general anesthesia, tracheal is routinely intubated i.e. a tube is passed through the mouth into the trachea for continuous supply of oxygen through out the surgery. Various methods are available for doing the same namely endotracheal intubation using direct laryngoscopy and FOB.

What are the advantages and disadvantages of both the techniques?

Laryngoscopy is done after giving anesthesia and muscle paralysis during which you will be totally unconscious and will not have any pain. But due to the anticipated difficult airway in you, neurological assessment cannot be done after anesthetizing or sometimes intubation can become difficult.

FOB is done either under sedation or after giving anesthesia. FOB can be done under sedation by giving some drugs like in this study during which you will be sedated but will respond for oral commands. You will not have pain as your oral cavity will be anesthetized and you will be sedated. The advantage is that FOB is the gold standard for intubating a patient with anticipated difficult airway. Your neurological status can also be assessed after intubation.

FOB can also be done after giving anesthesia and muscle paralysis during which you will be totally unconscious and will not have any pain. But the disadvantage of this technique is that you neurological examination cannot be done as you are completely anesthetized and sometimes it might be difficult doing FOB guided intubation in anesthetized condition.

Both these techniques are routinely done in our hospital and are found to be safe.

You have the right to choice as to by which method you would like to get intubated either by using laryngoscopy or by FOB method.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdrawpermission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way. In addition, if you experience any side effects, the study will be stopped and you will be given additional treatment.

What will happen if you develop any study related injury?

We do not expect any injury to happen to you since the anaesthesia technique, drugs used and monitoring tools are standard technology used worldwide and in our institution,would be same even if you were not part of the study. However if you do develop any side effects or problems due to the study, these will be treated at no cost to you. We are unable to provide any monetary compensation, however.

Will you have to pay for the cost of using the devices?

Awake FOB is used as a part of routine anaesthesia procedures where patients are suspected to have difficult airway prior to the surgery. Any extra charge for monitoring purpose will be borne by the Principal Investigator.

What happens after the study is over?

Awake FOB guided intubation is routinely done in neurosurgical patients posted for surgery with anticipated difficult airway. After the study is over the general anaesthesia will be induced and the planned surgery will be conducted. After the surgery, general anaesthesia will be stopped and based on whether patient is fit for extubation or not he/ she will be either extubated (endotracheal tube will be removed) or shifted to ICU on

ventilator.

Will your personal details be kept confidential?

The results of this study will be used for thesis submission as a part of academic research and will be submitted to a medical journal for publication, but you will not be identified by name in any publication or presentation of results. However, only the people associated with the study may review your medical notes, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask *Dr. B. Madhusudhana Rao* (Principal investigator) mobile number :09048656800. Email id: drmaddy@sctimst.ac.in

Participant's name: . Date of Birth / Age (in years):

I_____, son/daughter of _____

Declare that (Please tick boxes)

- I have read and understood the above information provided to me regarding this study: Comparison between infusion of Dexmedetomidine alone and Propofol with Fentanyl combination for fiberoptic guided intubation in neurosurgical patient's with anticipated difficult airway using Bispectral index guided conscious sedation. A Prospective, Randomized Case Control Study. [ ]
- I have clarified any doubts that I had. [ ]
- I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ]

- I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access [ ]
- I understand that my identity will not be revealed in any information released to third parties or published [ ]
- I voluntarily agree to take part in this study [ ]
- I have been provided with the contact numbers of the principle investigator, in case I want to know more about the study and participants rights [ ].
- I received a copy of this signed consent form [ ]

Name: Name of witness:

Signature: Relation to participant:

Date: Signature:

Person Obtaining Consent:

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form,including any risks and adverse reactions that may reasonably be expected too occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

Signature: Date:

Name:

Annexures: III

PROFORMA

COMPARISON BETWEEN DEXMEDETOMIDINE ALONE AND PROPOFOL WITH FENTANYL COMBINATION FOR FIBEROPTIC GUIDED ENDOTRACHEAL INTUBATION IN NEUROSURGICAL PATIENTS USING BISPECTRAL INDEX GUIDED CONSCIOUS SEDATION.A PROSPECTIVE, RANDOMISED CASE CONTROL STUDY.

Serial No. /40Group: D / PF

Name: **I.P number:**

Diagnosis : **Proposed surgery**:

Age / Sex/Weight:Yrs/ M / F/ Kgs. **BMI:** **Date of surgery:**

Checklist:

Factors	Include	Exclude	Factors	Include	Exclude
Patient consent	Yes	No	**Cervical spine disease/ atlanto-axial dislocation**	Yes	No
Nature of procedure	Elective	Emergency	**History of previous difficult laryngoscopy or intubation**	Yes	No
Age	19-50	<18 or >50	**MMP class 3 and 4**	Yes	No
ASA grade	I or II	III, IV or V	**Thyromental distance less than 60 mm**	Yes	No
GCS	15	< 15	**Interincisor distance less than 30mm**	Yes	No
Features of raised ICP or Herniation syndrome	No	Yes	**Head and neck movement less than 80° and obesity.**	Yes	No
Anticipated difficult airway	Yes	No	**History of allergy to Lignocaine/ Propofol/ Fentanyl or Dexmedetomidine**	No	Yes
Systemic HTN stage III or above	No	Yes	**History of TIA/ Stroke**	No	Yes
Heart block / Bradycardia< 50bpm	No	Yes	**Coagulation abnormality**	Present	Absent
Pregnancy/ Nursing	No	Yes	**Presence of CAD/ Left ventricular dysfunction**	No	Yes

Observations:

Parameters	**HR**	**SpO_2**	**SBP**	**Mean BP**	**DBP**	**BIS**	**OAA/S**
Baseline ("0" min)							
After 1 min							
After 3 min							
After 6 min							
After 9 min							
After 12 mins							
After 15mins							
After 20mins							
After 25 mins							
After 30mins							

Table 1: Cough severity. [109]

Cough severity	Number of coughs	Score	Total Score
No cough	**No cough**	**1**	
Slight cough	**<3**	**2**	
Moderate cough	**3-5**	**3**	
Severe cough	**>5**	**4**	

Table2:Intubation score (Anaesthesia quality, Vocal cords relaxation, Immediate tracheal tube tolerance): [100]

Criteria	Evaluation	Score	Total score
Anaesthesia quality	Asleep, deep sedation	2	
	Slight, resistance	0	
Vocal cords relaxation	No	0	
	In part, middle	1	
	Relaxed, open	2	
Immediate tracheal tube tolerance	Bad, disturbing: cough, swallowing	0	
	Middle; coughing or swallowing not disturbing the procedure	2	
	Good, no coughing or swallowing	4	

Total score < 3: difficult or impossible fibreoptic intubation. Three < total score < 7: disturbed procedure for fibreoptic intubation;successed tracheal intubation. Total score > 7: easy fibreoptic intubation; successful tracheal intubation.

Table3:The observer's assessment of alertness/sedation score. [83]

Responsive	**Speech**	**Facial expression**	**Eyes**	**Complete score**
Responds readily to name spoken in normal tone	Normal	Normal	Clear; no ptosis	**5 (alert)**
Lethargic response to name spoken in normal tone	Mild slowing or thickening	Mild relaxation	Glazed or mild ptosis (less than half the eye)	**4**
Responds only after name is called loudly/or repeatedly	Slurring or prominent slowing	Marked relaxation (slack jaw)	Glazed or marked ptosis (half the eye or more)	**3**
Responds only after mild prodding or shaking	Few recognizable words	-	-	**2**
Does not respond to mild prodding or shaking	-	-	-	**1**

Table 4: Adverse events:

Adverse events	**Management**
Total episodes of desaturations	
Arrhythmias/ Bradycardia / Tachycardia	
Hypotension /hypertension	
Allergies	
Other	

- Infusion started time
- Total Dose of Lignocaine:
- Total Dose of Dexmedetomidine:
- Total time for intubation:
- Additional manoeuvres required:
- Postoperative sore throat:
- Postoperative hoarseness:
- Postoperative recall of memory:

Infusion completed time:
Total Dose of Propofol& Fentanyl:
Time to achieve BIS - 70:
Total intubation attempts:

- **Name & Signature of Investigator:**

Annexures: IV

Table 1: Cough severity. [109]

Cough severity	Number of coughs	Score	Total Score
No cough	**No cough**	**1**	
Slight cough	**<3**	**2**	
Moderate cough	**3-5**	**3**	
Severe cough	**>5**	**4**	

Table2: Intubation score (Anaesthesia quality, Vocal cords relaxation, Immediate tracheal tube tolerance): [100]

Criteria	Evaluation	Score	Total score
Anaesthesia quality	Asleep, deep sedation	2	
	Slight, resistance	0	
Vocal cords relaxation	No	0	
	In part, middle	1	
	Relaxed, open	2	
Immediate tracheal tube tolerance	Bad, disturbing: cough, swallowing	0	
	Middle; coughing or swallowing not disturbing the procedure	2	
	Good, no coughing or swallowing	4	

- Total score < 3: difficult or impossible fibreoptic intubation. Three < total score < 7: disturbed procedure for fibreoptic intubation;successed tracheal intubation. Total score > 7: easy fibreoptic intubation; successful tracheal intubation.

Table 3: The observer's assessment of alertness/sedation score. [83]

Responsive	**Speech**	**Facial expression**	**Eyes**	**Complete score**
Responds readily to name spoken in normal tone	Normal	Normal	Clear; no ptosis	**5 (alert)**
Lethargic response to name spoken in normal tone	Mild slowing or thickening	Mild relaxation	Glazed or mild ptosis (less than half the eye)	**4**
Responds only after name is called loudly/or repeatedly	Slurring or prominent slowing	Marked relaxation (slack jaw)	Glazed or marked ptosis (half the eye or more)	**3**
Responds only after mild prodding or shaking	Few recognizable words	-	-	**2**
Does not respond to mild prodding or shaking	-	-	-	**1**

Annexures: V

Plagiarism Check

Thesis_Dr.Rao.docx

ORIGINALITY REPORT

19%

SIMILARITY INDEX

KEY TO MASTER CHART

1. Gp D- Group Dexmedetomidine
2. Gp. F- Group Propofol with Fentanyl
3. M=Male
4. F=Female
5. BMI: Body mass index
6. Anticipated Difficult Airway: 1= Yes, 2= No
7. C Spine Disease/AAD): 1= Yes, 2= No
8. Neck Extension <80degree: 1= Yes, 2= No
9. HR: Heart Rate
10. SBP : Systolic Blood Pressure
11. DBP: Diastolic Blood Pressure
12. MBP: Mean Blood Pressure
13. BIS: Bispectral Index
14. OAA/S: Observer's Assessment of Alertness/ Sedation score**.**

SL. NO.	Groups	Sex(M=1, F=2)	Weight	Height	BMI	ASA GRADE	ADA	C Spine Disease/AAD	MMP	TMD	Neck Extension <80^0	Mouth Opening	0-HR (mins)	1 HR (mins)	3 HR (mins)	6 HR (mins)	9 HR (mins)	12 HR (mins)	15 HR (mins)	20 HR (mins)	25 HR (mins)	30 HR (mins)	0-SpO2 (mins)	1 SpO2 (mins)	3 SpO2 (mins)	6 SpO2 (mins)	9 (mins)SpO2	12 SpO2 (mins)	15 SpO2 (mins)	20 SpO2 (mins)	25 SpO2 (mins)	30 SpO2 (mins)
D1	D	1	80	170	29	II	1	1	4	6	1	3	89	78	76	86	70	73	72	69	74	77	100	100	100	100	100	100	100	100	100	100
D2	D	2	60	152	26	I	1	1	4	6	1	3	61	68	62	60	58	54	52	68	64	65	100	100	100	100	100	100	100	100	100	100
D3	D	1	85	172	29	I	1	2	4	6	1	3	71	65	64	62	64	72	70	68	68	70	100	100	100	100	100	100	100	100	100	100
D4	D	1	50	160	20	I	1	2	3	6	2	2.5	67	62	58	51	52	43	66	88	80	78	100	100	100	100	100	100	100	100	100	100
D5	D	1	70	172	24	II	1	1	4	6.5	1	3	80	86	75	71	76	81	84	84	84	80	100	100	100	100	100	100	100	100	100	100
D6	D	2	70	160	27	II	1	2	3	5.5	1	2	67	65	61	62	66	65	63	62	62	61	98	98	98	98	98	98	98	98	98	99
D7	D	1	90	175	29	I	1	1	4	6.5	1	3	56	58	60	64	60	60	62	65	65	65	100	100	100	100	100	100	100	100	100	100
D8	D	1	75	164	28	I	1	2	4	5.5	1	3	78	90	86	84	84	80	76	74	74	72	100	99	99	99	99	99	99	99	99	99
D9	D	2	70	167	25	I	1	2	3	6	1	3	76	67	66	64	63	51	53	64	58	60	100	100	100	100	100	100	100	100	100	100
D10	D	1	72	172	24	I	1	2	4	6	1	3	64	52	59	45	57	52	53	52	54	58	100	100	100	100	100	100	100	100	100	100
D11	D	1	80	168	28	I	1	2	3	6	1	3	59	62	74	70	51	52	55	54	56	60	100	100	100	100	100	100	100	100	100	100
D12	D	2	70	158	28	I	1	2	3	5.5	1	3	80	73	65	73	60	52	52	54	54	56	100	100	100	100	100	100	100	100	100	100
D13	D	1	50	148	23	I	1	2	3	5.5	1	3	76	78	74	70	70	68	68	70	68	70	100	100	100	100	100	100	100	100	100	100
D14	D	1	79	167	28	I	1	1	4	5.5	1	3	78	68	66	56	58	58	56	58	60	60	100	100	100	100	100	100	100	100	100	100
D15	D	1	50	163	19	I	1	2	3	6.5	2	2.5	75	80	69	68	54	79	70	75	72	70	99	99	100	100	98	100	98	100	98	98
D16	D	2	56	156	23	II	1	1	3	6.5	2	3	77	77	73	72	72	70	72	70	72	74	100	100	100	100	100	100	100	100	100	100
D17	D	1	75	169	24	I	1	2	3	5.5	1	3	64	60	62	59	58	62	61	60	60	58	100	100	100	100	100	100	100	100	100	100
D18	D	1	80	178	25	I	1	2	4	6	1	3	57	66	62	68	60	66	65	62	70	72	100	100	100	100	100	100	100	100	100	100
D19	D	1	75	166	27	I	1	2	3	6	1	2.5	78	82	88	83	66	65	68	62	63	63	100	100	100	100	100	100	100	100	100	100

SL. NO.	0- SBP (mins)	1 SBP (mins)	3 SBP (mins)	6 SBP (mins)	9 SBP (mins)	12 SBP (mins)	15 SBP (mins)	20 SBP (mins)	25 SBP (mins)	30 SBP(mins)	0-MBP (mins)	1 MBP (mins)	3MBP (mins)	6 MBP (mins)	9 MBP(mins)	12 MBP(mins)	15 MBP(mins)	20 MBP(mins)	25 MBP(mins)	30 MBP(mins)	0-DBP (mins)	1 DBP(mins)	3 DBP(mins)	6 DBP(mins)	9 DBP(mins)	12 DBP(mins)	15 DBP (mins)	20 DBP(mins)	25 DBP(mins)	30 DBP (mins)
D1	165	153	151	153	157	157	152	119	120	120	103	111	111	109	111	112	105	87	95	95	85	100	101	80	82	82	73	67	80	80
D2	120	116	98	92	101	102	120	120	122	122	78	75	66	61	68	70	78	78	78	78	65	64	58	48	52	54	64	64	64	64
D3	128	134	132	146	127	112	134	124	116	116	96	99	98	107	94	84	67	86	86	83	86	89	88	94	84	67	86	63	62	63
D4	135	138	153	150	156	122	114	134	135	138	104	101	103	104	117	98	90	110	104	100	97	88	87	89	104	83	76	97	97	88
D5	162	125	121	144	138	110	114	116	110	110	101	89	84	90	91	75	82	82	78	78	80	80	72	70	80	56	64	64	60	60
D6	133	124	116	116	115	110	128	120	115	117	90	86	83	84	83	81	89	82	74	78	65	63	62	63	63	63	69	61	55	59
D7	150	120	118	110	117	112	110	110	118	112	104	83	81	88	96	91	90	88	96	90	104	83	80	81	74	82	76	76	82	76
D8	136	130	120	136	130	126	124	126	130	126	100	94	89	92	99	97	99	95	99	97	84	76	74	70	84	82	86	80	84	82
D9	144	154	114	136	126	136	124	138	144	134	119	118	110	100	99	108	99	104	104	98	112	108	108	78	81	90	80	80	78	80
D10	148	148	162	122	142	125	125	122	124	122	95	92	85	84	83	94	94	94	84	84	80	75	102	58	50	72	72	58	72	58
D11	130	126	128	128	136	124	128	128	136	124	94	89	93	97	98	90	93	97	98	90	72	70	70	80	72	70	70	80	72	70
D12	145	148	132	136	136	136	148	132	136	136	105	102	93	103	102	98	104	92	103	102	94	89	80	94	92	88	88	80	94	92
D13	102	102	126	116	110	120	112	126	116	110	67	75	83	76	73	79	73	82	76	74	49	57	59	55	53	56	53	59	56	54
D14	110	118	123	97	109	107	109	110	118	124	84	90	92	75	84	84	84	84	90	92	70	75	73	64	71	72	71	70	75	73
D15	127	122	124	140	145	138	101	126	122	124	97	84	87	109	107	107	78	97	84	88	89	93	95	99	96	90	64	89	93	95
D16	137	148	146	143	141	142	141	136	146	142	103	108	108	106	106	106	106	102	108	106	79	82	82	83	82	83	82	82	82	83
D17	118	143	112	130	125	102	104	102	102	104	89	109	81	96	88	76	78	76	76	78	80	97	71	84	76	69	65	69	69	65
D18	131	140	135	140	137	137	135	130	130	130	92	97	94	97	92	88	95	92	92	92	81	84	83	84	79	82	82	80	81	81
D19	130	122	119	121	115	100	116	116	116	120	89	91	84	78	76	84	94	94	94	84	78	81	72	56	54	54	76	76	76	74

SL. NO.	0- BIS (mins)	1 BIS (mins)	3BIS (mins)	6 BIS (mins)	9 BIS(mins)	12 BIS (mins)	15 BIS(mins)	20 BIS (mins)	25 BIS (mins)	30 BIS (mins)	0- OAA/S (mins)	1 OAA/S (mins)	3 OAA/S (mins)	6 OAA/S(mins)	9 OAA/S (mins)	12 OAA/S (mins)	15 OAA/S (mins)	20 OAA/S(mins)	25 OAA/S(mins)	30 OAA/S (mins)	Cough severity Total	Anesthesia Quality	VC Relaxation	ETT Tolerance	Total Intubation Score	Total Infusion Time	Total LIGNO DOSE	Total PROPOFOL (mg)	Total FENTANYL (mcg)	Total DEXMED (mcg)	Intubation Time(sec)	Time to Achieve BIS< 7	Add Manoevers Req	Intubation Attempts	Complications.	Treatment	Post op Discomfort	post of Recall
D1	100	98	96	84	78	72	70	70	50	50	5	5	5	4	3	2	2	2	1	1	2	2	1	2	5	15	500	0	0	100	48	13	2	2	1	1	1	2
D2	98	96	82	78	70	68	56	55	51	50	5	5	3	2	2	1	1	1	1	1	1	2	2	4	8	10	300	0	0	100	8	9	2	1	1	1	2	2
D3	97	97	92	80	70	70	60	55	51	50	5	5	4	3	2	2	1	1	1	1	2	2	2	2	6	10	450	0	0	120	6	9	2	1	2	2	2	2
D4	98	96	92	84	70	68	56	52	50	50	5	4	4	3	2	2	1	1	1	1	1	2	2	4	8	9	250	0	0	50	6	8	2	1	1	1	2	2
D5	98	96	90	84	72	70	48	52	50	50	5	5	4	3	2	2	1	1	1	1	1	2	2	4	8	10	360	0	0	90	30	9	2	1	1	1	2	2
D6	98	98	97	84	80	74	70	58	54	52	5	5	5	3	2	2	2	1	1	1	2	2	2	2	6	10	400	0	0	100	40	14	2	1	1	1	2	2
D7	98	96	90	84	80	70	68	48	52	50	5	5	4	3	3	2	1	1	1	1	1	2	2	4	8	12	400	0	0	90	10	11	1	1	1	1	2	2
D8	100	97	97	94	86	80	72	70	65	52	5	5	5	4	4	3	3	2	1	1	3	2	1	2	5	15	500	0	0	80	15	16	2	1	1	1	2	2
D9	98	96	94	86	82	70	70	60	58	52	5	5	4	4	3	2	2	1	1	1	1	2	2	4	8	10	400	0	0	70	8	11	2	1	1	1	2	2
D10	100	98	98	92	86	78	70	60	54	56	5	5	5	4	3	3	2	1	1	1	2	2	2	4	8	14	300	0	0	100	30	14	2	1	2	1	2	2
D11	98	97	93	88	78	70	60	56	55	54	5	5	4	3	3	2	1	1	1	1	2	2	1	2	5	11	400	0	0	100	90	11	2	1	1	1	1	2
D12	98	98	92	84	78	70	60	55	52	48	5	5	4	3	3	2	1	1	1	1	2	2	2	2	6	15	120	0	0	75	45	14	2	1	1	1	2	2
D13	97	97	97	94	84	71	70	60	54	56	5	5	5	4	3	2	2	1	1	1	2	2	2	4	8	12	200	0	0	60	40	10	2	1	1	1	2	2
D14	98	98	97	96	84	76	70	60	55	56	5	5	5	5	4	3	2	1	1	1	1	2	2	4	8	15	160	0	0	75	30	15	2	1	1	1	2	2
D15	100	96	94	89	80	74	70	60	48	55	5	5	4	3	2	2	1	1	1	1	1	2	2	4	8	11	260	0	0	75	35	13	1	1	1	1	2	2
D16	97	94	90	84	78	70	70	60	54	54	5	5	4	4	3	3	3	2	1	1	1	2	2	4	8	10	400	0	0	60	45	9	2	1	1	1	2	2
D17	100	97	93	82	75	70	60	58	54	52	5	5	4	4	3	2	1	1	1	1	1	2	2	4	8	11	350	0	0	75	20	11	2	1	1	1	2	2
D18	100	98	95	84	78	72	70	60	54	58	5	5	5	4	3	2	2	1	1	1	1	2	2	4	8	15	250	0	0	80	10	15	2	1	1	1	2	2
D19	100	96	90	80	74	70	58	52	55	53	5	5	4	3	2	2	1	1	1	1	1	2	2	2	6	15	300	0	0	90	12	14	2	1	1	1	2	2

SL. NO.	Groups	Sex(M=1, F=2)	Weight	Height	BMI	ASA GRADE	ADA	C Spine Disease/AAD	MMP	TMD	Neck Extension <80^0	Mouth Opening	0-HR (mins)	1 HR (mins)	3 HR (mins)	6 HR (mins)	9 HR (mins)	12 HR (mins)	15 HR (mins)	20 HR (mins)	25 HR (mins)	30 HR (mins)	0-SpO2 (mins)	1 SpO2 (mins)	3 SpO2 (mins)	6 SpO2 (mins)	9 (mins)SpO2	12 SpO2 (mins)	15 SpO2 (mins)	20 SpO2 (mins)	25 SpO2 (mins)	30 SpO2 (mins)
PF1	PF	1	50	150	22	I	1	2	3	5.5	1	2.5	82	78	70	71	82	75	70	70	70	70	100	100	100	100	100	100	100	100	100	100
PF2	PF	2	56	150	25	I	1	2	3	5.5	1	3	89	97	86	63	70	79	89	90	88	82	100	100	100	100	100	100	100	100	100	100
PF3	PF	2	60	151	26	I	1	2	3	5.5	1	3	61	68	62	60	58	54	52	68	64	65	100	100	100	100	100	100	100	100	100	100
PF4	PF	2	70	169	25	I	1	1	3	6.5	1	3	65	66	64	63	65	67	68	66	68	67	100	100	100	100	100	100	100	100	100	100
PF5	PF	2	50	154	21	I	1	2	3	6	2	3	89	97	86	63	70	79	89	90	88	82	100	100	100	100	100	100	100	100	100	100
PF6	PF	1	75	162	29	I	1	1	4	6	1	3	68	69	68	74	70	70	74	68	67	69	100	100	100	100	100	100	100	100	100	100
PF7	PF	2	50	152	22	I	1	1	4	6	1	3	56	54	52	56	64	66	68	66	64	64	100	100	100	99	99	99	99	99	99	99
PF8	PF	1	50	154	21	I	1	2	4	5.5	1	2	110	118	120	116	100	100	92	88	86	88	100	100	100	100	95	100	100	100	100	100
PF9	PF	2	60	155	25	I	1	1	3	6.5	1	2.5	100	100	100	96	96	94	86	84	80	80	100	100	100	100	100	100	100	100	100	100
PF10	PF	1	70	167	25	I	1	2	3	6	1	3	63	72	69	78	71	65	69	82	74	62	100	100	100	100	100	100	100	100	100	100
PF11	PF	1	54	155	22	II	1	1	4	6	1	3	57	86	92	96	95	96	87	77	78	78	100	100	100	100	100	100	100	100	100	100
PF12	PF	1	50	155	21	II	1	1	4	6	1	3	68	66	64	56	58	62	64	66	60	62	100	100	100	100	100	100	100	100	100	100
PF13	PF	1	70	158	28	II	1	2	4	6	1	3	56	58	62	72	79	72	61	60	60	58	100	100	100	100	100	100	100	100	100	100
PF14	PF	1	75	174	25	I	1	2	3	6.8	2	3	65	65	61	60	59	59	61	60	58	58	100	100	95	100	100	100	100	100	100	100
PF15	PF	1	66	163	29	II	1	2	3	6.5	2	3	68	67	66	67	78	67	69	72	72	69	100	100	100	100	100	100	100	100	100	100
PF 16	PF	1	70	162	27	I	1	2	4	6	1	3	90	97	86	63	72	79	88	90	89	82	100	100	100	100	100	100	100	100	100	100
PF17	PF	1	75	164	28	II	1	1	4	6	1	3	61	68	62	60	58	54	52	68	64	65	100	100	100	100	100	100	100	100	100	100
PF18	PF	1	75	158	30	I	1	2	3	6	1	3	64	58	62	72	79	72	61	60	60	58	100	100	100	100	100	100	100	100	100	100
PF19	PF	2	70	150	31	I	1	2	4	5.5	1	3	90	100	100	96	92	90	86	84	80	80	100	100	100	100	100	100	100	100	100	100
PF20	PF	2	65	158	26	I	1	2	4	6.6	2	2.5	70	65	64	62	64	72	70	68	68	70	100	100	100	100	100	100	100	100	100	100

SL. NO.	0- SBP (mins)	1 SBP (mins)	3 SBP (mins)	6 SBP (mins)	9 SBP (mins)	12 SBP (mins)	15 SBP (mins)	20 SBP (mins)	25 SBP (mins)	30 SBP(mins)	0-MBP (mins)	1 MBP (mins)	3MBP (mins)	6 MBP (mins)	9 MBP(mins)	12 MBP(mins)	15 MBP(mins)	20 MBP(mins)	25 MBP(mins)	30 MBP(mins)	0-DBP (mins)	1 DBP(mins)	3 DBP(mins)	6 DBP(mins)	9 DBP(mins)	12 DBP(mins)	15 DBP (mins)	20 DBP(mins)	25 DBP(mins)	30 DBP (mins)
PF1	101	92	107	120	122	116	116	112	110	106	75	74	85	91	92	88	87	83	81	78	68	59	68	70	71	88	87	83	81	78
PF2	130	122	119	121	115	100	116	116	116	120	89	91	84	78	76	84	94	94	94	84	78	81	72	56	54	54	76	76	76	74
PF3	120	116	98	92	101	102	120	120	122	122	78	75	66	61	68	70	78	78	78	78	65	64	58	48	52	54	64	64	64	64
PF4	118	134	126	117	128	130	136	134	126	118	92	103	95	76	87	96	103	103	95	76	76	82	75	64	74	78	82	82	76	64
PF5	130	122	119	121	115	100	116	116	116	120	89	91	84	78	76	84	94	94	94	84	78	81	72	56	54	54	76	76	76	74
PF6	118	125	122	127	120	110	112	110	112	110	78	81	95	92	84	78	72	78	72	110	67	78	89	81	73	69	60	69	60	69
PF7	135	133	132	134	130	133	126	124	124	126	102	100	100	101	102	100	90	89	89	90	92	90	91	90	95	92	78	78	79	79
PF8	140	150	152	147	97	118	114	117	113	120	104	99	102	100	63	98	76	97	76	80	100	100	94	86	52	90	66	90	97	68
PF9	130	124	110	122	120	120	110	110	120	122	93	90	86	84	82	84	80	80	84	84	70	70	64	64	62	60	62	60	60	64
PF10	137	130	102	96	136	124	120	113	107	112	102	94	78	72	106	95	93	84	80	84	91	79	72	59	90	98	76	68	64	68
PF11	131	140	135	140	137	137	135	130	130	130	92	97	94	97	92	88	95	92	92	92	81	84	83	84	79	82	82	80	81	81
PF12	133	110	102	108	129	103	108	110	102	102	96	83	82	82	98	81	82	83	81	81	84	76	74	67	79	67	67	76	74	74
PF13	118	143	112	130	125	102	104	102	102	104	89	109	81	96	88	76	78	76	76	78	80	97	71	84	76	69	65	69	69	65
PF14	135	133	132	134	130	133	126	124	124	126	102	100	100	101	102	100	90	89	89	90	92	90	91	90	95	92	78	78	79	79
PF15	163	166	165	144	144	121	122	121	122	122	104	103	103	96	95	88	81	88	81	80	86	90	84	80	80	79	72	79	71	71
PF 16	130	122	119	121	115	100	116	116	116	120	89	91	84	78	76	84	94	94	94	84	78	81	72	56	54	54	76	76	76	74
PF17	120	116	98	92	101	102	120	120	122	122	78	75	66	61	68	70	78	78	78	78	65	64	58	48	52	54	64	64	64	64
PF18	118	143	112	130	125	102	104	102	102	104	89	109	81	96	88	76	78	76	76	78	80	97	71	84	76	69	65	69	69	65
PF19	130	124	110	122	120	120	110	110	120	122	93	90	86	84	82	84	80	80	84	84	70	70	64	64	62	60	62	60	60	64
PF20	128	134	132	146	127	112	134	124	116	116	96	99	98	107	94	84	67	86	86	83	86	89	88	94	84	67	86	63	62	63

SL. NO.	0- BIS (mins)	1 BIS (mins)	3BIS (mins)	6 BIS (mins)	9 BIS(mins)	12 BIS (mins)	15 BIS(mins)	20 BIS (mins)	25 BIS (mins)	30 BIS (mins)	0- OAA/S (mins)	1 OAA/S (mins)	3 OAA/S (mins)	6 OAA/S(mins)	9 OAA/S (mins)	12 OAA/S (mins)	15 OAA/S (mins)	20 OAA/S(mins)	25 OAA/S(mins)	30 OAA/S (mins)	Cough severity Total	Anesthesia Quality	VC Relaxation	ETT Tolerance	Total Intubation Score	Total Infusion Time	Total LIGNO DOSE	Total PROPOFOL (mg)	Total FENTANYL (mcg)	Total DEXMED (mcg)	Intubation Time(sec)	Time to Achieve BIS< 7	Add Manoevers Req	Intubation Attempts	Complications.	Treatment	Post op Discomfort	post of Recall
PF1	96	94	90	80	70	60	56	55	52	50	5	4	3	3	2	1	1	1	1	1	1	2	2	4	8	8	350	60	60	0	30	7	2	1	1	1	2	2
PF2	98	96	88	78	70	56	58	52	55	53	5	5	4	3	2	1	1	1	1	1	1	2	2	4	8	8	300	70	70	0	8	7	2	1	1	1	2	2
PF3	98	96	82	78	70	68	56	55	51	50	5	5	3	2	2	1	1	1	1	1	1	2	2	4	8	10	200	80	80	0	8	8	2	1	1	1	2	2
PF4	98	97	92	86	70	70	60	55	52	50	5	5	4	2	2	2	1	1	1	1	1	2	2	4	8	8	400	80	80	0	5	9	2	1	1	1	2	2
PF5	98	96	90	84	70	70	60	52	55	53	5	5	4	3	2	2	1	1	1	1	2	2	2	4	8	10	300	65	50	0	5	9	2	1	1	1	2	2
PF6	98	98	94	86	78	72	70	60	55	52	5	5	5	4	4	3	3	1	1	1	3	2	2	2	6	12	350	100	100	0	45	11	1	2	1	1	2	2
PF7	100	96	94	86	80	70	64	58	52	52	5	5	4	3	3	2	1	1	1	1	1	2	2	4	8	8	300	60	60	0	10	10	2	1	1	1	2	2
PF8	100	100	94	86	74	70	60	52	56	54	5	5	4	3	3	2	1	1	1	1	2	2	2	4	8	10	200	70	70	0	10	10	1	1	2	2	2	2
PF9	98	98	94	89	74	70	58	56	56	52	5	5	5	4	3	2	1	1	1	1	1	2	2	4	8	10	160	100	100	0	16	11	2	1	1	1	2	2
PF10	97	97	97	90	86	76	70	66	50	50	5	5	5	4	3	3	2	1	1	1	2	2	2	4	8	12	300	100	100	0	20	12	2	1	1	1	2	2
PF11	100	96	95	79	75	73	70	60	54	58	5	5	5	4	3	2	2	1	1	1	3	2	2	2	6	15	180	80	80	0	10	15	2	1	1	1	2	2
PF12	99	99	96	86	78	68	71	50	56	54	5	5	4	4	3	3	3	1	1	1	2	2	2	4	8	12	200	80	80	0	22	10	2	1	1	1	2	2
PF13	100	98	94	84	76	70	70	60	54	52	5	5	4	4	3	3	3	1	1	1	1	2	2	4	8	13	300	140	70	0	30	11	2	1	1	1	2	2
PF14	100	98	90	86	70	70	60	50	50	50	5	4	3	3	2	2	1	1	1	1	2	2	2	4	8	10	250	120	75	0	30	8	1	1	2	2	2	2
PF15	99	98	96	90	86	80	70	50	50	50	5	5	5	4	3	3	3	1	1	1	1	2	2	4	8	18	400	120	70	0	20	15	2	1	1	1	2	2
PF 16	98	94	89	80	70	60	60	52	55	53	5	5	4	3	2	1	1	1	1	1	1	2	2	4	8	10	300	75	75	0	5	9	2	1	1	1	2	2
PF17	100	96	82	78	70	68	56	55	51	50	5	5	3	2	2	1	1	1	1	1	1	2	2	4	8	9	300	75	75	0	8	9	2	1	1	1	2	2
PF18	100	98	92	80	74	70	60	58	54	52	5	5	4	4	3	2	1	1	1	1	1	2	2	4	8	11	300	90	90	0	20	11	2	1	1	1	2	2
PF19	98	97	92	86	72	70	58	56	56	52	5	5	4	3	2	2	1	1	1	1	1	2	2	4	8	10	160	75	75	0	14	9	2	1	1	1	2	2
PF20	97	96	90	80	70	60	60	55	51	50	5	5	4	3	2	1	1	1	1	1	1	2	2	4	8	9	250	70	70	0	6	9	2	1	1	1	2	2

Annexures: V

Plagiarism Check

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ORIGINALITY REPORT

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SIMILARITY INDEX