Comparison Of Propofol + Ketamine, Propofol And Dexmedetomidine Sedation In Children On Antiepileptic Therapy For Magnetic Resonance Imaging

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

by

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DECLARATION

I hereby declare that this thesis entitled **“Comparison of propofol + ketamine, propofol and dexmedetomidine sedation in children on antiepileptic therapy for magnetic resonance imaging”**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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This is to certify that this thesis entitled**"Comparison of propofol+ketamine, propofol and dexmedetomidine sedation in children on antiepileptic therapy for magnetic resonance imaging"** is a bonafide work of **Dr.N.V.VINOTH KUMAR,** 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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Introduction

INTRODUCTION

Epilepsy is the most common neurologic disorder in children with an incidence of approximately 4%. Upto 70% of patients diagnosed with epilepsy can be rendered seizure-free by currently available anti-epileptic drugs (AEDs) when administered as monotherapy.[1,2] Among old generation AEDs, phenobarbital is the most commonly used AED in pediatric population and is a prototypic P-450 enzyme inducer. It stimulates the activity of a variety of cytochrome P-450 (CYP- 450) enzymes, including CYP1A2, CYP2C9, CYP2C19, and CYP3A4, as well as glucuronyl transferases and UDP-glucuronosyltransferase (UGT).[2-4] These isoenzymes are also involved in the metabolism of more than 50% of all drugs including anesthetics.[5,6]

The clinical efficacy of concomitantly administered anesthetics that use the common metabolic pathway with phenobarbital might be reduced by an increase in distribution and clearance.[7] The rationale of the present study is the possible pharmacodynamic and kinetic alterations to the sedation regimen by the prior use of AED. It is not only the enzyme induction / inhibition by AEDs but other mechanisms such as alterations to the free drug level of sedatives due to protein binding, sedative side effect of the AED themselves both can interfere with sedation.[8-14,17]

Magnetic resonance imaging (MRI) is the preferred radiologic imaging technique for diagnosis and follow up of epilepsy. The important concern is the selection of sedative anesthetic agents for successful sedation during MRI procedures because of the potential drug interactions with AEDs. The selection would be arranged among the anesthetics that have anticonvulsant effects like thiopental, benzodiazepines, etomidate, ketamine, propofol, and inhalation anesthetics.[14,17] All of these anesthetic agents are also metabolized with cytochrome P-450 izoenzymes.[15] Thereby, the effective duration of sedation and the required amount of sedatives might increase when either of the anesthetic agents is co-administered with an AED. In clinical practice, anesthesiologists should keep in mind that additional sedative consumption for the sedation management of epileptic children might be required and the possibilities of short sleeping time should be considered for the children under antiepileptic therapy.[16] AED not only causes enzyme induction but also causes significant pharmacokinetic and pharmacodynamic interactions with sedatives and anesthetics because of following mechanisms- hepatic enzyme inhibition, alterations in protein binding thereby altering the free plasma concentration and in addition the sedative side effect of their own.[8-14,17]

There is a general paucity of information regarding the effects of prior AED use on anesthesia. It has been shown that patients on AEDs have resistance to the action of neuromuscular blocking drugs and they require higher doses of fentanyl (opioid) to maintain comparable depth of anesthesia. The cause or causes for this resistance to neuromuscular blocking drugs and opioids are not known.[13] However the reasons that are suggested include changes in the number of receptors, alterations to drug metabolism, alterations in the endogenous neurotransmitters and alterations to the free drug levels due to protein binding. Propofol is discussed to be the best of all intravenous (i.v) drugs for paediatric sedation. However, its narrow therapeutic window and the vulnerability of children to the sedative effects may lead quickly to unintended deep anaesthesia with loss of protective reflexes even after small dosage increase. Thus, an appropriate low dosage of propofol, which nevertheless ensures sufficient sleep for successful MRI completion, would probably minimize these adverse events.[18] The ideal sedation protocol is one that has an easy route of administration, with little or no adverse reactions, and allows for a quick, complete recovery. In our institute, we achieve sedation of these patients by propofol, ketamine, midazolam, and dexmedetomidine either alone or combination of drugs.

Phenobarbital, phenytoin, and carbamazepine are hepatic enzyme inducers, whereas phenytoin, benzodiazepine, and valproic acid are highly protein bound. Valproic acid is an enzyme inhibitor. In addition, AEDs have many adverse effects, many of which are unique to each specific drug. However, the adverse effect which is shared by a significant number of AEDs includes somnolence and sedation. Therefore this study was designed to compare the efficacy, incidence of adverse events, cardiovascular profile, respiratory profile and recovery profile following MRI sedation by various sedation techniques commonly followed in our institute in epileptic patients on anti epileptic therapy.

Basic science
&
Review of literature

Review of literature

The concept of intravenous (IV) anesthesia has evolved from primarily induction of anesthesia to total IV anesthesia (TIVA). TIVA has assumed increasing importance for therapeutic, as well as diagnostic, procedures in both adults and children. This change has been a result of the development of rapid, short-acting IV hypnotic, analgesic, and muscle relaxant drugs; the availability of pharmacokinetic and dynamic-based IV delivery systems; and the development ofthe electroencephalogram (EEG) base cerebral monitor, which measures the hypnotic component of the anesthetic state.

Following its introduction into clinical practice, thiopental quickly became the gold standard of IV anesthetics against which all the newer IV drugs were compared. Many different hypnotic drugs are currently available for use during IV anesthesia. However, the “ideal” IV anesthetic has not yet been developed. The physical and pharmacologic properties that an ideal IV anesthetic would possess include the following:

1. Drug compatibility and stability in solution.

2. Lack of pain on injection, veno-irritation, or local tissue damage from extravasation.

3. Low potential to release histamine or precipitate hypersensitivity reactions.

4. Rapid and smooth onset of hypnotic action without excitatory activity.

5. Rapid metabolism to pharmacologically inactive metabolites.

6. A steep dose-response relationship to enhance titratability and minimize accumulation.

7. Lack of acute cardiovascular and respiratory depression.

8. Decreases in cerebral metabolism and intracranial pressure.

9. Rapid and smooth return of consciousness and cognitive skills with residual analgesia.

10. Absence of postoperative nausea and vomiting, amnesia, psychomimetic reactions, dizziness,headache, or prolonged sedation ("hangover").[21]

Propofol:

Propofol (2,6-disopropylphenol), an alkylphenol compound, is virtually insoluble in aqueoussolution. [21] The initial cremophor EL formulation of propofol was withdrawn from clinical testingbecause of the high incidence of anaphylactic reactions. Subsequently, propofol (10 mg/mL) wasreintroduced as an egg lecithin emulsion formulation (Diprivan), consisting of 10% soybean oil,2.25% glycerol, and 1.2% egg phosphatide. Pain on injection occurs in 32 to 67% of patients when injected into small hand veins but can be minimized by injection into larger veins and byprior administration of either lidocaine or a potent opioid analgesic (e.g., fentanyl or remifentanil). A wide variety of drugs have been used for reducing pain on injection of propofol(e.g., metoprolol, granisetron, dolasetron, and even thiopental). Diluting the formulation with additional solvent (Intralipid) or changing the lipid carrier (Lipofundin) also reduced propofol induced injection pain, probably because of a decrease in the concentration of free propofol in the acqueous phase of the emulsion. A new propofol formulation with sodium metabisulphite (insteadof disodium edetate) as an antimicrobial has recently been shown to be associated with less severe pain on injection. Although the presence of the metabisulphite has raised concerns regarding its use in sulphite-allergic patients, this does not appear to be a clinically important problem. Of interest, a 2% formulation is available for long-term sedation to decrease the fluid volume infused as well as the lipid load. Recently, a lower-lipid formulation of propofol (Ampofol) has been introduced into clinical practice for both general anesthesia and sedation. The increased "free" fraction of propofol leads to increased pain when it is injected into small veins. Therefore, it is important to add lidocaine to the Ampofol formulation to minimize the pain on injection. A new water-soluble prodrug of propofol (Aquavan) is rapidly hydrolized in the circulation to release propofol. It has a slower onset than propofol but a similar recovery profile.Although Aquavan does not produce injection site discomfort, a burning perineal sensation hasbeen reported.

Propofol's pharmacokinetics has been studied using single bolus dosing and continuous infusions.In studies using a two-compartment kinetic model, the initial distribution half-life is 2 to 8minutes and the elimination half-life is 1 to 3 hours. Using a three-compartment model, the initial and slow distribution half-life values are 1 to 8 minutes and 30 to 70 minutes, respectively. The elimination half-life depends largely on the sampling time after discontinuing the administration of propofol and ranges from 2 to 24 hours. This long elimination half-life is indicative of the existence of a poorly perfused compartment from which propofol slowly diffuses back into the central compartment. Propofol is rapidly cleared from the central compartment by hepatic metabolism and the context-sensitive half-life for propofol infusions up to 8 hours is less than 40minutes. Propofol is rapidly and extensively metabolized to inactive, water-soluble sulphate and glucuronic acid metabolites, which are eliminated by the kidneys. Propofol's clearance rate (1.5 to2.2 l/min) exceeds hepatic blood flow, suggesting that an extrahepatic route of elimination (lungs) also contributes to its clearance. Nevertheless, changes in liver blood flow would be expected to produce marked alterations in propofol's clearance rate. Surprisingly, few changes in propofol'spharmacokinetics have been reported in the presence of hepatic or renal disease.

The induction dose of propofol in healthy adults is 1.5 to 2.5 mg/kg, with blood levels of 2 to 6μg/mL producing unconsciousness depending on the concomitant medications (e.g., opioidanalgesics), the patient's age and physical status, and the extent of the surgical stimulation. Inone of the first reports describing the use of propofol for induction and maintenance of anesthesiawith nitrous oxide, an average infusion rate of 120 μg/kg/min was required. The recommended maintenance infusion rate of propofol varies between 100 and 200 μg/kg/min for hypnosis and 25to 75 μg/kg/min for sedation. Awakening typically occurs at plasma propofol concentrations of 1 to1.5 μg/mL.Because a 50% decrease in the plasma propofol concentration is usually required for awakening, emergence following anesthesia is rapid even following prolonged infusions.

Analogous to the barbiturates, children require higher induction and maintenance doses of propofol on a mg/kg basis as a result of their larger central distribution volume and higher clearance rate. Elderly and patients in poor health require lower induction and maintenance doses of propofol as a result of their smaller central distribution volume and decreased clearance rate.

Although subhypnotic doses of propofol produce sedation and amnesia,awareness has been reported even at higher infusion rates when propofol is used as the sole anesthetic.Propofol often produces a subjective feeling of well-being and even euphoria, and may have some abuse potential as a result of these effects.Propofol possesses dose-dependent effects on thalamocortical transfer of nociceptiveinformation. However, pain-evoked cortical activity remains intact after loss of consciousness.

Propofol decreases CMRO2 and CBF, as well as ICP. However, when larger doses are administered, the marked depressant effect on systemic arterial pressure can significantly decrease CPP. Cerebrovascular autoregulation in response to changes in systemic arterial pressure and reactivity of the cerebral blood flow to changes in carbon dioxide tension are not affected by propofol. Evidence for a possible neuroprotective effect has been reported in in vitro preparations,and the use of propofol to produce EEG burst suppression has been proposed as a method for providingneuroprotection during aneurysm surgery. Its neuroprotective effect may at least partially be related to the antioxidant potential of propofol's phenol ring structure, which may actas a free-radical scavenger, decreasing free-radical induced lipid peroxidation. A recent study reported that this antioxidant activity may offer many advantages in preventing the hypoperfusion/reperfusion phenomenon that can occur during major laproscopic surgery.

Although TIVA with propofol and an opioid analgesic is a safe and effective alternative to standard inhalation techniques (i.e., volatile anesthetic with nitrous oxide) for maintenance of anesthesia,concerns have been raised regarding the cost-effectiveness of this technique.

Propofol produces cortical EEG changes that are similar to thiopental. However, sedative doses of propofol increase β-wave activity analogous to the benzodiazepines. Induction of anesthesia with propofol is occasionally accompanied by excitatory motor activity (so-called nonepileptic myoclonia). In a study involving patients without a history of seizure disorders, excitatory movements following propofol were not associated with EEG seizure activity.Propofol appears to possess profound anticonvulsant properties.Propofol has been reported to decrease spike activity in patients with cortical electrodes implanted for resection of epileptogenic foci and has been used successfully to terminate status epilepticus. The duration of motor and EEG seizure activity following electroconvulsive therapy is significantly shorter with propofol than with other IVanesthetics. Propofol produces a decrease in the early components of somatosensory and motor evoked potentials but does not influence the early components of the auditory evoked potentials.

Propofol produces dose-dependent respiratory depression, with apnea occurring in 25 to 35% of patients after a typical induction dose. A maintenance infusion of propofol decreases tidal volume and increases respiratory rate. The ventilatory response to carbon dioxide and hypoxia is also significantly decreased by propofol. Propofol can produce bronchodilation in patients with chronic obstructive pulmonary disease and does not inhibit hypoxic pulmonary vasoconstriction.

Propofol's cardiovascular depressant effects are generally considered to be more profound than those of thiopental. Both direct myocardial depressant effects and decreased systemic vascular resistance have been implemented as important factors in producing cardiovascular depression.Direct myocardial depression and peripheral vasodilation are dose and concentration dependent.In addition to arterial vasodilation, propofol produces venodilation (due both to a reduction in sympathetic activity and to a direct effect on the vascular smooth muscle), which further contributes to its hypotensive effect. The relaxation of the vascular smooth muscle may be because of an effect on intracellular calcium mobilization or because of an increase in the production of nitric oxide. Experiments in isolated myocardium suggest that the negative inotropiceffect of propofol results from a decrease in intracellular calcium availability secondary to inhibition of transsarcolemmal calcium influx.

Propofol also alters the baroreflex mechanism, resulting in a smaller increase in heart rate for a given decrease in arterial pressure. The smaller increase in heart rate with propofol may accountfor the larger decrease in arterial pressure than with an equipotent dose of thiopental. Recent studies suggest that induction of anesthesia with propofol attenuates desflurane-mediated sympathetic activation. Age enhances the cardio depressant response to propofol and a reduced

dosage is required in the elderly. Patients with limited cardiac reserve seem to tolerate the cardiac depression and systemic vasodilation produced by carefully titrated doses of propofol and maintenance infusions are increasingly used at the end of cardiac surgery when early extubation is desired.

Propofol appears to possess antiemetic properties that contribute to a lower incidence of emetic sequelae after general anesthesia. In fact, subanesthetic doses of propofol (10 to 20mg) have also been successfully used to treat nausea and emesis in the early postoperative period. The postulated mechanisms include antidopaminergic activity, depressant effect on the chemoreceptor trigger zone and vagal nuclei, decreased release of glutamate and aspartate in the olfactory cortex, and reduction of serotonin concentrations in the area postrema. Interestingly,propofol also decreases the pruritus produced by spinal opioids.

Propofol does not trigger malignant hyperthermia (MH) and may be considered the induction agent of choice in MH-susceptible patients. The use of propofol infusions for sedation in the pediatric intensive care unit has been linked to several deaths following prolonged administration because of lipid accumulation and hypotension. Although clinical doses of propofol do not affect cortisolsynthesis or the response to adrenocorticotropic hormone (ACTH) stimulation, propofol has been reported to inhibit phagocytosis and killing of bacteria in vitro and to reduce proliferative responses when added to lymphocytes from critically ill patients. Because fat emulsions are known to support the growth of microorganisms, contamination can occur as a result of dilution or fractionated use.

Ketamine:

Ketamine (Ketalar or Ketaject) is an arylcyclohexylamine that is structurally related to phencyclidine.[21] Ketamine is a water-soluble compound with a pKa of 7.5 and is available in 1%, 5%, and 10% aqueous solutions. The ketamine molecule contains a chiral center producing two optical isomers. The S(+) isomer of ketamine possesses more potent anesthetic and analgesic properties despite having a similar pharmacokinetic and pharmacodynamic profile as the racemicmixture (or the R[-] isomer). Although the S(+)-ketamine is approved for clinical use in Europe, the commonly used solution is a racemic mixture of the two isomers. Ketamine is extensively metabolized by hepatic microsomal cytochrome P-450 enzymes and its primary metabolite, norketamine, is one third to one fifth as potent as the parent compound. The metabolites of norketamine are excreted by the kidney as water-soluble hydroxylated andglucuronidated conjugates. Analogous to the barbiturates and propofol, ketamine has relatively short distribution and redistribution half-life values. Ketamine also has a high hepatic clearancerate (1 L/min) and a large distribution volume (3 L/kg), resulting in an elimination half-life of 2 to3 hours. The high hepatic extraction ratio suggests that alterations in hepatic blood flow can significantly influence ketamine's clearance rate.

Ketamine produces dose-dependent CNS depression leading to a so-called dissociative anesthetic state characterized by profound analgesia and amnesia, even though patients may be conscious and maintain protective reflexes. The proposed mechanism for this cataleptic state includes electrophysiologic inhibition of thalamocortical pathways and stimulation of the limbic system. Although it is most commonly administered parenterally, oral and intranasal administration of ketamine (6 mg/kg) hasbeen used for premedication of pediatric patients. Following benzodiazepine premedication,ketamine 1 to 2 mg/kg IV (or 4 to 8 mg/kg IM) can be used for induction of anesthesia. The duration of ketamine-induced anesthesia is in the range of 10 to 20 minutes after a single induction dose; however, recovery to full orientation may require an additional 60 to 90 minutes.

Emergence times are even longer following repeated bolus injections or a continuous infusion. S(+)-ketamine has a shorter recovery time compared with the racemic mixture. The therapeutic window for maintenance of unconsciousness with ketamine is between 0.6 and 2 mg/mL in adultsand between 0.8 and 4 mg/mL in children. Analgesic effects are evident at subanesthetic doses of 0.1 to 0.5 mg/kg IV and plasma concentrations of between 85 and 160 ng/mL. A low-dose infusionof 4 μg/kg/min IV was reported to result in equivalent postoperative analgesia as an IV morphine infusion of 2 mg/h.As a result of its NMDA-receptor blocking activity, it has been suggested that ketamine should be highly effective for preemptive analgesia and opioid-resistant chronic pain states. Unfortunately,a well-controlled study failed to demonstrate a preemptive effect when ketamine was administered prior to the surgical incision.

An important consideration in the use of ketamine anesthesia relates to the high incidence of psychomimetic reactions (namely, hallucinations, nightmares, altered short-term memory and cognition) during the early recovery period. The incidence of these reactions is dose dependent and can be reduced by coadministration of benzodiazepines, barbiturates, or propofol.

Ketaminehas been traditionally contraindicated for patients with increased ICP or reduced cerebral compliance because it increases CMRO2, CBF, and ICP.

However, there is recent evidence that IVinduction doses of ketamine actually increases ICP in traumatic–brain-injury patients during controlled ventilation with propofol sedation. Prior administration of thiopental or benzodiazepines can blunt ketamine-induced increases in CBF. Since ketamine has antagonistic activity at the NMDA receptor, it has been suggested that it possesses some inherent protective effects against brain ischemia. Nevertheless, ketamine can adversely affect neurologic outcome in the presence of brain ischemia despite its NMDA-receptor blocking activity.

Cortical EEG recordings following ketamine induction are characterized by the appearance of fast β activity (30to 40 Hz) followed by moderate-voltage θ activity, mixed with high-voltage δ waves recurring at 3to 4 second intervals. At higher dosages, ketamine produces a unique EEG burst-suppression pattern.

Although ketamine-induced myoclonic and seizure-like activity has been observed in normal (nonepileptic) patients, ketamine appears to possess anticonvulsant activity.

Recently, several have demonstrated the opioid-sparing effects of low-dose Ketamine (75 to 200mcg/kg) when administered as an adjuvant during anesthesia. Interestingly, small-dose ketamine has also been used in the treatment of severe depression in patients with chronic pain syndromes. However, ketamine can produce adverse effects when administered in the presence of tricyclic antidepressants because both drugs inhibit norepinephrine reuptake and could producesevere hypotension, heart failure, and/or myocardial ischemia.

Ketamine has well-characterized bronchodilatory activity. In the presence of active bronchospasm,ketamine is considered to be the IV induction agent of choice. Ketamine has been used in subanesthetic dosages to treat persistent bronchospasm in the operating room and ICU. It is also used in combination with midazolam to provide sedation and analgesia for asthmatic patients. In contrast to the other IV anesthetics, protective airway reflexes are more likely to be preserved with ketamine. However, it must be emphasized that the use of ketamine does not obviate theneed for tracheal intubation in the patient with a full stomach (because tracheal soiling has been reported in this situation). Ketamine causes minimal respiratory depression in clinically relevant doses and can facilitate the transition from mechanical to spontaneous ventilation after anesthesia. However, its ability to increase oral secretions can lead to laryngospasm during “light”anesthesia.Ketamine has prominent cardiovascular stimulating effects secondary to direct stimulation of the sympathetic nervous system. Ketamine is the only anesthetic that actually increases peripheral arteriolar resistance. As a result of its vasoconstrictive properties, ketamine can reduce the magnitude of redistribution hypothermia. Induction of anesthesia with ketamine often produces significant increases in arterial blood pressure and heart rate. Although the mechanism of the cardiovascular stimulation is not entirely clear, it appears to be centrally mediated. There is evidence to suggest that ketamine attenuates baroreceptor activity via an effect on NMDAreceptors in the nucleus tractus solitarius. Because of the increased cardiac work and myocardial oxygen consumption, ketamine negatively affects the balance between myocardial oxygen supplyand demand. Consequently, its use is not recommended in patients with severe coronary arterydisease. In contrast to the secondary cardiovascular stimulation, ketamine has intrinsic myocardial depressant properties that only become apparent in the seriously ill patient with depleted catecholamine reserves. Because ketamine can also increase pulmonary artery pressure, its use is contraindicated in adult patients with poor right ventricular reserve. Interestingly, the effect on the pulmonary vasculature seems to be attenuated in children.

The anesthetic and analgesic potency of S(+)-ketamine is three times greater than R(-)-ketamine and twice that of the racemic mixture , reflecting its fourfold greater affinity at the phencyclidine binding site on the NMDA receptor compared with the R(-) isomer. The therapeutic index of S(+)-ketamine is 2.5 times greater than both the R(-)and the racemic forms. In addition, hepatic biotransformation of S(+)-ketamine occurs 20% fasterthan that of the R(-)

enantiomer, contributing to shorter emergence times and a faster return of cognitive function. Both isomers produce similar cardiovascular stimulating effects and hormonal responses during surgery. Although the incidence of dreaming is similar with S(+)-ketamine and the racemic mixture, subjective mood and patient acceptance are higher with the S(+) isomer[6].

Dexmedetomidine:

The α2-adrenergic agonists are sub-classified into 3 groups: imidazolines, phenylethylamines,and oxalozepines.[22-96] Dexmedetomidine (Precedex®, Hospira Worldwide Inc, Lake Forest, IL) and clonidine are members of the imidazole subclass which exhibits a high ratio of specificity for the α2 versus the α1 receptor. Clonidine exhibits an α2 : α 1 specificity ratio of 200:1 while that ofdexmedetomidine is 1600:1, thereby making it a complete agonist at the α 2adrenergic receptor.Dexmedetomidine has a short half-life (2-3 hours vs. 12-24 hours for clonidine) and is commercially available for intravenous administration. Its physiologic effects are mediated via post-synaptic α 2-adrenergic receptors and activation of a pertussis toxin-sensitive guanine nucleotide regulatory protein (G protein) resulting in decreased adenylyl cyclase activity. A reduction of intracellular cyclic adenosine monophosphate (cAMP) and cAMP-dependent protein kinase activity results inthe dephosphorylation of ion channels. Alterations in ion channel function, ion translocation, andmembrane conductance lead to decreased neuronal activation and the clinical effects of sedation andanxiolysis. Centrally acting α 2-adrenergic agonists also activate receptors in the medullary vasomotor center reducing norepinephrine with a resultant central sympatholytic effect leading to decreased heart rate (HR) and blood pressure (BP). Central CNS stimulation of parasympatheticoutflow and inhibition of sympathetic outflow from the *locus cereleus*in the brainstem play a prominent role in the sedation and anxiolysis produced by these agents. Decreased noradrenergicoutput from the *locus cereleus*allows for increased firing of inhibitory neurons including gamma aminobutyric acid (GABA). Primary analgesic effects and potentiation of opioid-induced analgesia result from the activation of α 2-adrenergic receptors in the dorsal horn of the spinal cord and the inhibition of substance P release.

Pharmacokinetics:

In healthy adult volunteers, dexmedetomidine's pharmacokinetic profile includes a rapid distribution phase (distribution half-life of 6 minutes); an elimination half-life of 2 hours; and a steady-state volume of distribution of 118 liters. In the dosing range of 0.2 to 0.7 mcg/kg/hr deliveredvia continuous intravenous infusion for up to 24 hours, the pharmacokinetics are linear.Dexmedetomidine is 94% protein bound to serum albumin and α 1-glycoprotein. It undergoes hepatic metabolism with limited unchanged drug excreted in the urine or stool. Data regardingdexmedetomidine pharmacokinetics in the pediatric population have been similar to those reported in the adult population. Petroz GC et al. randomized 36 children, rangingin age from 2 to 12 years, to receive dexmedetomidine infused for 10 minutes at 2, 4 or 6 μg/kg/hr(0.33, 0.6 and 1 μg/kg). Using a two-compartment model, they reported no dose-dependentkinetics, protein binding of 92.6%, weight adjusted total body clearance of 13 mL/kg/min, a volume of distribution of the peripheral compartment of 1.0 liter/kg, and a terminal elimination half-life of1.8 hours. Rodarte et al. administered a continuous infusion in a dose ranging from 0.2-0.7 μg/kg/hrfor 8-24 hours to 10 children (0.3 to 7.9 years of age) following cardiac procedures (n=9) or craniofacial procedures (n=1). Using a two-compartment model, they reported a volume ofdistribution of 1.53 ± 0.37 liter/kg, clearance of 0.57 ± 0.14 liters/kg/hr (approximately 9.5mL/kg/min), and a terminal elimination half-life of 2.65 ± 0.88 hours. They commented that their data demonstrated that the pharmacokinetics of dexmedetomidine in children were predictableand consistent with results similar to that reported in adults. The final pharmacokinetic study in children includes infants, ranging in age from 1 to 24 months, following surgery for congenital heart disease. The authors reported a median clearance of 27.2 mL/kg/min, peripheral volume of distribution of 2.5 liters/kg, and a terminal elimination half-life of 83 minutes. They concluded that infants appear to clear dexmedetomidine more quickly than adults or older children. Given is dependence on hepatic metabolism, a prolonged half-life and delayed elimination has been noted in adults with hepatic dysfunction. Additionally, prolonged sedation has been noted in patients with renal insufficiency which is postulated to result from an increased free fraction related to alterations in protein binding.

Applications of dexmedetomidine in the Pediatric Population:

The first two reports in the literature regarding the use of dexmedetomidine in pediatricpatients were retrospective case series. The first of these described the use of dexmedetomidine in 4 pediatric patients in various clinical scenarios including sedation during mechanical ventilation,combined with remifentanil as an adjunct for controlled hypotension during posterior spinal fusion,and for procedural-sedation. Dexmedetomidine was effective in the first 2 scenarios; however, it was ineffective as the sole agent during upper gastrointestinal endoscopy. The second report outlined the use of dexmedetomidine in 3 patients in the Pediatric ICU setting and 2 in the postanesthesia care unit. In the PICU setting, dexmedetomidine was used for sedation during spontaneous ventilation without airway control in a 4-year-old with status asthmaticus whose agitation prevented the delivery of inhalational therapy, a 13-year-old who had significant anxiety

Following pectusexcavatum surgery despite effective pain management with a thoracic epidural catheter, and a 17-year-old with withdrawal from the recreational use of illicit drugs. In the other 2 patients, a single bolus dose of dexmedetomidine (0.4-0.5 mcg/kg) controlled postoperative emergence delirium and postoperative shivering.

PREVENTION OF EMERGENCE DELIRIUM FOLLOWING ANESTHESIA:

Five prospective,randomized trialdetail the successful use of dexmedetomidine to prevent emergence delirium following general anesthesia in an total of 288 pediatric patients. The first study randomized 90children to placebo or one of 2 doses of dexmedetomidine (0.15 mcg/kg or 0.3 mcg/kg) which wasadministered following anesthetic induction with sevoflurane. The incidence of emergence delirium was 37% in the placebo group, 17% with 0.15 mcg/kg of dexmedetomidine and 10% with0.3 mcg/kg. Similar efficacy was reported in the 4 subsequent studies. Dexmedetomidine was administered in doses ranging from

0.5 to 1 μg/kg as a bolus dose or an infusion of 0.2 μg/kg/hr inone of the studies. These studies demonstrate an approximate 10-fold decrease in the incidence of emergence delirium when compared with placebo. One of the studies noted that both time to emergence (5.03 ± 2.3 vs. 3.30 ± 1.3 minutes, $p<0.05$) and extubation (9.30 ± 2.9 vs. 7.20 ± 2.7minutes, $p<0.05$) were longer with dexmedetomidine versus placebo.

SEDATION IN THE PICU SETTING:

To date, only one prospective, randomized trial hasevaluated dexmedetomidine for sedation during mechanical ventilation in infants and children. Thirty infants and children requiring sedation during mechanical ventilation were randomized to receive either a continuous infusion of midazolam starting at 0.1 mg/kg/hr or a continuous infusion of dexmedetomidine starting at either 0.25 mcg/kg/hr or 0.5 mcg/kg/hr. Morphine (0.1 mg/kg) was provided as needed with an increase of the midazolam or dexmedetomidine infusion in 20%increments if necessary. The efficacy of the sedation regimens was assessed using the Ramsay sedation score and the need for supplemental morphine while the depth of sedation was comparedusing the Bispectral Index. Dexmedetomidine at 0.25 mcg/kg/hr was as effective as midazolam at 0.22mg/kg/hr while the higher dose of dexmedetomidine (0.5 mcg/kg/hr) was more effective. With the higher dose of dexmedetomidine, although sedation scores and the Bispectral Index were equivalent,there was a decreased need for supplemental morphine (0.28 ± 0.12 vs. 0.74 ± 0.5 mg/kg/24 hours).Two of 10 patients receiving dexmedetomidineat 0.5 μg/kg/hr had a Ramsay score of 1 at any timeversus 6 or 10 patients receiving midazolam. There was a decrease in the number of Ramsay scoresof 1 (5 with dexmedetomidineat 0.5 mcg/kg/hr versus 14 with midazolam at a mean dose of 0.22mg/kg/hr). The authors speculated that dexmedetomidine may be less effective in younger patientsas 5 of the 6 patients who manifested a Ramsay score of 1 in either of the 2 dexmedetomidine groups (0.25 or 0.5 mcg/kg/hr) were less than 12 months of age. Although there is likely significant clinical experience with the use of dexmedetomidine for longer than 24 hours as a sedative during mechanical ventilation, the only information currently available in the literature in children is anecdotal.

In another report from the PICU setting, Chrysostomou et al. retrospectively reviewed theirexperience with dexmedetomidine infusions following cardiac and thoracic surgical procedures in 38patients with a mean age of 8 ± 1 years. Seven patients (18%) were less than 1 year of age and 33(87%) were extubated and breathing spontaneously. The dexmedetomidine infusion without aloading dose was started following the surgical procedure at 0.1-0.5 μg/kg/hr (0.32 ± 0.15 μg/kg/hr).The infusion was continued for 3 to 26 hours (14.7 ± 5.5 hours) at 0.1-0.75 μg/kg/hr (0.3 ± 0.05μg/kg/hr). There was mild to moderate sedation achieved 93% of the time and no to mild pain 83%of the time. Forty-nine doses of rescue agents were required for either sedation or analgesia (1.3 ±0.26 boluses per patient). Twenty-nine (60%) were required during the first 5 hours of the dexmedetomidine infusion. There was a trend toward a requirement for a higher dexmedetomidine infusion and more rescue doses in patients less than 1 year of age compared to those more than 1year of age (0.4 ± 0.13 versus 0.29 ± 0.17 μg/kg/hr). Bradycardia occurred in 1 patient, 15 minutes after starting the dexmedetomidine infusion and resolved with its discontinuation. Transient hypotension was noted in 6 patients (15%) and resolved with decreasing the dexmedetomidine infusion in 3 and with discontinuation of the infusion in 3.

PROCEDURAL SEDATION (NON-INVASIVE PROCEDURES):

There is increasing interest and a growing number of reports of regarding the use of dexmedetomidine for non-invasive proceduralsedation.Preliminary data were provided by Nichols et al. who used dexmedetomidine for "rescue sedation" during radiologic imaging (CT and MR) in 5 patients, ranging in age from 11 months to 16years, when a combination of chloral hydrate and midazolam were ineffective. This has beenfollowed by prospective trials evaluating the efficacy of dexmedetomidine in the clinical scenario

.Koroglu et al. randomized 80 children (1-7 years of age) to dexmedetomidine or midazolam duringMR imaging. Dexmedetomidine was administered as a loading dose of 1 μg/kg over 10 minutes followed by an infusion of 0.5 μg/kg/hr while midazolam was administered as a loading dose of 0.2mg/kg followed by an infusion of 6 μg/kg/hr. The quality of sedation was better and the need for rescue sedation was less (8 of 40 versus 32 of 40) with dexmedetomidine compared to midazolam.Similar efficacy was reported by Berkenbosch et al. in an open label trial during MRI in 48 pediatric patients ranging in age from 5 months to 16 years. Dexmedetomidine was administered as a loadingdose of 0.5 μg/kg over 5 minutes and repeated as needed to achieve the desired level of sedation.

Following this, a continuous infusion was started at a rate in μg/kg/hr which was equivalent to the loading dose. The mean loading dose was 0.92 ± 0.36 μg/kg followed by an infusion of 0.69 ± 0.32μg/kg/hr. Effective sedation was achieved in all patients and the scan was completed without otheragents. Recovery time was longer in patients who had received other agents prior todexmedetomidine than in those who received dexmedetomidine as a primary agent (117 ± 41 versus69 ± 34 minutes). A subsequent study by the same investigators randomized 60 children to dexmedetomidine or propofol during MR imaging. The agents were equally effective in providing sedation. Induction time, recovery time, and discharge times were shorter with propofol whileadverse effects including hypotension and oxygen desaturation were more common with propofol.Oxygen desaturation requiring intervention (chin lift, discontinuation of the infusion, andsupplemental oxygen) occurred in 4 children receiving propofol versus 0 receiving dexmedetomidine.The largest experience with dexmedetomidine for procedural sedation comes from the Boston Children's Hospital. In a retrospective review of prospective data from their QA database,

Mason et al. presented data regarding dexmedetomidine for sedation in 62 children during radiologicalimaging. Dexmedetomidine was administered as a loading dose of 2 μg/kg over 10 minutes andrepeated as needed to achieve effective sedation. The loading dose was followed by an infusion,starting at 1 μg/kg/hr. The mean loading dose was 2.2 μg/kg with 52 patients requiring only the initialdose of 2 μg/kg for completion of the scan. The time to achieve sedation varied from 6 to 20minutes. Although HR and BP decreased in all patients, no treatment was necessary and no valuewas less than the 5th percentile for age. No effects on respiratory function were noted. Two patients manifested significant agitation during the administration of the loading dose and wereswitched to other sedative agents (propofol or pentobarbital). The ongoing experience from the Boston Children's Hospital has suggested that higher loading and infusion doses (up to 3 μg/kg) are needed to achieve a rapid onset and a high efficacy rate. Despite the use of higher doses and a more rapid infusion rate (3 μg/kg over 10 minutes), no significant increase in adverse effects has been noted. Anecdotal case reports have also demonstrated the efficacy of dexmedetomidine for sedationduring cardiac MR imaging and radiation therapy.

PROCEDURAL SEDATION (INVASIVE PROCEDURES):

There have been mixed results when using dexmedetomidine for invasive procedures. Although Tobias et al. reported that dexmedetomidine was not effective for upper GI endoscopy in an 11-year-old boy, Jooste et al. reported successful sedation with dexmedetomidine during fiberoptic intubation in 2 pediatric patients,both of whom were 10 years old, who presented for operative procedures and evidence of cervical spinal cord compromise. Similar success with dexmedetomidine for sedation during fiberoptic intubation of the trachea has been reported in adults. However, Jalowiecki et al. found dexmedetomidine to be ineffective during colonoscopy, associated with a high incidence of adverse effects, and to delay discharge in adults and therefore abandoned the study before completion.Similar issues were reported when comparing dexmedetomidine with midazolam for monitored anesthesia care in adults during cataract surgery.

In the first prospective evaluation of dexmedetomidine as the lone agent during aninvasive procedure in infants and children, Munro et al. reported their experience with dexmedetomidine during cardiac catheterization. Following premedication with midazolam and the placement of intravenous access with the inhalation of sevoflurane, the inhalational anesthetic agent was discontinued and dexmedetomidine administered (1μg/kg over 10 minutes followed byan infusion of 1 μg/kg/hr titrated up to 2 μg/kg/hr as needed). Five patients (25%) moved during local infiltration of the groin which did not require treatment or interfere with cannulae placement.Twelve (60%) of patients received a propofol bolus during the procedure for movement, an increasing BIS number, or anticipation of a stimulus.Anecdotal experience suggests that a combination of dexmedetomidine with ketamine may be effective for painful invasive procedures. Scher and Gitlin reported the successful use of dexmedetomidine (bolus of 1 mcg/kg followed by an infusion of 0.7 mcg/kg/hr) and ketamine (15 mgfollowed by an infusion of 20 mg/hr) for procedural sedation (awake fiberoptic intubation in an adult patient). Tosun et al. compared dexmedetomidine-ketamine with propofol-ketamine for sedation during cardiac catheterization in children with acyanotic congenital heart disease undergoing cardiac catheterization. Although sedation was managed effectively with both regimens, patients sedated with ketamine-dexmedetomidine required more ketamine (2.03 ± 1.33vs. 1.25 ± 0.67 mg/kg/hr, $P<0.01$), more supplemental doses of ketamine (10/22 vs. 4/22), and had longer recovery times (median time of 45 vs. 20 minutes, $p=0.01$) than patients sedated with a propofol-ketamine combination. No clinically significant differences were noted in hemodynamic and respiratory parameters. During the maintenance sedation phase, 2 patients receiving the dexmedetomidine-ketamine combination had convulsions. Neither had a history of previous neurological problems and the authors could not determine the cause of the seizure activity.

Despite the limited data, the combination of dexmedetomidine with ketamine makespharmacologic sense as the two medications have the potential to balance the hemodynamic and adverse effects of the other. Dexmedetomidine may prevent the tachycardia, hypertension,salivation, and emergence phenomena from ketamine while ketamine may prevent the bradycardia and hypotension which has been reported with dexmedetomidine. Additionally, ketamine as part of the sedation induction may speed the onset of sedation and eliminate the slow onset time when dexmedetomidine is used as the sole agent and the loading dose is administered over 10minutes.

TREATMENT OF WITHDRAWAL:

Regardless of the agent responsible for withdrawal, thepotential role of dexmedetomidine in treating such problems is supported by animal studies, casereports in adults and children, and one retrospective case series in infant. One reported experience with the use of dexmedetomidine to control withdrawal in 7 infants ranging in age from 3 to 24 months. The patients had received a continuous fentanyl infusion supplemented with intermittent doses of midazolam for during mechanical ventilation.

Withdrawal was documented by a Finnegan score ≥ 12. Dexmedetomidine was administered as a loading dose of 0.5 μg/kg/hr followed by an infusion of 0.5 μg/kg/hr. The loading dose was repeated and the infusion increased to 0.7 μg/kg/hr in the 2 patients who had received the highest doses of fentanyl (8.5 ± 0.7 versus 4.6 ± 0.5 μg/kg/hr, $p<0.0005$). Withdrawal was controlled and subsequent Finnegan scores were ≤ 7.

INTRAOPERATIVE APPLICATIONS:

In addition to the anecdotal report outlining the use of dexmedetomidine combined with remifentanil to provide controlled hypotension during posterior spinal fusion, there are 2 reports describing the successful intraoperative use of dexmedetomidine for awake neurosurgical procedures in pediatric patients.

Ard et al. used dexmedetomidine to provide sedation during awake craniotomy in 2 patients, both of whom were 12 years old. Anesthesia for skin incision, craniotomy and dural opening were provided by sevoflurane, fentanyl and nitrousoxide via a laryngeal mask airway (LMA). Dexmedetomidine (0.1-0.3 μg/kg/hr) provided sedation during the tumor resection and provided an awake and cooperative patient to allow identification of critical language areas. For this part of the procedure, the other anesthetic agents were discontinued and the LMA was removed. Similar success was reported by Everett et al. in 2 additional pediatric patients undergoing awake craniotomy, both of whom were 16 years of age.

MISCELLANEOUS APPLICATIONS:

Additional reports from the literature have described various other potential applications of dexmedetomidine in the pediatric population. Khasawinah etal. reported the successful use of dexmedetomidine in 3 patients to control the signs and symptoms of cyclic vomiting syndrome, a disorder thought to be related to alterations in the central control ofthe sympathetic nervous system, which manifests as recurrent bouts of vomiting. Zub et al.evaluated the potential efficacy of oral dexmedetomidine in 13 patients ranging in age from 4 to14years. Oral dexmedetomidine in doses ranging from 1.0 to 4.2 μg/kg was used as premedication prior to inhalational anesthetic induction or to facilitate IV cannula placement prior to procedural sedation in 9 patients with neurobehavioral disorders. Effective sedation was achieved in 11 of the 13 patients. An anecdotal report in a 14-year-old suggests the potential efficacy ofdexmedetomidine in the treatment of chronic regional pain (CRPS) syndrome type I. Finally,dexmedetomidine may be an effective agent to control shivering following general anesthesia.Dexmedetomidine (0.5 μg/kg over 3-5 minutes) was administered in a prospective, open label fashion to 24 children ranging in age from 7 to 16 years of age. Shivering behavior ceased within 5minutes with a mean onset time of 3.5 ± 0.9 minutes.

Summary of Dexmedetomidine:

It is an α2-adrenergic agonist which shares physiologic similarities with clonidine. It is currently approved by the FDA for continuous infusions for up to24 hours in adult ICU patients who are initially intubated and receiving mechanical ventilation. To date, there are no FDA-approved indications for its use in children, but with ongoing encouragement from the medical community, it is hoped that the manufacturers will seek FDA-approval for various clinical scenarios within the pediatric population. As with any sedative agent, the potential exists for adverse end-organ effects with dexmedetomidine. Although the current literature suggests that these events are relatively uncommon, such adverse effects have the potential for significant morbidity or even mortality in critically ill infants and children. Of concern in infants and children following cardiovascular surgery are animal data suggesting that the rapid administration of dexmedetomidine may increase pulmonary artery pressure and pulmonary vascular resistance. Todate, the literature contains reports of its use in approximately 1000 pediatric patients. Given is favorable sedative and anxiolytic properties combined with its limited effects on hemodynamic and respiratory function, there is growing interest in its use in the pediatric population in various clinicalscenarios.

Use of Intravenous Anesthetics for Sedation

The use of sedative–hypnotic drugs as part of a monitored anesthesia care (MAC) technique incombination with local anesthetics is becoming increasingly popular. During local or regional anesthesia, subhypnotic dosages of IV anesthetics can be infused to produce sedation, anxiolysis,and amnesia and enhance patient comfort. The optimum sedation technique achieves the desiredclinical end points without producing perioperative side effects (respiratory depression, nausea,and vomiting). In addition, it should provide for ease of titration to the desired level of sedation while providing for a rapid return to a “clear headed” state on completion of the surgicalprocedure. Sedation also constitutes an essential element in the management of patients in the ICU. The ideal sedative agent for critically ill patients would have minimal depressant effects on the respiratory and cardiovascular systems, would not influence biodegradation of other drugs, and would be independent of renal and hepatic function for its elimination. Recently, the BISmonitor has been used to monitor the depth of sedation in the ICU. For patients undergoingcardiac surgery, rapid reversibility of the sedative state may result in earlier extubation and lead to a shorter stay in the ICU. Although intermittent bolus injections of sedative–hypnotic drugs (e.g., diazepam 2.5 to5 mg, lorazepam 0.5 to 1 mg, midazolam 1.25 to 2.5 mg) have been administered during localanesthesia, continuous infusion techniques with propofol are becoming increasingly popular for maintaining a stable level of sedation in the OR and ICU settings.

Benzodiazepines, particularly midazolam, are still the most widely used for sedation in the ICU and for relief of acute situational anxiety during local and regional anesthesia. Midazolam has asteeper dose-response curve than diazepam, and therefore, careful titration is necessary to avoid oversedation and respiratory depression. Midazolam infusion, 0.05 to 5mg/kg/min, can be highly effective in providing sedation for hemodynamically unstable patients in the ICU. Use of a midazolam infusion has been shown to control agitation and decrease analgesic requirements without producing cardiovascular or respiratory instability. However, marked variability exists for midazolam in the individual patient dose-effect relationships. In addition,marked tolerance may develop to the CNS effects of midazolam with prolonged administration.

Propofol sedation offers advantages over the other sedative–hypnotics (including midazolam)because of its rapid recovery and favorable side effect profile. In addition, the degree of sedation is readily changeable from “light” to “deep” levels by varying the MIR. Following a propofol LD of 0.25 to 0.5 mg/kg, a carefully titrated subhypnotic infusion of 25 to 75 mg/kg/min produces a stable level of sedation with minimal cardiorespiratory depression and a short recovery period.

Because even low concentrations of propofol can depress the ventilatory response to hypoxia,supplemental oxygen should always be provided. Sedative infusions of propofol produce less perioperative amnesia than midazolam, and propofol-induced amnesia appears to be directly related to the infusion rate.

A small dose of midazolam (2 mg IV) administered immediately before a variable-rate infusion of propofol has also been shown to significantly decrease intraoperative anxiety and recall of uncomfortable events without compromising the rapid recovery from propofol sedation. Propofol sedation can also be supplemented with potent opioid and nonopioid analgesics to provide sedation analgesia. In comparing propofol and midazolam for patient-controlled sedation,midazolam was associated with less intraoperative recall and pain on injection than propofol, while propofol was associated with less residual impairment of cognitive function. Compared with midazolam in the ICU setting, use of propofol sedation allowed for more rapid weaning of critically ill patients from artificial ventilation. It has been suggested that the more rapid weaning after propofol sedation may be cost-saving compared with midazolam when only a limited period of sedation (<48 hour) is required. Although a pharmacokinetic study yielded no evidence of a change in receptor sensitivity or drug accumulation over a 4-day study period, preliminary data suggest that tolerance to the CNS effects of propofol may develop with more prolonged administration (>1 week).

Concerns have been raised about elevated lipid plasma levels in patients sedated with propofol for several days, especially when high infusion rates (>6 mg/kg/h) are utilized. However, the availability of a propofol formulation with reduced lipid content (Ampofol) should decrease the risk of this problem in the future. Because of conflicting evidence regarding increased mortality as a result of myocardial failure when propofol was used for sedation in the neonatal ICU, more safety data are needed to define the indications for the use of prolonged propofol infusions, especially in the pediatric population. Low-dose ketamine infusions (5 to 25 mg/kg/min) can also be used for sedation and analgesia during local or regional anesthetic procedures, as well as in the ICU setting. Midazolam, 0.07 to 0.15 mg/kg infused over 3 to 5 min, followed by ketamine,0.25 to 0.5 mg/kg IV over 1 to 3 min, produced excellent sedation, amnesia, and analgesia without significant cardiorespiratory depression.

Magnetic resonance imaging:

MRI is a noninvasive, radiation-free diagnostic procedure. A magnetic field with strength of 1.5–7T (140 000 times the Earth's natural magnetic field) is used to perform MRI clinically.[8] These magnetic forces orient all protons in the magnetic field in a longitudinal direction and create a spin. A high-frequency radio impulse is then applied with the same frequency as the spin. This triggers the protons to absorb energy. After stopping the radio frequency, the protons return to their initial position and emit radio waves that serve as raw material for the MRI. Depending on the diagnostic needs an MRI scan takes about 10–30 min, is quite noisy and the patient is moved into a narrow pipe with limited access. For optimum image quality enabling precise diagnosis patients have to remain motionless. Metallic materials have to be removed as they impair image quality and may induce undesirable side effects, e.g. warming. The high-frequency radio impulses can cause damage to or dysfunction of medical devices.For this reason an anaesthesia workstation in an MRI environment has to fulfil specific criteria to meet the highly specialized respective needs.

Nevertheless, it also has to perform as any other anaesthesia unit with a ventilator, anaesthetic gas measurement, capnography, pulse oximetry, ECGmonitor, blood pressure measurement and respiratory frequency monitor. For paediatric anaesthesia, the ventilator in the MRI setting has to be equipped with compliance compensation, and resuscitation material has to be within reach. Finally it must be pointed out that an MRI emergency stop takes some minutes to be effective and is expensive. The frequency of MRI scans in children has increased in recent years owing to significant improvements in MRI opening up new diagnostic perspectives . If young patients are unable to cooperate or to be at rest, either sedation or anaesthesia is required. Most children who need MRI diagnostic procedures have neurological diseases, vascular malformation or oncological tumour growth. Epilepsy and spastic or mental retardation are common symptoms in these patients . These facts must be taken into account when sedation or anaesthesia for MRI in children is required. In the end, however, the main goals to be achieved are maximum patient safety, successful scanning and paramount image quality.

Sedation for MRI:

Usually the Observer's Assessment of Alertness andSedation (OAAS) scale or the Ramsey score are used to describe sedation depth clinically.[97] For children theAmerican Academy of Pediatrics defined four sedationsteps: anxiolysis, conscious sedation, deep sedation and anaesthesia. Goals of sedation in the paediatric patient for diagnostic and therapeutic procedures are defined as:guard the patient's safety and welfare; minimize physical discomfort and pain; control anxiety, minimize psychological trauma, and maximize the potential for amnesia;control behaviour and/or movement to allow the safe completion of the procedure; and return the patient to a state in which safe discharge from medical supervision, as determined by recognized criteria, is possible. These goals can be achieved by selecting the lowest dose of one drug with the highest therapeutic index for the procedure.Concerning children and MRI, because of noise and tube narrowness, deep sedation is the required depth for examination in most cases. Stopping an MRI scan is expensive and ineffective, thus the failure rate has to be minimized.

Prerequisites for sedation are the same as for generalanaesthesia: fasting, intravenous access, vital signs monitoring, emergency equipment and physicians whoare experienced in using the technical equipment and trained in paediatric airway management.In this context it must be pointed out that disabled children do not need higher doses of sedatives but are three times more at risk of hypoxia under sedation.As the view of and access to the patient are limited in the MRI setting, the physician has to be very experienced inpaediatric medication and airway management in newborns and children. If hypoventilation occurs, stopping the scan, pulling the scan desk outside the tube and attending to the patient in this special surrounding is time consuming and needs to be practised. In newborns and infants immediately after oxygen desaturation occurs bradycardia starts. This has to be kept in mind when choosing a suitable procedure and monitoring for outpaediatric patients.A very safe and simple technique for newborns is the‘feed and scan’ technique in which children are fed and one has to wait until the young patient falls asleep.Remarkable disadvantages of this technique are the unpredictable ‘induction times’ and the high failure rates of the scanning procedure. This time-consuming procedure therefore seems not to be practicable in most modern medical centres. In 2008 Beauve and colleagues compared the feed and scan technique with moderate chloral hydrate sedation in neonates. The MRI failure rate was similar, but the time until MRI was started was shorter for chloral hydrate sedation . As still only a fewstudies exist on the exact mode of action of different sedative drugs in paediatric patients and off-label use has to be performed in many cases the feed and scan technique has to be considered as a relevant alternative.In another investigation melatonin was used for sleepinduction before MRI. The success of this sleep induction concept was not convincing. Nevertheless high doses of this substance combined with sleep withdrawal might have an effect but needs further proof .

In most countries in Europe and overseas,anaesthesiologists are responsible or indispensable owing to regulatory frameworks. In the UK or France, however,sedation is also provided by trained nurses. This topic has been discussed controversially .Krauss et al.described the advantages and disadvantages of the USmodel, which has helped to make sedation and analgesia significantly safer and more professional than procedures performed 20 years ago in the United States.

The Paediatric Sedation Research Consortium recently reported on 49836 sedation or anaesthesia cases involving propofol over a 3-year period. Two cardiac arrests, four aspiration events, and no deaths were among this cohort.One in 65 sedations was associated with stridor or laryngospasmor airway obstruction or expiratory wheezing or central apnea .In this context it has to be pointed out that chest excursions cannot be observed easily and saturation might fall late after cessation of breathing, particularly if oxygen is insufflated.For this reason end-tidal CO2 monitoring is indispensable in MRI sedation and anaesthesia procedures.Long-distance ventilator or capnometry tubes are often used in the MRI setting. Therefore there are significant drawbacks in using these devices. Another alternative to measure respiratory excursions is a special respiratory belt that monitors chest excursions during MRI scanning.There is a variety of drugs available for sedation.

Which of these substances are favourable for MRI sedation?When choosing an adequate sedative for MRI in children ,the review of Krauss et al. about procedural sedation and analgesia is helpful.

Effect of antiepileptic drug on anaesthetic drugs:

Epilepsy is the most common neurologic disorder in children with an incidence of approximately 4%.[16] Upto 70% of patients diagnosed with epilepsy can be renderedseizure-free by currently available anti-epileptic drugs (AEDs) when administered as monotherapy . Among old generation AEDs, phenobarbital is the most commonly used AED in pediatric population and is a prototypic P-450 enzyme inducer. It stimulates the activity of a variety of cytochrome P-450 (CYP-450) enzymes, including CYP1A2, CYP2C9, CYP2C19, and CYP3A4, as well as glucuronyltransferases and UDP-glucuronosyltransferase (UGT) .

These isoenzymes are also involved in the metabolism of more than 50% of all drugs including anesthetics . Thereby, the clinical efficacy of concomitantly administered anesthetics that use the common metabolic pathway with phenobarbital might be reduced by an increase in distribution and clearance .

Magnetic resonance imaging (MRI) is the preferred radiologic imaging technique for diagnosis and followup of epilepsy. The important concern is the selection

of sedative anesthetic agents for successful sedation during MRI procedures because of the potential drug interactions with AEDs. The selection would be arranged among the anesthetics that have anticonvulsanteffects like thiopental, benzodiazepines, etomidate,ketamine, propofol, and inhalation anesthetics .

All of these anesthetic agents are also metabolized with cytochrome P-450 isoenzymes. Thereby, the effective duration of sedation and the required amount of sedatives might increase when either of the anesthetic agents is co-administered with an AED.

Aim of the study

AIMS AND OBJECTIVES

The study was conducted with the following aims;

1) To compare the efficacy of Propofol+ketamine infusion, Propofol infusion, and Dexmedetomidine infusion regimens for sedation in paediatric patients on antiepileptic therapy undergoing magnetic resonance imaging.

2) To compare the following parameters between the three regimes;
    1. Cardiovascular profile,
    2. Respiratory profile ,
    3. Incidence of adverse events and
    4. Recovery profile.

Materials & Methods

Materials and methods

This randomized prospective case controlled study was approved by the ethical committee Children of age between 1-12 years scheduled to undergo MRI at our institute were included to participate in the study. Informed written consent was obtained from the parents of the children undergoing magnetic resonant imaging for diagnostic purposes.

Ninety epileptic patients between the age group of 1-12 years on antiepileptic therapy undergoing magnetic resonance imaging of brain between April 2013 and June 2014 were included in the study.

Inclusion and exclusion criteria followed in this study were below;

Inclusion criteria:

1. Children of age 1- 12 years
2. Patients on antiepileptic drugs
3. American Society of Anesthesiologist status 1 and 2

Exclusion criteria:

1.ASA status III and above

2.Presence of congenital heart disease,

3.Anatomic airway abnormalities,

4.Sleep apnoea,

5.History of intolerance or allergies to propofol,

6. A recent upper/lower respiratory infection,

7. A episode of acute asthma in the preceding 2 weeks,

8. Gastroesophageal reflux disease requiring treatment and

9. Those children not followed the fasting guidelines , which were explained in the preanaesthesia visit.

10. History of allergy or anaphylaxis to the drugs used

11. Patients unwilling to participate.

During pre anaesthetic checkup, patients assessed for fitness and instructions to be followed were given. Study protocol was explained to patient's relative who satisfied the inclusion and exclusion criteria. Informed consent was obtained from parents who were willing to include their children in this study. Patients were instructed to continue the AEDs, as per their scheduled time.

Fasting guidelines followed in this study were in accordance with standard practice guidelines on fasting proposed by the American society of anesthesiologists.[19] Patients were allowed,

1. Clear fluids (clear water, pulp free clear juice) till 2hours,

2. Breast milk till 4hrs and

3. Solids till 6hrs prior to anesthesia/ sedation.

The patients were shifted to MRI induction room accompanied by parents. Monitoring lines were attached which included electrocardiogram (ECG), non-invasive blood pressure (NIBP), and pulse oximetry for SpO2 monitoring. Baseline heart rate (HR), respiratory rate (RR) ,NIBP and SpO2 values were recorded. For securing intravenous line , patients were induced with sevoflurane in 100% oxygen through a face mask. The concentration of sevoflurane in the inspired mixture was gradually increased and adjusted. When the patient shows loss of responsiveness to verbal stimuli, intravenous line (IV) was secured. Dextrose normal saline was used as maintainance fluid, according to 4- 2- 1 formula[20]. Sevoflurane was discontinued as soon as IV line was secured and the study drug (sedation regimen) was started by IV infusion as per randomization. Randomization was done using a computer generated program.

Group- P (n-30),received propofol(1%) infusion at the rate of 1.2ml/kg/hr in the intial 10 mins, followed by 0.6ml/kg/hr till the completion of MR imaging .

Group- PK (n-30), receiving propofol-ketamine infusion in the ratio of 4:1(each ml containing 10mg of propofol and 2.5mg of ketamine) at 1.2ml/kg/hr of the study drug in the intial 10 mins, followed by 0.6ml/kg/hr till the completion of MR imaging .

Group D (n-30) receiving dexmedetomidine, an initial loading dose of 1mcg/kg over10 min followed by a continuous infusion at 0.5 mcg/ kg /h till the completion of MR imaging.

Baseline hemodynamic variables (HR, NIBP,SPO2 &RR)were noted during this time. Pulse oximetry (SPO2), HR and RR were monitored continuously throughout the anesthetic. Noninvasive arterial blood pressure was monitored at 10 min intervals throughout the anesthetic. If required, children were positioned with a soft roll under the shoulder and the neck extended to ensure an unobstructed airway. A stable respiratory pattern was established before proceeding. If evidence of airway obstruction were present, supplemental airway maneuvering and interventions (insertion of nasal airway, oral airway, Larnygeal mask airway) were instituted. Sedation levels was evaluated by the Ramsay sedation score (RSS) . The assessed sedation levels were recorded at 5-min intervals. Patients were shifted to MRI console and the imaging sequence was started if the sedation level is more than 4 in the RSS. If adequate sedation and immobilization was not achieved after infusion of study drug, midazolam was given at a dose of 50mcg/kg boluses to keep RSS>4 during scanning. After each administration of midazolam, the patient was observed for a minute duration to approve the adequate sedation level. If RSS was not achieved to the targeted point, an additional midazolam bolus was given as rescue drug. Interaction of midazolam with antiepileptic drug is unpredictable and midazolam induced depression of ventilation is exaggerated in presence of CNS depressant drugs. So arbitrarily 2 bolus doses (50mcg/kg) or depression of ventilation whichever occurs earlier were considered as maximum dose of midazolam. Children were planned to give GA with laryngeal mask airway(LMA) or endotracheal tube,if RSS>4 was not achieved , even after giving maximum midazolam .

After the imaging sequence was completed, the infusion was stopped and the child was transferred to a recovery room, where they were observed by a recovery nurse and the attending anesthesiologist . The observer was recording vital signs, all complications and side effects during or after the anesthetic. Recovery time was defined as the time from completion of the scan until achievement of a recovery score assessed with Modified Aldrete Scoring of 8. Children were discharged from recovery room when their vital signs returned to baseline, their level of consciousness was close to baseline, they could maintain a patent airway, and when their protective airway refluxes were effective.

Statistics

Statistical analysis

SPSS version 16 (SPSS inc, Chicago 2007) was used for statistical analysis. One way analysis of normal variance (ANOVA) was used to find difference between demographic parameters like age and weight between three groups. Chi-square test was used to assess the difference between gender distributions among three groups. One way ANOVA was used to compare changes in hemodynamic parameters within the groups. Repeated measure ANOVA(Greenhouse-Geisser) was used to find difference in variation of vital parameters throughout the study period among the three groups.

Chi-square test was used to analyse airway support measures (shoulder roll use and nasal airway use) and for hypotension among three groups. ANOVA was used to find difference in duration of imaging, recovery time and for requirement of rescue drug among three groups. A ‘p’ value less than 0.05 was considered statistically significant.

Results

Table1showing the demographic data of the three groups

Patient characteristics	Group PK (N=30)	Group P (N=30)	Group D (N=30)	P
Age in years(mean±SD)	6.257±2.756	5.183±2.762	5.067±3.183	0.223
Weight in Kg (mean ± SD)	22.83±6.449	22.37±9.379	21.03±10.604	0.774
Male/ Female	19/11	16/14	21/9	0.407

P value <0.05 was considered significant

SD- Standard deviation

Group-PK- propofol-ketamine group

Group-P- Propofol group

Group-D- Dexmedetomidine group

Results

A total of ninety patientswere includedwith thirty patients in each group.

Table 1 shows the comparison of the demographic data of the three groups.

Mean age in Group-PK was 6.257 with SD of 2.756 years. Mean age in Group-P was 5.183 with SD of 2.762 years. Mean age in Group-D was 5.067 with SD of 3.183 years. The mean difference in age between three groups was not statistically significant (p-0.223).

Gender distribution (Male : Female) were19:11,16:14 and 21:9 among Group-PK, Group-P and Group-D respectively. The difference of gender distribution was not statistically significant (p-0.407).

Mean weight of patients were 22.83 ±6.449 Kg in Group-PK,22.37 ± 9.379 Kgin Group-P and 21.03±10.604 Kg in Group-D and their difference were not statistically significant (p-0.774).

Table2 showing duration of imaging and recovery time in three groups

Patient characteristics		Group PK	Group P	Group D	P Value
Imaging Duration (in min)	Mean ±SD	68.50±5.438	69.00±5.318	64.33±3.407	**0.004# 0.001**
	Range	60-75	60-75	60-70	
Recovery time (in min)	Mean ±SD	12.97±1.426	2.60±0.724	21.10±5.689	**0.0 (between groups)$**
	Range	10-15	2-4	3-35	

#,$- P value <0.05.

SD: standard deviation

Imaging Duration: Duration of time in the MRI scanning room.

Recovery time: Time to achieve modified Aldrette score of 8.

Mean duration of imaging for patients were 68.50 ±5.438 minutes in Group-PK,69.00 ± 5.318 minutes in Group-P and 64.33 ± 3.407minutes in Group-D. Though the difference in duration of imaging between Group-D and other two groups were statistically significant(p value=0.004,0.001), it is not clinically significant. The range of imaging duration were 60- 75 minutes,60- 75 minutes and 60-70 minutes in Group-PK,Group- P and Group-D respectively.

The time to achieve modified aldrette score of eight in the three groups following sedation for magnetic resonance imaging were 12.97±1.426 minutes, 2.60±0.724 minutes and 21.10±5.689 minutes in Group-PK,Group-P and Group-D respectively. The difference in recovery time ,between the groups was statistically significant (pvalue-0.00). The imaging duration and time to achieve modified aldrette score of eight in the three groups is given in table 2.

Table 3 showing vital parameters(mean ±SD) in Group PK

(n=30)	Baseline	10min	20min	30 min	40 min	50 min	60min	70min	P
HR Beats/Min	83.47 ±13.4	83.6 ±11.9	83.83 ±11.2	83.23 ±12.1	84.1 ±12.2	83.97 ±11.5	84.1 ±12.7	85.07 ±12.4	1.00
SBP *(mmHg)*	90.8 ±12.43	91.1 ±12.49	90.23 ±11.69	92.17 ±11.98	91.43 ±11.42	91.5 ±10.96	92.4 ±11.59	91.97 ±11.19	0.99
DBP*(mmHg)*	53.37 ±13.64	51.77 ±13.20	50.5 ±11.72	51.03 ±12.75	51.87 ±12.59	52.43 ±11.98	53.63 ±12.32	52.37 ±11.24	0.98
MAP (mmHg)	65.84 ±12.95	64.88 ±12.53	63.74 ±11.19	64.74 ±12.03	65.06 ±11.83	65.46 ±11.36	66.56 ±11.78	65.57 ±10.71	0.99
RR (Breaths/min)	20.53 ±4.64	19.57 ±4.86	19.87 ±4.23	20.67 ±4.24	21.3 ±4.41	20.9 ±4.01	21.2 ±3.62	21.33 ±3.68	0.64

P value<0.05 was considered significant

SD: Standard deviation

HR- Heart rate

SBP- Systolic blood pressure, DBP- Diastolic blood pressure, MAP- Mean blood pressure

RR- Respiratory rate

Table 3 displays the average value of theparameters(heart rate, systolic blood pressue,diastolic blood pressure,mean blood pressure and respiratory rate) at various time points, starting from baseline to the end of imaging in patients, in patients who received propofol-ketamine infusion. Hemodynamic parameters in group- PK were maintained throughout imaging. HR, systolic, diastolic, mean blood pressure and respiratory rate changes werenot statistically significant with p value of 1.00,0.99,0.98,0.99 and 0.64 respectively.

Table 4 showing vital parameters(mean ±SD) in Group P

(n=30)	Baseline	10min	20min	30 min	40 min	50 min	60min	70min	P
HR Beats/Min	91 ±10.11	92.2 ±9.97	91 ±10.05	92.17 ±10.70	92.53 ±11.63	90.97 ±9.01	90.07 ±8.93	89.43 ±10.01	0.93
SBP *(mmHg)*	93.7 ±9.35	91.7 ±8.65	92.03 ±8.26	92.27 ±9.64	93.07 ±7.58	92.77 ±7.2	92.6 ±8.27	93.27 ±8.46	0.98
DBP*(mmHg)*	51.8 ±9.14	48.13 ±8.39	49.2 ±5.20	50.83 ±7.13	51.7 ±7.92	52.97 ±8.56	49.97 ±7.07	52.03 ±5.95	0.21
MAP (mmHg)	65.77 ±8.22	62.66 ±7.59	63.48 ±5.35	64.64 ±6.97	65.49 ±7.03	66.23 ±7.70	64.18 ±6.37	65.78 ±5.94	0.44
RR (Breaths/min)	21.93 ±3.34	21.33 ±3.45	20.73 ±3.34	21.67 ±3.48	21.87 ±2.28	22.07 ±2.75	21.27 ±2.19	21.93 ±2.54	0.66

P value<0.05 was considered as significant

SD: Standard deviation,

HR- Heart rate

SBP- Systolic blood pressure, DBP- Diastolic blood pressure, MAP- Mean blood pressure,

RR- Respiratory rate

Table 4 shows average value of the parameters(heart rate, systolic blood pressue,diastolic blood pressure,mean blood pressure and respiratory rate) at various time points, starting from baseline to the end of imaging in patients who received propofol infusion. Hemodynamic parameters in group- P were maintained throughout imaging. HR, systolic, diastolic, mean blood pressure and respiratory rate change werenot statistically significant with p value of 0.93,0.98,0.21,0.44 and 0.66 respectively.

Table 5 showing vital parameters(mean ±SD) in Group D

(n=30)	Base line	10min	20min	30 min	40 min	50 min	60min	70min	P
HR Beats/Min	98.27 ±11.76	95.47 ±9.83	88.33 ±12.20	82.4 ±9.25	78.13 ±10.17	76.2 ±10.89	74.27 ±11.57	72.47 ±12.86	**0.001#**
SBP *(mmHg)*	92.73 ±6.35	86.2 ±6.12	79.23 ±7.21	74.4 ±6.52	76.97 ±7.99	76.13 ±5.88	75.2 ±6.20	76.13 ±8.32	**0.00#**
DBP*(mmHg)*	46.33 ±8.99	45.33 ±6.13	41.27 ±3.69	41 ±3.95	42.4 ±4.34	43.2 ±3.66	43.07 ±4.29	42.4 ±3.87	**0.001#**
MAP (mmHg)	61.8 ±7.80	58.96 ±5.77	53.92 ±4.17	52.13 ±3.74	53.92 ±5.31	54.18 ±3.88	53.78 ±4.35	53.64 ±3.95	**0.00#**
RR (Breaths/min)	21.13 ±2.90	21.73 ±3.35	21.47 ±3.01	21.27 ±2.43	21.2 ±2.26	22.27 ±2.44	22 ±2.57	20.6 ±1.97	0.30

#P value<0.05 was considered as significant

SD: standard deviation

HR- Heart rate

SBP- Systolic blood pressure, DBP- Diastolic blood pressure, MAP- Mean blood pressure

RR- Respiratory rate

Table 5 shows average value of the parameters(heart rate, systolic blood pressue,diastolic blood pressure,mean blood pressure and respiratory rate)) at various time points, starting from baseline to the end of imaging in patients, in patients who receiveddexmedetomidine infusion. There was significantdecrese in hemodynamic parameters in Group D, throughout imaging. Heat rate, systolic, diastolic and mean blood pressure decrese were statistically significant with p value of 0.001,0.00,0.001, and 0.00 respectively.There was no significant variation in respiratory rate in this group (P value-0.30).

Table 6Comparing mean values of systolic blood pressure among three groups

Group	Baseline	10min	20min	30min	40 min	50min	60min	70min
PK	90.8	91.1	90.23	92.17	91.43	91.5	92.4	91.97
P	93.7	91.7	92.03	92.27	93.07	92.77	92.6	93.27
D$	92.73	86.2	79.23	74.4	76.97	76.13	75.2	76.13

PK:propofol-ketamine, P : propofol, D: dexmedetomidine.

Values were expressed in mmHg

$: P value <0.05.

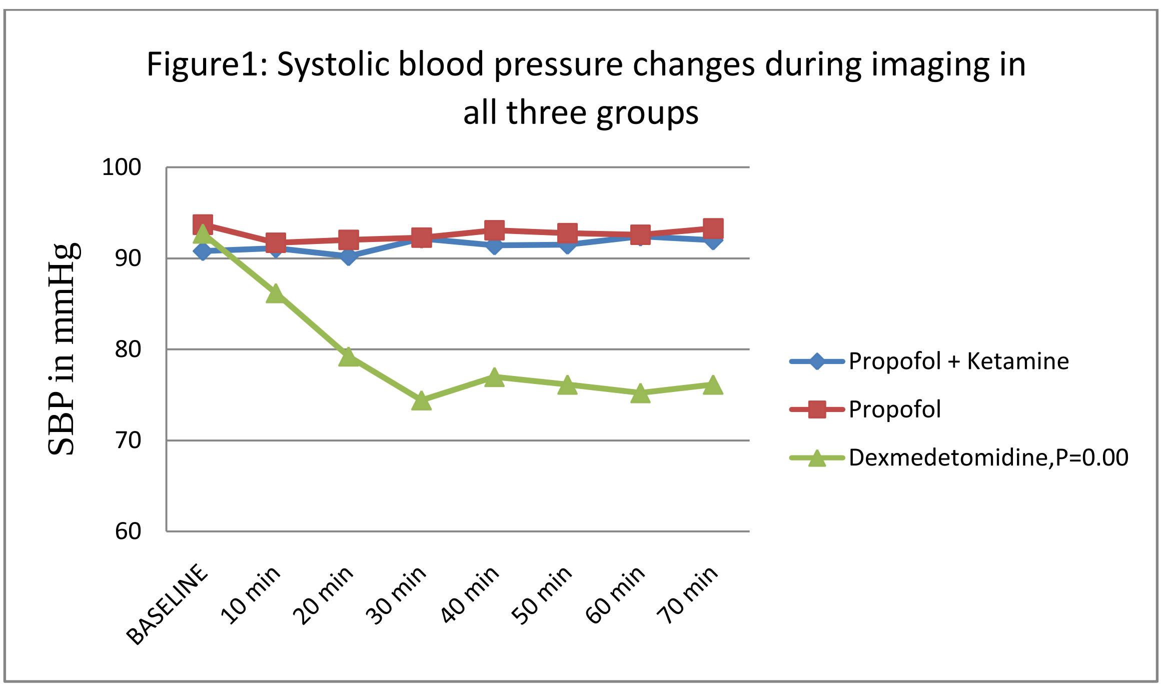

Table 6 displays the mean values of systolic blood pressures at various time points during imaging in all the three groups. The variation in systolic blood pressure was statistically significant with p value of 0.00, if the comparison of variation was made among the three groups

Figure 1 displays the systolic blood pressure changes in all the three groups. In Group PK and Group P, the systolic blood pressure were maintained around baseline, whereas in group D shows decrease in systolic blood pressure from baseline.These changes in systolic blood pressure was statistically significant with p value of 0.00, if the comparison of systolic blood pressure variation was made among the three groups.

Table 7 Comparing mean values of diastolic blood pressure among three groups

Group	Baseline	10min	20min	30min	40 min	50min	60min	70min
PK	53.37	51.77	50.5	51.03	51.87	52.43	53.63	52.37
P	51.8	48.13	49.2	50.83	51.7	52.97	49.97	52.03
D$	46.33	45.33	41.27	41	42.4	43.2	43.07	42.4

PK:propofol-ketamine, P : propofol, D: dexmedetomidine.

Values were expressed in mmHg

$: P value <0.05.

Figure 2:Diastolic blood pressure changes during imaging

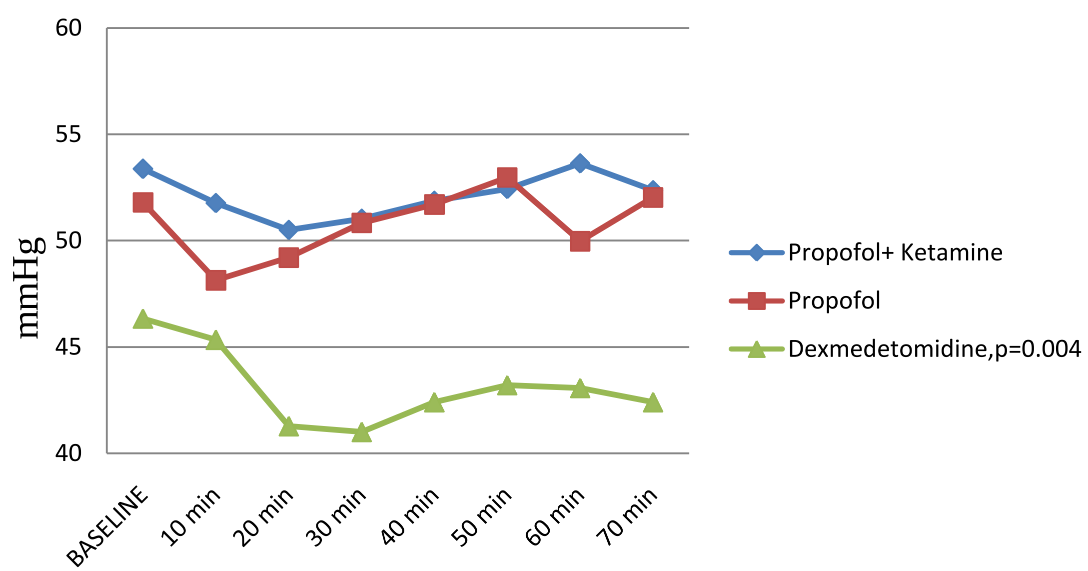

Table 7 displays the mean values of diastolic blood pressures at various time points during imaging in all the three groups. The variation in diastolic blood pressure was statistically significant with p value of 0.004, if the comparison of variation was made among the three groups

Figure 2 displays the diastolic blood pressure changes in all the three groups. In Group PK and Group P, the diastolic blood pressure weremaintained around baseline, whereas in group D shows decrease in diastolic blood pressure from baseline. These changes in diastolic blood pressure was statistically significant with p value of 0.004, if the comparison of diastolic blood pressure variation was made among the three groups.

Table 8 Comparing mean values of mean blood pressure among three groups

Group	Baseline	10min	20min	30min	40 min	50min	60min	70min
PK	65.84	64.88	63.74	64.74	65.06	65.46	66.56	65.57
P	65.77	62.66	63.48	64.64	65.49	66.23	64.18	65.78
D$	61.8	58.96	53.92	52.13	53.92	54.18	53.78	53.64

PK:propofol-ketamine, P : propofol, D: dexmedetomidine.

Values were expressed in mmHg

$: P value <0.05.

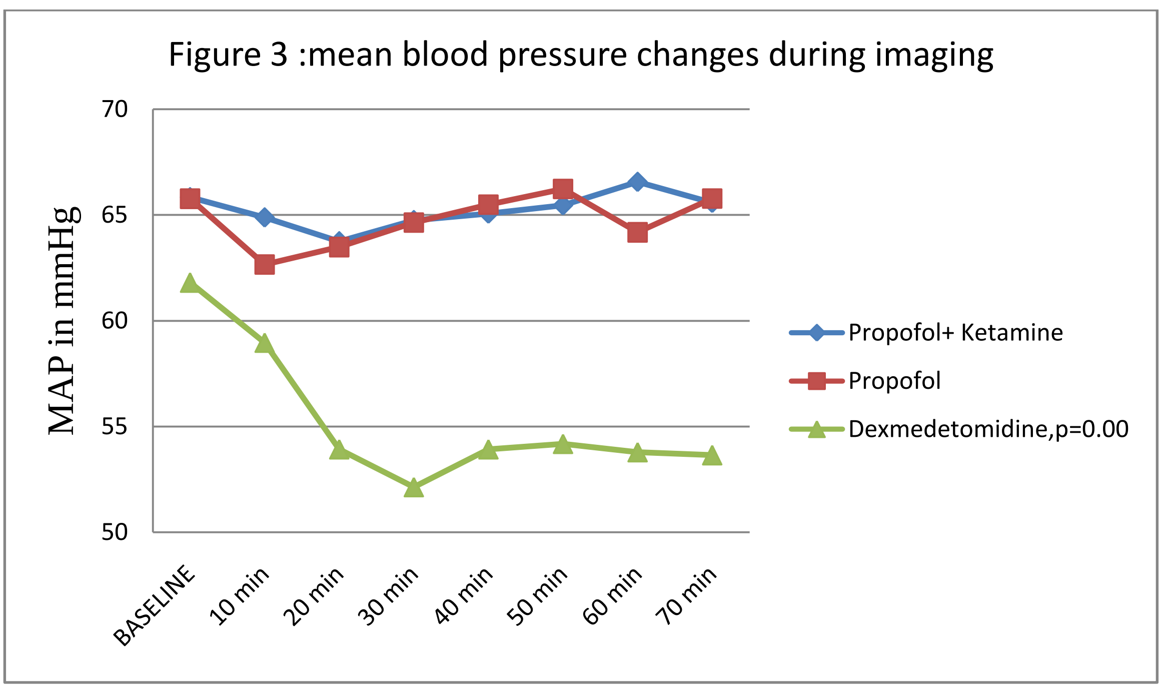

Table 8 displays the mean values of mean blood pressures at various time points during imaging in all the three groups. The variation in mean blood pressure was statistically significant with p value of 0.00, if the comparison of variation was made among the three groups

Figure 3 displays the mean blood pressure changes in all the three groups. In Group PK and Group P, the mean blood pressure were maintained around baseline, whereas in group D showsdecrese in mean blood pressure from baseline. These changes in mean blood pressure was statistically significant with p value of 0.00, if the comparison of mean blood pressure variation was made among the three groups.

Table 9 Comparing mean values of heart rate among three groups

Group	Baseline	10min	20min	30min	40 min	50min	60min	70min
PK	83.47	83.6	83.83	83.23	84.1	83.97	84.1	85.07
P	91	92.2	91	92.17	92.53	90.97	90.07	89.43
D$	98.27	95.47	88.33	82.4	78.13	76.2	74.27	72.47

PK:propofol-ketamine, P : propofol, D: dexmedetomidine.

Values were expressed in beats per minute

$: P value <0.05.

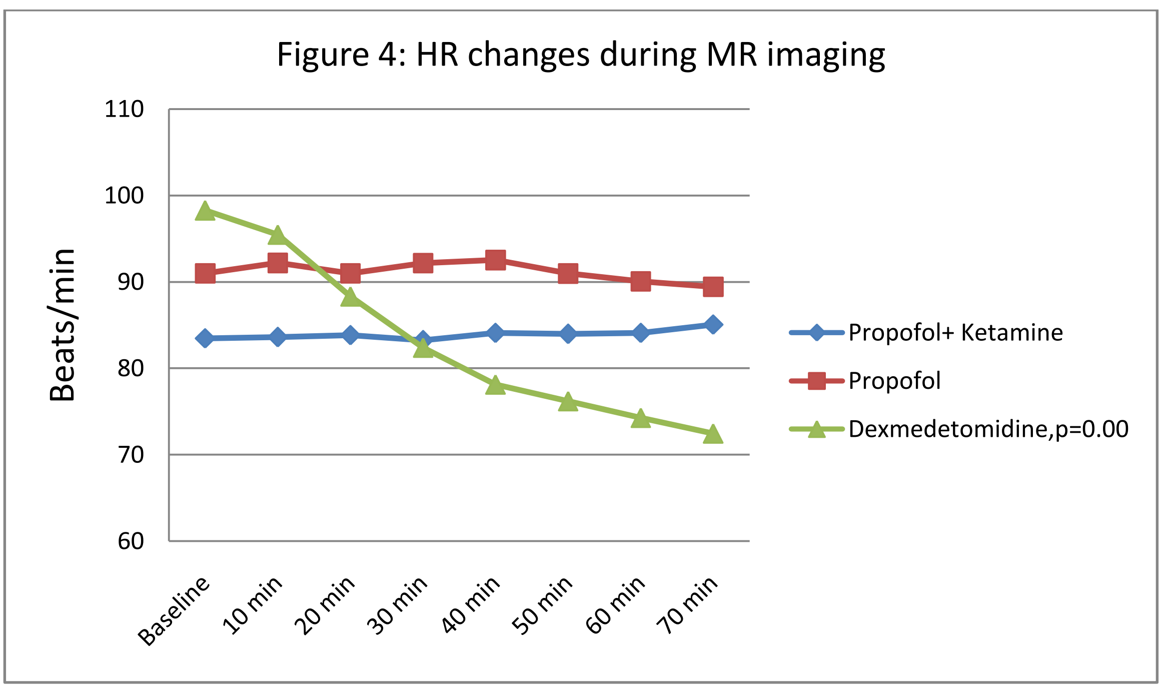

Table 9 displays the mean values of heart rate at various time points during imaging in all the three groups. The variation in heart rate was statistically significant with p value of 0.00, if the comparison of variation was made among the three groups

Figure 4 displays the heart rate changes in all the three groups. In Group PK and Group P, heart rate were maintained around baseline, whereas in group D shows decrease in heart rate from baseline. These changes in heart rate was statistically significant with p value of 0.00, if the comparison of variation was made among the three groups.

Table 10 Comparing mean values of respiratory rate among three groups

Group	Baseline	10min	20min	30min	40 min	50min	60min	70min
PK	20.53	19.57	19.87	20.67	21.3	20.9	21.2	21.33
P	21.93	21.33	20.73	21.67	21.87	22.07	21.27	21.93
D	21.13	21.73	21.47	21.27	21.2	22.27	22	20.6

PK:propofol-ketamine, P : propofol, D: dexmedetomidine.

Values were expressed in breaths per minute

P value <0.05 was considered as significant

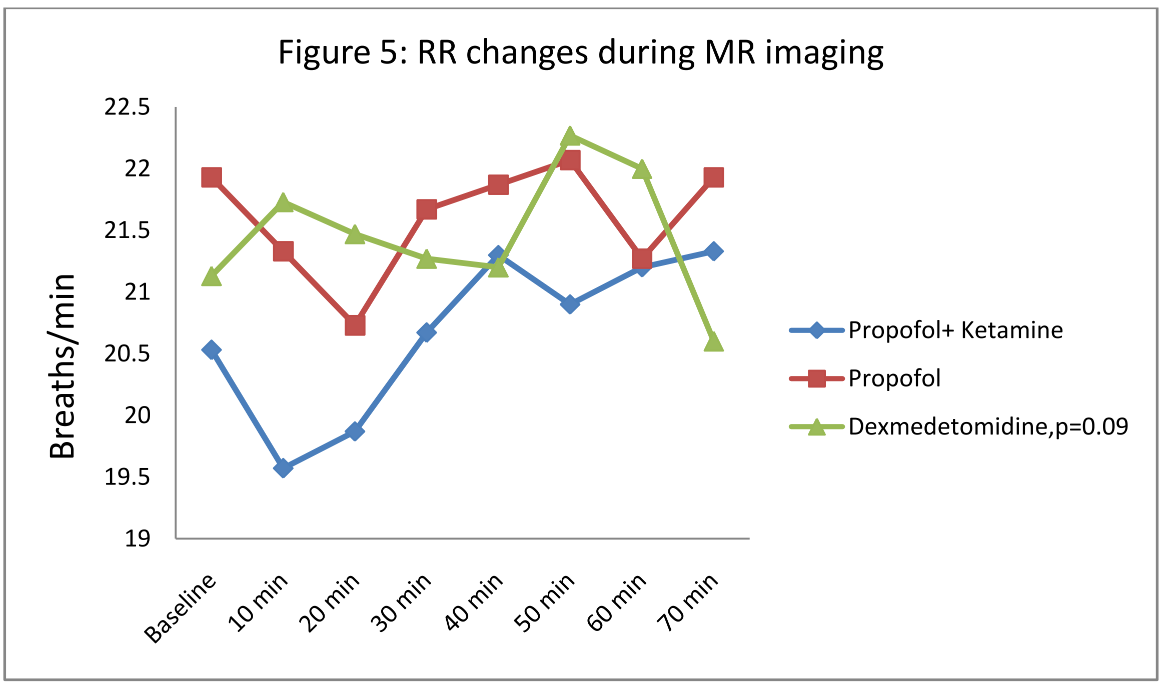

Table 10 displays the mean values of respiratory rate at various time points during imaging in all the three groups. The variation in respiratory rate was not statistically significant with p value of 0.09, if the comparison of variation was made among the three groups

Figure 5 displays the respiratory rate changes in all the three groups. In all the threegroups respiratory rate was maintained around baseline. Respiratory rate variation was not statistically significant (P = 0.09) among the three groups.

Table 11 Comparing mean values of oxygen saturation among three groups

Group	Baseline	10min	20min	30min	40 min	50min	60min	70min
PK	99.53	99.1	99.03	99	98.97	99.13	99	98.97
P	99.4	98.83	98.57	98.37	98.57	98.63	98.5	98.73
D	99.33	98.7	98.67	98.8	98.37	98.6	98.6	98.53

PK:propofol-ketamine, P : propofol, D: dexmedetomidine.

Values were expressed in percentage

P value <0.05 was considered as significant

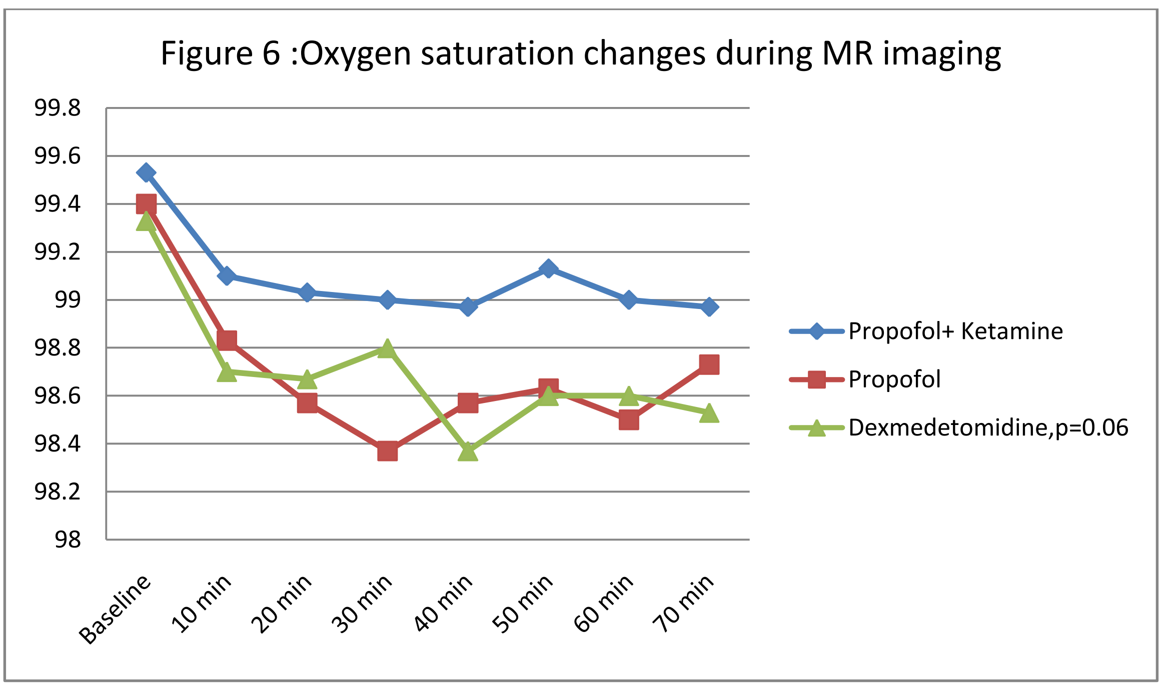

Table 11 displays the mean values of oxygen saturation at various time points during imaging in all the three groups. The variation in oxygen saturation was not statistically significant with p value of 0.06, if the comparison of variation was made among the three groups

Figure 6 displays the oxygen saturation changes in all the three groups. In all the three groups oxygen satuation was maintained around baseline. Oxygen saturation variation was not statistically significant (P = 0.06) among the three groups

Table12 compares the adverse events and use of rescue drugs among groups

Events	Group PK	Group P	Group D	P Value
Airway use No of Pts (%)	6 (20)	11(36.7)	4(13.3)	0.08
Shoulder roll use No of Pts (%)	16(53.3)	22(73.3)	19(63.3)	0.275
Incidence of hypotension No of Pts (%)	0(0)	2(6.7)	27(90)	**0.0**#
Rescue drug use No of Pts (%)	0 (0)	3(10)	30(100	**0.0**)≠
Nausea No of Pts(%)	0(0)	0(0)	(0)	NS
Vomiting No of Pts(%)	0(0)	0(0)	0(0)	NS
Seizures No of Pts(%)	0(0)	0(0)	0(0)	NS
Patient requiring admission in hospital(Post imaging)	0(0)	0(0)	0(0)	NS

P Value <0.05

Values entered as number of patients and percentage within the bracket.

Nasal airways were used for 6 patients in Group PK, 11patients in Group P and 4 patients in Group D. The difference between the usage of nasal airway in the three groups were not statistically significant (P value=0.08). Similarly shoulder rolls were used in 16, 22 and 19 patients in Group PK, Group P and Group D respectively. There was no statistical difference between the shoulder roll use between the three groups (P value=0.275)

Twenty seven patients in Group D and two patients in Group P had hypotension during sedation for magnetic resonance imaging,whereas,none of the patients in Group PK had hypotension . The difference between the incidence of hypotension in the three groups were statistically significant (P value=0.00).

All the patients in Group D and three patients in Group-P required midazolam as rescue drug during sedation for magnetic resonance imaging, whereas none of the patients in Group PK required rescue drug. The difference between the requirement of rescue drug in the three groups was statistically significant (P value=0.0). None of the patients in the study had nausea ,vomiting and seizures during the study period. Similarly, none of the patients required hospital admission in the post imaging period. Complications and rescue drug requirement during sedation for magnetic resonance imaging is presented in table 12.

Discussion

Discussion

Our study compared the efficacy of monitored anaesthesia care with three regimens namely propofol, propofol + ketamine and Dexmedetomidine in children with epilepsy undergoing MRI procedures. This is the first study to compare these drug infusions in epileptic patients on antiepileptic therapy.

Though MRI could be completed with all the regimes, all patients, who received dexmedetomidine infusion required rescue midazolam for successful magnetic resonance imaging, whereas none of the patients in Group PK required additional midazolam for uninterrupted imaging. Only three patients in propofol required rescue midazolam for successful conduct of magnetic resonance imaging.Among the patients, who received dexmedetomidine infusion for sedation, 18 patients required one rescue dose of midazolam(50µg/kg) ,whereas 12 patients required rescue midazolam twice (100µg/kg).Our study shows Dexmedetomidine infusion alone is not effective for children undergoing MRI.

Dexmedetomidine has been investigated as an anesthetic for ambulatory radiological procedures inchildren, including MRI. Most of these reports have been case series with wide variations in the dosing regimens and success rates. Christopher heard et al, in a study compared dexmedetomidine-midazolam combination with propofol for maintainence of anesthesia in children undergoing magnetic resonance imaging.[99] But in their study , they excluded patients on anti epileptic therapy.

Dexmedetomidine was compared with midazolam and propofol for MRI in children in randomized, controlled trials. In thecomparison with propofol, the failure rates (as evidenced by movement during the scan) with dexmedetomidine and propofol were 16% and 10%, respectively,the scan times were uncharacteristically brief (25 min) and hemoglobin desaturation occurred in theperioperative period. As a result of the scan failureswith dexmedetomidine, the scans had to be rescheduled. The results of these studies suggested that when dexmedetomidine was administered in accordancewith these study protocols, it did not provideadequate anesthesia for MRI in children.To address the substantial failure rates during MRI

scans, larger doses of dexmedetomidine have been studied for MRI in children. However, many clinicians have been hesitant to administer large doses of dexmedetomidine for these outpatient surgeries as the elimination half-life of dexmedetomidine in childrenis prolonged, approximately 2 h,and there is concern of hypotension and bradycardia.

Manson et al, in their study recommend a high dose of dexmedetomidine (3µg/kg IV loading dose, followed by infusion of 2µg/kg/hr) as a sole sedative for pediatric MRI.[101,102]

We could not escalate our dexmedetomidine dose , because almost 90% of patients in this group had hypotension and received vasopressors.Only 2 patients, who received propofol infusion in propofol group had hypotension,whereas none of the patients in propofol ketamine group had hypotensive episode.

Christopher et al, in their study found more hypotension in the propofol group but they used high dose of propofol,almost twice the dose used in our study.[99] Mohammad Dabis et al, in their study on assessment of different concentration of ketofol for procedural operation found hemodynamic stability with propofol +ketamine combination.[98] Similarly in our study, none of the patients ,who received propofol +ketamine combination for magnetic resonance imaging had hypotensive episode.

In the present study shoulder rolls were used in 16, 22 and 19 patients in Group PK, Group P and Group D respectively. There was no statistical difference between the shoulder roll use between the three groups (P value=0.275).Nasal airways in addition to shoulder roll were used for 6 patients in Group PK, 11patients in Group P and 4 patients in Group D. The difference between the usage of nasal airway in the three groups were not statistically significant (P value=0.08)

In our study shoulder roll was tried initially to relieve the airway obstruction, nasal airway was inserted then, if the stable respiratory pattern was not achieved. We ensured a stable respiratory pattern , before perfoming magnetic resonance scanning.All the patients in our study were managed with these airway support measures, none of the patients required bag mask ventilation or laryngeal mask airway or endotracheal intubation for successful conduct of magnetic resonance imaging.

Machata et al, in their prospective study on propofol-based sedation regimen for 500 infants and children undergoing ambulatory magnetic resonance imaging found respiratory adverse events in five patients (1%).[18] All of their patients suffered from oxygen desaturation(SPO2 <92%). Three children in their study experienced partial airway obstruction, which was treated immediately with slight neck extension and chin support. Two other children in their study required short-time assistanceof spontaneous respiration via bag-valve-mask ventilation and afterwards further reposition of neck and shoulders.Sufficient spontaneous respiration reoccurred in all of their patients, so that MRI scanning could be completed without further airway support. In our study almost 57 patients of total 90 patients(63.33%) required shoulder roll as airway support technique. 23.33% of patients required nasal airway in addition to shoulder roll for maintainance of airway. So we recommend that the physician involved in the sedation for magnetic resonance imaging should anticipate this and necessary equipments should be readily available.

Our study shows that the time to achieve modified aldrette score of eight in the three groups following sedation for magnetic resonance imaging were 12.97±1.426 minutes, 2.60±0.724 minutes and 21.10±5.689 minutes in Group-PK, Group-P and Group-D respectively.The difference between the groups was statistically significant (pvalue-0.00).Hence propofol group had rapid awakening compared to other groups.

Mason et al,in their study on pediatric CT Sedation, comparing dexmedetomidine and pentobarbital used dexmedetomidine at a dose of 2 µg/kg ,followed by infusion at 1µg/kg/hr.[101] They found a recovery time of 32±18 min, as assessed by modified aldrette score . But the present study has demonstrated recovery time of 21.10±5.689 minutes in the dexmedetomidine group.

Christopher et al, in a study comparing the Dexmedetomidine-midazolam combination with propofol for maintainence of anesthesia in children undergoing magnetic resonance imaging used dexmedetomidine infusion at the same dose used in our study.[99] They found a recovery time of 44.2±18 minutes in their patients in dexmedetomidine group. But they used midazolam 0.1mg/kg to all their patients, in addition to dexmedetomidine and they assessed their recovery time by modified aldrette score of 10. But , we assessed recovery time, by modified Aldrette score of 8.

In the same study propofol recovery time was 29.7±11.1 minutes, but their infusion dose of propofol was 250- 300µg/kg/min and they excluded patients on antiepileptic therapy. Our study has shown the recovery time of 2.6±0.724 minutes in patients who received propofol infusion.

JE Cho et al, in their study comparing titrated propofol induction and continuous infusion in children undergoing magnetic resonance imaging found a recovery time of 1 min in patients ,who received propofol infusion for sedation. They used intravenous induction with propofol 2mg/kg given over 30seconds , followed by infusion at 50µg/kg/min. and they excluded patients on anticonvulsant medications.[100]

Dabis et al in their study on assessment of different concentration of ketofol on procedural operation found a recovery time of 8.2±6.7 minutes.[98] In this study the recovery time in patients ,who received propofol+ ketamine infusion were 12.97±1.426 minutes.

Our study is the first study to compare the recovery time in these anaesthetic regimens in peaditric patients on antiepileptic therapy.

To facilitate ambulatory radiological procedures inchildren, the anesthetic prescription should facilitate rapid recovery. Recovery after administration of propofol for MRI in children is rapid, complete andassociated with few complications.Recent pharmacokinetic data for dexmedetomidine

in children indicated that the elimination half-life after a single bolus, 2 h, although similar to that in adults,far exceeds that of propofol (approximately 25min). Consequently, one might expect that recovery after receiving dexmedetomidine may be delayed compared with propofol.One might be tempted to attribute the delay in recovery after dexmedetomidine in this study to the rescue dose of midazolam, although this is unlikely to be the case as 0.1mg/kg of midazolam did not delay recovery after dexmedetomidine in a previous study.

No side effects or complications were attributed toeither anesthetic in this study. None of the patients had seizures during the study period. Nausea and vomiting did not occur after either treatment during the hospital stay or after discharge. The lack of nausea and vomiting after receiving propofol is consistent with its antiemetic action.[99] Whether dexmedetomidine prevents nausea and vomiting cannot be established with any certainty given the small number of children in the group.

The present study has showed that the respiratory rate and oxygen saturation variation between the three groups as statistically not significant(P value-0.08 and 0.09).Christopher et al in their study comparing dexmedetomidine-midazolam with propofol for maintenance of anesthesia in children undergoing magnetic resonance imaging found that respiratory responses to both dexmedetomidine-midazolam and propofol were similar and unchanged over time.[99] In the same study they found that the heart rate at all

times in the dexmedetomidine group was significantly less than baseline , whereas heart rate in the propofol group did not differ significantly from

baseline at any time. In our study ,we found that the heart rate variation from baseline was more in patients who received dexmedetomidine ,whereas there was no significant variation from baseline in patients who received propofol and propofol- ketamine.The hemodynamic responses to dexmedetomidine

and propofol have been documented. Decrease in heart rate have been reported over time with dexmedetomidine in children. Our results are consistent with those data. However, there were no instances of bradycardia requiring treatment in this study.

Limitations of the Study:

Among the limitations of this study, the time to onset of the anesthesia with dexmedetomidine, propofol and propofol-ketamine could not be evaluated because we induced anesthesia with an inhaled induction with sevoflurane. We do not believe that sevoflurane affected the success rate of the MRI scans as the exposure to sevoflurane was brief and the solubility of sevoflurane is very small. The advantages of inducing anesthesia by inhalation in children include the ability to establish IVaccess after the child is anesthetized and that the residual sevoflurane could bridge the interval between recovery from the initial loading dose of study drug and start of the infusion. In addition,residual sevoflurane may have bridged the need for an induction dose of propofol, thereby reducing the risk of apnea during transition to the propofol infusion. Disadvantages of this technique include the exclusion of non anesthesiology practitioners from using it, as they are not qualified to administer inhaled anesthesia.

We could not monitor sedation level during imaging, by bispectral index(BIS), because of non availability of MRI compatible BIS monitor and we monitored sedation level during imaging by ramsay sedation score.

Although, none of our patients had seizures, there is a substantial risk of seizures, because of drug interactions, in sedating these patients for magnetic resonance imaging.

The external validity of this study is limited, because we studied, only patients on anti epileptic therapy.

So to conclude, dexmedetomidine as sole sedative required more rescue midazolam than propofol and propofol+ketamine for successful conduct of magnetic resonance scanning in patients on antiepileptic therapy. Dexmedetomidine infusion was associated with more hypotension, greater heart rate variability and greater recovery time than patients receiving propofol and propofol +ketamine for magnetic resonance imaging in patients on anti epileptic therapy.We included only 30 patients in each group, so its validity need to be confirmed by large scale studies.

Conclusion

Conclusion

Our study was the first to compare the efficacy of propofol or propofol with ketamine or dexmedetomidine for monitored anaesthesia care in pediatric patients with epilepsy undergoing MRI procedure. Our study shows that dexmedetomidine alone was not useful and all the patients receiving dexmedetomidine required supplemental midazolam for rescue sedation. In addition, patients receiving dexmedetomidine recovered late compared to the other two regimes. Between propofol alone or propofol+ketamine groups, few patients in propofol alone required midazolam, these patients can otherwise be managed by increasing the dose of propofol infusion. Propofol alone group has the best recovery time compared to propofol+ ketamine group.There was no significant differences in the incidence of adverse effects between propofol and propofol+ ketamine group. Hence both the regimes of propofol and propofol+ketamine combination can be useful for sedation in pediatric patients with epilepsy undergoing MRI procedures.

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Appendix

Abbreviations

NIBP: Non invasive blood pressure

RSS: Ramsay sedation score

MAS: Modified Aldrette score

MRI: Magnetic resonance imaging

AED : Antiepileptic drug

CYP450 : CytochromeP-450

UGT: UDP-glucuronosyltransferase

SPO2: Pulse oximetry

RR: Respiratory rate

HR: Heart rate

LMA: Larngeal mask airway

Group PK: Propofol+ketamine group

Group P: Propofol group

GroupD: Dexmedetomidine group

Modified Aldrette Score

Activity level

2- Moves all limbs on command.

1-Moves only 2 limbs.

0- Not moving.

Respiration

2-Breathes deeply &coughs freely.

1- Dysponoeic& shallow limited breathing.

0- Apnoeic.

Circulation

2-SBP upto 20mmHg↑ to baseline.

1-20 to 50mmHg↑.

0- >50mmHh↑.

Consciousness

2-Fully awake.

1-Arousable on calling.

0-Not responding.

SPO_2

2- >90% on room air.

1- Requires oxygen to maintain >90%.

0- <90%, even with oxygen supplementation.

Ramsay Sedation Scale

1.Ptawake,anxious or restless or both.

2.Pt awake, cooperative,oriented and tranquil.

3.Ptawake,responds to command only.

4.Ptasleep,brisk response to light glabellar tap or loud auditory stimulus.

5. Ptasleep,sluggish response to light glabellar tap or loud auditory stimulus.

6.Ptasleep,brisk response to light glabellar tap or loud auditory stimulus.

Proforma

Name:Age/sex:Diagnosis:Wt:Hosp no:

1.**Parameters noted:**

Parameters/Time	Baseline (after sevo,before IV line													
HR(beats/min)														
NIBP (mmHg)														
SPO2(%)														
RR (b/min)														
Rescue drug														
Ptmovt Yes/ No														
Episodes of Desaturation <92%(1/2/3)														
Use of airway Yes/ No														
Use of shoulder roll. Yes/No														
Use of LMA Yes/No														

2.MRI completion time:

3.Time of arrival in recovery room:

4.Time to achieve modified Aldrette score 8:

5.Mephetramine used/dose:

6.Nausea / vomiting : Yes □ No □.

7.Other events:

8.Drugs :

.

Master chart Group PK

Patient No	Name	age	weight	Gender	Diagnosis
1	Anandasudevan(PK)	4	12	Male	cps
2	rupali	8	28	Female	seizures with GDD
3	Sivaganga	2	14	Male	cps
4	Anoop	9	32	Male	static encephalopathy
5	muhammadbilal	4	18	Male	cps
6	Abhiram	6	24	Male	LGsyndrome
7	JessKJoby	10	32	Male	post encephalitis MCA stoke
8	Mishal G Mariya	3.4	17	Female	
9	KrupavipaulVekari	11	32	Female	CPS
10	shloksurendrayelwe	6.5	24	Male	cps
11	sradha	6	24	Female	GDD static encephalopathy
12	chandru	4	18	Male	Hydrocephalus with seizures
13	Devuashoks	12	35	Male	CPS
14	Nethulpramod	8	26	Male	seizure for evaluation
15	RoneSThomas	8	26	Male	seizures for evaluation
16	Amanibrahim	7	24	Male	seizure for evaluation
17	Nautami Ajay panchal	8.1	32	Female	Lt temporal glioma
18	Dhayandev	3	15	Male	CPS
19	Abijit	8	28	Male	CPS
20	Vigneshwaran	8	24	Male	encepalomalacia
21	Nandanasuresh	6	24	Female	tuberculoma
22	AjithKBiju	7.7	26	Male	mitochondrial encephalopathy
23	Gauthamshibu	7	22	Male	CPS
24	Adityakrishnan	2	14	Male	Frontal DNET
25	RiyaFathima	2	14	Female	Sympotamatic west syn
26	Mithra	2	14	Female	static encephalopathy
27	Nandana	7	22	Female	cps
28	Shobna	7	22	Female	cps
29	Chandan das	8	26	Male	cps
30	Riyaaju john	3	16	Female	optic tract glioma

Blood pressure changes

Pt No	NIBP_s 0	NIBP_d 0	NIBP_mo	NIBP_s 1	NIBP_d1	NIBP_m1	NIBP2	NIBP_d2	NIBP_m2	NIBP3	NIBP_d3	NIBP_m3	NIBP4	NIBP_d4	NIBP_m4	NIBP5	NIBP_d5	NIBP_m5	NIBP6	NIBP_d6	NIBP_m6	NIBP7	NIBP_d7	NIBP_m7
1	90	60	70	92	64	73.3	84	54	64	88	52	64.0	84	48	60.0	88	50	62.7	84	54	64.0	82	52	62.0
2	76	37	50.0	79	40	53.0	76	42	53.3	77	38	51.0	75	44	54.3	79	40	53.0	80	40	53.3	82	42	55.3
3	80	50	60.0	82	50	60.7	84	48	60.0	82	52	62.0	84	42	56.0	84	50	61.3	84	48	60.0	82	44	56.7
4	110	70	83.3	116	72	86.7	112	74	86.7	110	74	86.0	112	76	88.0	108	72	84.0	110	70	83.3	112	72	85.3
5	80	40	53.3	82	40	54.0	82	42	55.3	80	40	53.3	82	40	54.0	86	44	58.0	80	40	53.3	82	42	55.3
6	83	44	57.0	82	44	56.7	80	40	53.3	83	40	54.3	82	48	59.3	80	40	53.3	83	44	57.0	86	46	59.3
7	115	86	95.7	107	85	92.3	102	84	90.0	110	84	92.7	112	82	92.0	110	80	90.0	112	84	93.3	110	82	91.3
8	70	40	50.0	72	40	50.7	71	41	51.0	78	42	54.0	77	50	59.0	76	40	52.0	78	42	54.0	80	42	54.7
9	84	50	61.3	88	52	64.0	84	50	61.3	80	50	60.0	82	48	59.3	84	50	61.3	82	48	59.3	84	50	61.3
10	107	81	89.7	103	70	81.0	102	58	72.7	107	55	72.3	103	60	74.3	102	70	80.7	100	68	78.7	104	70	81.3
11	114	74	87.3	106	53	70.7	108	52	70.7	110	70	83.3	112	70	84.0	112	72	85.3	108	70	82.7	102	54	70.0
12	103	62	75.7	107	60	75.7	98	62	74.0	101	59	73.0	95	62	73.0	103	62	75.7	100	60	73.3	95	62	73.0
13	89	54	65.7	95	52	66.3	93	51	65.0	86	44	58.0	89	43	58.3	85	47	59.7	98	47	64.0	103	52	69.0
14	84	40	54.7	76	32	46.7	74	32	46.0	80	34	49.3	86	32	50.0	75	36	49.0	84	40	54.7	76	32	46.7
15	84	40	54.7	79	40	53.0	80	40	53.3	76	32	46.7	82	40	54.0	84	48	60.0	84	40	54.7	80	40	53.3
16	92	40	57.3	93	48	63.0	92	40	57.3	96	40	58.7	93	42	59.0	96	60	72.0	92	58	69.3	90	54	66.0
17	100	60	73.3	102	58	72.7	104	60	74.7	104	58	73.3	100	60	73.3	106	60	75.3	103	70	81.0	104	72	82.7
18	83	40	54.3	80	40	53.3	82	48	59.3	85	42	56.3	90	46	60.7	88	46	60.0	82	42	55.3	90	48	62.0
19	84	44	57.3	82	40	54.0	82	44	56.7	93	40	57.7	92	42	58.7	82	40	54.0	82	48	59.3	92	48	62.7
20	95	52	66.3	93	40	57.7	89	40	56.3	92	42	58.7	90	44	59.3	93	44	60.3	90	40	56.7	92	46	61.3
21	104	63	76.7	102	64	76.7	100	60	73.3	102	68	79.3	104	63	76.7	103	44	63.7	110	70	83.3	103	44	63.7
22	98	62	74.0	99	60	73.0	100	60	73.3	102	60	74.0	98	62	74.0	98	64	75.3	100	60	73.3	98	62	74.0
23	106	67	80.0	110	70	83.3	100	60	73.3	102	64	76.7	103	68	79.7	104	68	80.0	100	62	74.7	100	60	73.3
24	84	44	57.3	88	42	57.3	86	46	59.3	90	48	62.0	88	42	57.3	88	48	61.3	90	52	64.7	88	50	62.7
25	84	43	56.7	82	44	56.7	80	40	53.3	86	46	59.3	80	46	57.3	90	50	63.3	92	50	64.0	90	48	62.0
26	71	34	46.3	72	36	48.0	76	32	46.7	78	40	52.7	71	34	46.3	77	34	48.3	72	36	48.0	70	40	50.0
27	102	68	79.3	108	72	84.0	112	64	80.0	118	64	82.0	108	70	82.7	100	60	73.3	114	70	84.7	100	60	73.3
28	84	48	60.0	86	40	55.3	93	48	63.0	86	42	56.7	86	50	62.0	84	48	60.0	90	52	64.7	90	48	62.0
29	90	54	66.0	94	55	68.0	100	54	69.3	98	59	72.0	99	54	69.0	98	60	72.7	103	52	69.0	112	59	76.7
30	78	54	62.0	76	50	58.7	81	49	59.7	85	52	63.0	84	48	60.0	82	46	58.0	85	52	63.0	80	50	60.0

Heart rate, SpO2 and respiratory rate changes :

Pt No	HR0	HR1	HR2	HR3	HR4	HR5	HR6	HR7	Sat0	sat1	sat2	sat3	sat4	sat5	sat6	sat7	RR0	RR1	RR2	RR3	RR4	RR5	RR6	RR7
1	100	104	102	106	104	100	104	106	100	99	99	99	99	99	99	99	18	16	18	16	20	22	20	20
2	60	61	63	60	62	64	62	64	99	98	98	98	98	98	98	99	14	16	14	20	22	16	20	22
3	72	74	72	74	75	75	74	75	99	98	98	99	99	99	99	99	18	14	20	22	24	25	28	20
4	80	84	86	86	88	85	88	86	100	100	100	100	100	100	99	99	16	16	14	20	22	18	20	22
5	85	84	88	82	84	86	88	90	100	100	100	100	100	100	100	99	20	18	22	24	22	16	18	20
6	89	90	92	94	90	92	94	96	100	100	100	100	100	100	100	99	18	14	20	22	24	25	24	22
7	50	60	62	56	55	55	54	58	99	99	99	99	99	99	99	99	14	14	16	18	16	18	20	22
8	106	100	98	102	107	103	101	100	100	99	99	99	99	99	99	99	16	14	20	22	20	24	26	24
9	85	82	82	82	80	82	80	84	100	100	100	100	100	100	100	99	22	20	18	18	22	24	26	20
10	72	73	70	74	78	80	82	84	99	99	99	98	99	99	99	98	16	16	14	12	12	14	16	16
11	72	78	80	74	78	70	68	70	100	99	98	99	98	99	98	99	16	15	14	16	15	16	14	18
12	100	99	97	89	92	94	96	100	100	100	98	99	98	99	98	99	24	22	18	20	20	22	18	18
13	76	80	82	82	84	86	84	90	100	99	98	98	99	99	98	99	14	16	20	20	22	20	20	18
14	84	74	76	70	68	72	70	84	100	99	98	99	98	99	98	99	24	20	22	24	22	20	24	22
15	84	82	84	80	84	88	78	75	100	99	99	99	99	99	99	99	24	26	28	30	28	24	22	26
16	90	84	82	88	84	82	88	88	100	99	100	100	100	100	100	99	24	28	26	24	26	22	24	26
17	92	88	86	90	94	90	92	94	100	99	100	100	100	100	100	99	24	22	20	22	22	20	22	20
18	92	90	92	94	88	86	90	92	99	99	99	99	99	99	99	99	28	26	24	28	26	28	22	26
19	64	68	70	66	62	64	66	68	99	99	99	99	99	99	99	99	25	28	26	22	24	22	22	24
20	95	94	96	92	90	94	94	94	99	99	99	98	99	99	98	99	24	22	24	22	24	25	22	28
21	98	96	94	96	94	98	96	92	99	99	98	99	99	99	99	99	22	24	22	24	24	24	22	22
22	84	82	84	80	88	88	84	88	99	99	99	99	99	99	99	99	18	18	20	18	20	20	20	20
23	106	104	102	102	100	102	106	99	99	99	99	99	98	99	100	99	30	28	26	28	30	30	28	30
24	92	94	92	96	98	88	86	84	99	98	99	98	97	98	98	99	16	15	14	14	12	16	16	14
25	82	83	85	80	78	78	74	72	99	99	100	98	99	99	99	99	24	25	24	22	20	22	24	22
26	70	84	82	84	88	86	82	80	99	99	99	99	99	99	99	98	23	22	22	20	24	22	22	22
27	78	74	72	80	84	88	92	90	99	98	99	98	99	98	99	99	24	20	22	24	26	20	24	24
28	94	98	96	90	92	90	96	99	100	100	100	99	99	99	99	99	28	24	20	18	20	22	20	20
29	84	80	82	80	82	83	86	90	100	99	98	99	98	99	99	99	16	14	14	16	14	16	18	16
30	68	64	66	68	72	70	68	60	100	100	100	100	100	100	100	100	16	14	14	14	16	14	14	16

Complications and rescue drug use

Pt No	desatepisode	airwayuse	shoulderrolluse	LMAuse	MRItime	MAS8time	Adverseevents	Rescue
1	nil	nil	nil	nil	75	15	nil	nil
2	nil	nil	yes	nil	65	14	nil	nil
3	nil	nil	yes	nil	75	14	nil	nil
4	nil	nil	nil	nil	65	13	nil	nil
5	nil	nil	nil	nil	65	13	nil	nil
6	nil	nil	yes	nil	60	12	nil	nil
7	nil	nil	yes	nil	60	13	nil	nil
8	nil	yes	yes	nil	60	13	nil	nil
9	nil	nil	yes	nil	65	14	nil	nil
10	nil	nil	yes	nil	60	12	nil	nil
11	nil	yes	yes	nil	75	13	nil	nil
12	nil	nil	nil	nil	70	13	nil	nil
13	nil	nil	yes	nil	70	10	nil	nil
14	nil	nil	nil	nil	75	12	nil	nil
15	nil	nil	nil	nil	70	15	nil	nil
16	nil	nil	nil	nil	70	15	nil	nil
17	nil	nil	nil	nil	65	12	nil	nil
18	nil	nil	yes	nil	75	13	nil	nil
19	nil	yes	yes	nil	70	14	nil	nil
20	nil	yes	yes	nil	70	12	nil	nil
21	nil	yes	yes	nil	70	13	nil	nil
22	nil	nil	nil	nil	75	12	nil	nil
23	nil	nil	nil	nil	70	13	nil	nil
24	nil	nil	nil	nil	70	10	nil	nil
25	nil	nil	nil	nil	60	12	nil	nil
26	nil	nil	nil	nil	60	13	nil	nil
27	nil	nil	yes	nil	70	15	nil	nil
28	nil	yes	yes	nil	75	14	nil	nil
29	nil	nil	yes	nil	70	10	nil	nil
30	nil	nil	nil	nil	75	15	nil	nil

Master chart Group P :

Patient No	Name	age	weight	Gender	Diagnosis
1	Ayisharizam	4	18	Female	cerebellar astrocytoma
2	Altaf	8	32	Male	cps
3	Mariya David	10	40	Female	cps
4	Ahsana	9	36	Female	recurrent seizures
5	Anila SR	9	36	Female	cortical dysplasia
6	Figo	1	5	Female	post encephalitic sequalae
7	Nehajan	6	24	Female	seizure disorder
8	Abinavdarsan	3	16	Male	global developmental delay
9	Alsabithajas	5	20	Male	ststic encephalopathy
10	Dineshwaran	1	5	Male	west syndrome
11	Abin	2	14	Male	cps
12	Harikrishnan	7	28	Male	cps
13	Archana	3	32	Female	symp LGS
14	VaneshYadav	4	18	Male	cps
15	Ayyapadas	3	16	Male	neurometabolic syndrome
16	Joyel	4	18	Male	rasmussen encephalitis
17	Gautamkrishna	8	32	Male	seizure disorder
18	Aleyavinod	2.5	15	Female	cps
19	ShahidNafees	3	16	Male	MCF arachanoid cyst
20	Janaki	4	18	Female	focal seizures
21	Mithilesh	2	14	Male	IC tuberculosis
22	Neelambaripradeep	3	16	Female	cps
23	Anusree	4	18	Female	cps
24	Susan antony	8	32	Female	global devolp delay
25	Jeevithaharishini	6	22	Female	cerebellar astrocytoma
26	Amirthaudayam	6	20	Female	cps
27	Aaronarum	5	20	Male	cps
28	Antonpaulsaju	5	18	Male	cps
29	Jishnu	10	36	Male	cps
30	Hariharan	10	36	Male	cps

Blood pressure changes

Pt No	NIBP _s 0	NIBP_ d 0	NIBP_ mo	NIBP _s 1	NIBP _d1	NIBP _m1	NIBP 2	NIBP _d2	NIBP_ m2	NIB P3	NIBP _d3	NIBP_ m3	NIB P4	NIBP _d4	NIBP_ m4	NIB P5	NIBP _d5	NIBP_ m5	NIB P6	NIBP _d6	NIBP_ m6	NIB P7	NIBP _d7	NIBP_ m7
1	103	64	77.0	105	61	75.7	96	57	70.0	98	55	69.3	97	55	69.0	100	61	74.0	103	55	71.0	105	51	69.0
2	96	54	68.0	93	46	61.7	92	40	57.3	101	48	65.7	94	48	63.3	94	56	68.7	95	50	65.0	101	48	65.7
3	104	68	80.0	102	70	80.7	110	58	75.3	104	48	66.7	110	68	82.0	103	72	82.3	100	60	73.3	102	62	75.3
4	103	64	77.0	105	61	75.7	100	58	72.0	99	56	70.3	98	60	72.7	100	60	73.3	103	64	77.0	100	60	73.3
5	110	68	82.0	103	48	66.3	104	50	68.0	110	70	83.3	102	48	66.0	103	68	79.7	104	50	68.0	110	68	82.0
6	82	48	59.3	80	42	54.7	82	50	60.7	83	48	59.7	80	40	53.3	80	42	54.7	80	42	54.7	82	50	60.7
7	96	54	68.0	93	58	69.7	90	48	62.0	92	56	68.0	90	60	70.0	92	54	66.7	90	48	62.0	92	50	64.0
8	92	48	62.7	90	42	58.0	88	42	57.3	92	50	64.0	93	52	65.7	94	52	66.0	94	52	66.0	90	50	63.3
9	92	44	60.0	90	42	58.0	94	48	63.3	95	50	65.0	95	50	65.0	92	56	68.0	88	52	64.0	95	50	65.0
10	83	42	55.7	84	48	60.0	82	50	60.7	88	50	62.7	83	52	62.3	85	50	61.7	83	52	62.3	88	50	62.7
11	74	50	58.0	83	50	61.0	74	42	52.7	75	56	62.3	82	48	59.3	80	40	53.3	72	50	57.3	74	50	58.0
12	103	42	62.3	104	40	61.3	103	48	66.3	93	54	67.0	102	50	67.3	94	48	63.3	92	50	64.0	94	48	63.3
13	82	46	58.0	74	48	56.7	84	48	60.0	80	42	54.7	82	50	60.7	82	48	59.3	78	48	58.0	82	50	60.7
14	92	48	62.7	93	46	61.7	94	48	63.3	88	52	64.0	92	50	64.0	92	50	64.0	94	48	63.3	90	54	66.0
15	86	54	64.7	88	52	64.0	92	50	64.0	84	48	60.0	85	50	61.7	90	54	66.0	92	50	64.0	90	52	64.7
16	96	52	66.7	94	48	63.3	90	42	58.0	92	50	64.0	93	46	61.7	95	50	65.0	88	52	64.0	90	50	63.3
17	93	42	59.0	90	40	56.7	88	52	64.0	86	50	62.0	88	52	64.0	90	44	59.3	93	40	57.7	90	42	58.0
18	84	48	60.0	83	40	54.3	84	48	60.0	80	42	54.7	93	40	57.7	88	52	64.0	90	44	59.3	94	48	63.3
19	83	40	54.3	94	48	63.3	96	54	68.0	92	58	69.3	94	50	64.7	92	48	62.7	90	40	56.7	82	46	58.0
20	103	48	66.3	102	50	67.3	96	54	68.0	98	52	67.3	100	54	69.3	102	48	66.0	104	50	68.0	103	48	66.3
21	112	48	69.3	103	48	66.3	100	50	66.7	106	48	67.3	104	50	68.0	102	50	67.3	100	50	66.7	102	52	68.7
22	102	70	80.7	103	68	79.7	104	49	67.3	110	60	76.7	100	68	78.7	103	68	79.7	104	50	68.0	102	68	79.3
23	102	68	79.3	94	56	68.7	94	40	58.0	106	48	67.3	102	70	80.7	100	68	78.7	103	70	81.0	106	50	68.7
24	100	60	73.3	90	48	62.0	102	62	75.3	104	68	80.0	100	62	74.7	102	64	76.7	100	60	73.3	100	60	73.3
25	94	58	70.0	83	40	54.3	84	48	60.0	90	42	58.0	88	54	65.3	90	52	64.7	88	54	65.3	92	54	66.7
26	92	48	62.7	83	40	54.3	86	48	60.7	81	52	61.7	90	46	60.7	92	54	66.7	92	48	62.7	92	54	66.7
27	84	48	60.0	83	40	54.3	84	48	60.0	80	42	54.7	93	40	57.7	88	52	64.0	90	44	59.3	84	48	60.0
28	82	48	59.3	80	42	54.7	82	50	60.7	83	48	59.7	80	40	53.3	80	42	54.7	82	48	59.3	84	50	61.3
29	92	40	57.3	90	40	56.7	94	48	63.3	90	42	58.0	92	50	64.0	90	44	59.3	94	40	58.0	92	50	64.0
30	94	42	59.3	92	42	58.7	92	46	61.3	88	40	56.0	90	48	62.0	88	42	57.3	92	38	56.0	90	48	62

Heart rate, SpO2 and respiratory rate changes :

Pt No	HR0	HR1	HR2	HR3	HR4	HR5	HR6	HR7	Sat0	sat1	sat2	sat3	sat4	sat5	sat6	sat7	RR0	RR1	RR2	RR3	RR4	RR5	RR6	RR7
1	82	80	78	76	72	75	75	73	100	99	98	99	98	99	98	98	16	14	14	16	16	18	16	14
2	84	80	82	88	78	82	82	84	100	99	98	99	99	98	99	99	22	20	18	18	20	22	22	18
3	88	86	84	84	84	80	82	80	100	99	99	98	99	98	99	99	24	22	24	20	22	20	20	22
4	88	86	84	80	84	84	80	82	99	99	99	99	99	99	99	99	22	24	20	22	22	24	24	22
5	100	98	96	92	102	98	96	99	99	99	99	99	99	99	99	99	20	22	24	24	22	22	20	24
6	98	96	98	99	96	98	90	98	99	99	99	99	99	99	99	99	24	28	22	26	24	28	22	26
7	96	98	96	99	100	102	92	90	100	100	98	99	99	99	99	99	20	18	16	20	22	20	22	20
8	98	90	88	92	94	94	96	96	99	99	99	98	97	98	98	99	24	22	22	22	20	24	24	22
9	94	100	98	102	100	102	104	98	100	99	99	99	98	99	99	99	18	16	20	22	22	20	20	22
10	98	94	92	88	82	86	96	94	100	99	98	97	99	99	98	99	24	22	20	24	22	22	20	24
11	74	82	80	86	80	82	84	72	100	100	100	100	100	100	99	99	28	26	24	26	22	24	22	26
12	102	104	102	100	106	100	96	98	100	99	99	99	98	99	98	99	20	18	16	16	18	20	20	22
13	98	96	94	90	90	92	99	94	99	98	99	99	99	99	99	98	20	24	22	22	24	20	22	24
14	94	90	88	88	84	90	92	98	100	99	99	99	99	98	99	98	24	28	22	24	22	24	20	24
15	110	108	106	104	104	98	94	100	99	98	97	97	98	97	97	97	28	24	26	26	24	22	24	24
16	100	108	110	110	114	112	106	104	98	97	98	98	98	98	98	99	24	22	26	24	22	24	20	22
17	110	114	112	116	120	104	108	106	98	97	97	97	97	97	98	99	24	22	20	24	22	22	24	22
18	88	94	92	98	96	86	84	80	99	99	99	98	99	98	99	99	28	18	20	22	24	24	22	20
19	98	100	98	102	104	98	96	99	99	98	99	97	98	99	98	99	16	18	20	22	24	20	18	18
20	84	80	78	88	82	84	90	94	99	99	99	99	99	99	98	99	16	18	16	14	18	18	20	22
21	94	98	96	96	90	88	84	86	98	98	97	96	97	97	97	99	24	22	20	18	22	20	24	22
22	78	88	86	84	82	88	78	80	99	99	99	99	99	99	98	98	20	20	22	28	24	22	20	20
23	84	82	80	80	88	90	92	84	99	98	98	98	98	99	98	98	20	22	22	24	20	20	26	24
24	94	96	98	99	100	96	98	100	99	98	98	97	99	99	99	99	18	16	14	18	20	22	20	22
25	74	78	76	64	72	74	72	74	100	99	98	99	99	99	99	99	24	22	20	26	24	22	22	20
26	100	102	100	102	104	98	96	98	100	100	99	98	99	99	99	98	24	26	24	22	24	24	22	26
27	88	94	92	98	96	86	84	80	100	100	99	98	99	99	99	99	24	22	20	22	26	24	24	22
28	72	74	72	82	86	80	82	84	100	99	98	99	98	99	98	99	20	18	18	16	18	16	20	22
29	80	84	86	88	94	92	88	78	100	100	100	99	99	99	99	99	20	24	26	22	24	28	20	22
30	82	86	88	90	92	90	86	80	100	99	99	99	99	99	99	99	22	22	24	20	22	26	18	20

Complications and rescue drug use

Pt No	desatepisode	airwayuse	shoulderrolluse	LMAuse	MRItime	MAS8time	Adverseevents	Rescue
1	NIL	YES	YES	NIL	75	4	NIL	NIL
2	NIL	NIL	YES	NIL	70	2	NIL	NIL
3	NIL	YES	YES	NIL	65	3	NIL	NIL
4	NIL	NIL	YES	NIL	60	2	NIL	NIL
5	NIL	YES	YES	NIL	75	2	NIL	NIL
6	NIL	NIL	YES	NIL	70	4	NIL	NIL
7	NIL	YES	YES	NIL	65	2	NIL	NIL
8	NIL	NIL	YES	NIL	70	4	NIL	NIL
9	NIL	YES	YES	NIL	75	2	NIL	NIL
10	NIL	YES	YES	NIL	70	2	NIL	NIL
11	NIL	NIL	YES	NIL	75	2	V1	YES
12	NIL	YES	YES	NIL	75	3	V1	YES
13	NIL	YES	YES	NIL	70	2	NIL	NIL
14	NIL	YES	YES	NIL	75	3	NIL	NIL
15	NIL	NIL	YES	NIL	70	2	NIL	NIL
16	NIL	NIL	YES	NIL	65	3	NIL	NIL
17	NIL	NIL	NIL	NIL	60	2	NIL	NIL
18	NIL	NIL	NIL	NIL	70	2	NIL	NIL
19	NIL	NIL	NIL	NIL	75	3	NIL	NIL
20	NIL	NIL	YES	NIL	70	2	NIL	NIL
21	NIL	NIL	YES	NIL	65	2	NIL	NIL
22	NIL	NIL	NIL	NIL	70	3	NIL	NIL
23	NIL	NIL	NIL	NIL	75	3	NIL	NIL
24	NIL	NIL	YES	NIL	60	2	NIL	NIL
25	NIL	NIL	YES	NIL	60	2	NIL	NIL
26	NIL	NIL	NIL	NIL	75	3	NIL	NIL
27	NIL	YES	YES	NIL	70	3	NIL	NIL
28	NIL	YES	YES	NIL	60	2	NIL	NIL
29	NIL	NIL	NIL	NIL	70	3	NIL	YES
30	NIL	NIL	NIL	NIL	65	4	NIL	NIL

Master chart Group D

Patient No	Name	age	weight	Gender	Diagnosis
1	Nivedita(D)	6	22	Female	Rt frontal DNET
2	Anju	10	40	Female	Focal cortical dysplasia
3	Roopesh	3	16	Male	cps
4	Afnafathima	1	5	Female	porencephalic cyst
5	Shalbin	5	20	Male	cps
6	Sanjay nai	7	26	Male	cps
7	Subham Thakur	8	30	Male	cps
8	Tobin john	12	48	Male	cps
9	Sreehari	3	16	Male	Global DDD
10	Godwin	4	18	Male	cps
11	Dhrupad vipin	5	20	Male	cps
12	Yadesh	6	24	Male	cps
13	Athul	7	28	Male	myoclonic seizures
14	Jagan	4	18	Male	cps
15	Gowri	8	30	Female	occipital encephalopathy
16	Kasimkunju	7	25	Male	cps
17	Afseenazad	2	12	Male	static encephalopathy
18	Veda krishnan	2	12	Male	Cps
19	Sandra elizabeth	8	32	Female	seizure disorder
20	Nauttami	9	33	Female	cps
21	Prammanathan	1	6	Male	seizure
22	Mithilesh	2	15	Male	static encephalopathy
23	Vijayalakshmi	1	6	Female	Hydrocephalus with seizures
24	Ethan babu	1	7	Male	static encephalopathy
25	Antony kebish	4	15	Male	static encephalopathy
26	Ananthakrishnan	12	40	Male	cps
27	Nithin	4	18	Male	developmental delay
28	Asim	2	15	Female	frontal lobe epilepsy
29	Vyga	4	17	Female	cps
30	Pranav	4	17	Male	cps

Blood pressure changes

Pt No	NIBP_s 0	NIBP_d 0	NIBP_mo	NIBP_s 1	NIBP_d1	NIBP_m1	NIBP2	NIBP_d2	NIBP_m2	NIBP3	NIBP_d3	NIBP_m3	NIBP4	NIBP_d4	NIBP_m4	NIBP5	NIBP_d5	NIBP_m5	NIBP6	NIBP_d6	NIBP_m6	NIBP7	NIBP_d7	NIBP_m7
1	92	40	57.3	83	44	57.0	80	40	53.3	72	38	49.3	70	40	50.0	72	42	52.0	74	44	54.0	72	42	52.0
2	90	40	56.7	88	42	57.3	82	40	54.0	80	40	53.3	92	50	64.0	83	50	61.0	84	50	61.3	93	40	57.7
3	84	40	54.7	80	42	54.7	72	42	52.0	70	40	50.0	82	42	55.3	80	40	53.3	70	40	50.0	72	42	52.0
4	92	50	64.0	88	50	62.7	84	40	54.7	82	50	60.7	74	40	51.3	72	40	50.7	82	50	60.7	72	48	56.0
5	90	48	62.0	92	50	64.0	82	40	54.0	80	42	54.7	73	40	51.0	70	42	51.3	72	46	54.7	82	50	60.7
6	108	72	84.0	100	60	73.3	84	40	54.7	80	40	53.3	82	44	56.7	80	44	56.0	76	50	58.7	74	40	51.3
7	94	48	63.3	82	50	60.7	84	40	54.7	70	42	51.3	68	38	48.0	74	40	51.3	74	40	51.3	72	42	52.0
8	108	68	81.3	100	60	73.3	94	50	64.7	72	50	57.3	74	48	56.7	84	48	60.0	74	42	52.7	74	50	58.0
9	92	42	58.7	84	40	54.7	75	50	58.3	64	38	46.7	74	40	51.3	72	48	56.0	70	38	48.7	72	40	50.7
10	94	42	59.3	80	42	54.7	68	38	48.0	70	40	50.0	72	42	52.0	76	42	53.3	70	42	51.3	68	42	50.7
11	86	40	55.3	84	40	54.7	80	38	52.0	70	36	47.3	66	36	46.0	72	40	50.7	68	38	48.0	74	40	51.3
12	96	52	66.7	94	50	64.7	70	44	52.7	66	38	47.3	72	42	52.0	70	40	50.0	72	42	52.0	82	44	56.7
13	90	40	56.7	88	42	57.3	82	40	54.0	80	40	53.3	92	50	64.0	83	50	61.0	84	50	61.3	93	40	57.7
14	90	40	56.7	88	42	57.3	82	40	54.0	80	40	53.3	92	50	64.0	83	50	61.0	84	50	61.3	93	40	57.7
15	98	42	60.7	88	40	56.0	80	38	52.0	78	36	50.0	74	40	51.3	72	42	52.0	78	38	51.3	78	40	52.7
16	92	54	66.7	80	38	52.0	74	36	48.7	88	40	56.0	72	40	50.7	68	38	48.0	74	40	51.3	72	40	50.7
17	92	40	57.3	90	40	56.7	94	48	63.3	90	42	58.0	92	50	64.0	90	44	59.3	94	40	58.0	92	50	64.0
18	92	40	57.3	83	44	57.0	80	40	53.3	72	38	49.3	70	40	50.0	72	42	52.0	74	44	54.0	72	42	52.0
19	92	50	64.0	88	50	62.7	84	40	54.7	82	50	60.7	74	40	51.3	72	40	50.7	82	50	60.7	72	48	56.0
20	90	40	56.7	88	42	57.3	82	40	54.0	80	40	53.3	92	50	64.0	83	50	61.0	84	50	61.3	93	40	57.7
21	84	40	54.7	80	42	54.7	72	42	52.0	70	40	50.0	82	42	55.3	80	40	53.3	70	40	50.0	72	42	52.0
22	92	50	64.0	84	48	60.0	80	42	54.7	69	42	51.0	72	38	49.3	70	44	52.7	72	42	52.0	70	38	48.7
23	90	48	62.0	82	46	58.0	78	40	52.7	68	40	49.3	70	36	47.3	68	42	50.7	70	40	50.0	68	36	46.7
24	84	40	54.7	80	42	54.7	72	42	52.0	70	40	50.0	82	42	55.3	80	40	53.3	70	40	50.0	72	42	52.0
25	98	42	60.7	88	40	56.0	80	38	52.0	78	36	50.0	74	40	51.3	72	42	52.0	78	38	51.3	78	40	52.7
26	108	68	81.3	100	60	73.3	94	50	64.7	72	50	57.3	74	48	56.7	84	48	60.0	74	42	52.7	74	50	58.0
27	94	42	59.3	80	42	54.7	68	38	48.0	70	40	50.0	72	42	52.0	76	42	53.3	70	42	51.3	68	42	50.7
28	84	40	54.7	80	42	54.7	72	42	52.0	70	40	50.0	82	42	55.3	80	40	53.3	70	40	50.0	72	42	52.0
29	92	50	64.0	84	48	60.0	80	42	54.7	69	42	51.0	72	38	49.3	70	44	52.7	72	42	52.0	70	38	48.7
30	94	42	59.3	80	42	54.7	68	38	48.0	70	40	50.0	72	42	52.0	76	42	53.3	70	42	51.3	68	42	50.7

Heart rate, SpO2 and respiratory rate changes :

Pt No	HR0	HR1	HR2	HR3	HR4	HR5	HR6	HR7	Sat0	sat1	sat2	sat3	sat4	sat5	sat6	sat7	RR0	RR1	RR2	RR3	RR4	RR5	RR6	RR7
1	92	94	80	78	68	64	62	64	100	99	99	99	98	99	99	98	22	24	22	20	18	22	18	18
2	94	90	88	82	80	78	70	68	100	99	98	99	98	99	99	98	20	24	22	20	18	22	24	22
3	110	108	106	88	84	90	90	96	99	98	99	99	98	99	98	99	20	18	16	20	22	20	22	20
4	98	96	94	92	94	82	74	70	98	99	98	99	98	99	98	98	18	18	20	22	24	22	20	20
5	98	92	94	82	66	64	98	72	99	98	99	99	98	99	98	99	16	16	22	20	24	22	24	22
6	82	84	64	60	72	74	60	58	100	100	99	99	99	98	98	99	20	22	24	22	20	24	24	22
7	r	72	68	64	58	56	58	52	98	99	99	98	99	98	98	99	24	22	20	26	22	20	18	18
8	84	82	74	76	62	58	54	52	99	98	98	99	99	98	99	98	24	26	22	20	24	28	22	20
9	98	94	80	82	80	80	72	64	99	98	99	98	99	99	98	99	20	18	18	16	20	22	24	22
10	100	96	78	72	74	72	68	68	99	98	99	98	99	98	99	99	22	24	26	22	20	20	18	18
11	92	90	70	68	72	66	72	70	100	99	99	99	99	98	99	98	18	18	20	22	24	26	22	24
12	90	88	88	84	72	68	82	66	100	99	100	100	99	99	99	99	28	24	24	26	24	22	24	26
13	94	90	88	82	80	78	70	68	100	99	98	99	98	99	99	98	20	24	22	20	18	22	24	22
14	94	90	88	82	80	78	70	68	100	99	98	99	98	99	99	98	20	24	22	20	18	22	24	22
15	102	100	98	94	72	70	72	74	100	99	99	99	96	99	98	98	16	18	18	20	22	24	22	20
16	110	108	100	94	92	88	80	72	100	99	98	98	99	98	99	98	28	30	28	24	22	20	28	20
17	80	84	86	88	94	92	88	78	100	100	100	99	99	99	99	99	20	24	26	22	24	28	20	20
18	92	94	80	78	68	64	62	64	100	99	99	99	98	99	99	98	22	24	22	20	18	22	18	18
19	98	96	94	92	94	82	74	70	98	99	98	99	98	99	98	98	18	18	20	22	24	22	20	18
20	94	90	88	82	80	78	70	68	100	99	98	99	98	99	99	98	20	24	22	20	18	22	24	22
21	110	108	106	88	84	90	90	96	99	98	99	99	98	99	98	99	20	18	16	20	22	20	22	20
22	120	110	100	92	90	88	84	88	99	99	98	99	99	98	99	99	24	20	22	24	22	20	24	22
23	118	108	98	90	88	86	82	86	99	99	98	98	99	98	99	99	20	24	22	20	18	22	24	22
24	110	108	106	88	84	90	90	96	99	98	99	99	98	99	98	99	20	18	16	20	22	20	22	20
25	102	100	98	94	72	70	72	74	100	99	99	99	96	99	98	98	20	22	24	22	20	24	24	22
26	84	82	74	76	62	58	54	52	99	98	98	99	99	98	99	98	24	22	20	26	22	20	18	18
27	100	96	78	72	74	72	68	68	99	98	99	98	99	98	99	99	24	26	22	20	24	28	22	20
28	110	108	106	88	84	90	90	96	99	98	99	99	98	99	98	99	20	18	18	16	20	22	24	22
29	120	110	100	92	90	88	84	88	99	99	98	99	99	98	99	99	24	20	22	24	22	20	22	20
30	100	96	78	72	74	72	68	68	99	98	99	98	99	98	99	99	22	24	26	22	20	20	18	18

Complications and rescue drug use

Pt No	desatepisode	airwayuse	shoulderrolluse	LMAuse	MRItime	MAS8time	Adverseevents	Rescue
1	nil	nil	nil	nil	70	15	nil	Once
2	nil	nil	nil	nil	65	18	v2	Twice
3	nil	nil	yes	nil	65	20	v1	Twice
4	nil	nil	yes	nil	60	22	v2	Once
5	nil	nil	nil	nil	65	20	v3	Once
6	nil	nil	yes	nil	60	20	v2	Once
7	nil	nil	yes	nil	65	18	v3	Once
8	nil	nil	yes	nil	65	25	v2	Once
9	nil	nil	yes	nil	60	20	v2	Twice
10	nil	yes	yes	nil	65	25	v2	Once
11	nil	yes	yes	nil	70	30	v2	Twice
12	nil	nil	yes	nil	70	35	v3	Twice
13	nil	nil	nil	nil	65	18	v2	Twice
14	nil	nil	nil	nil	65	18	v2	Twice
15	nil	yes	yes	nil	65	25	v2	Once
16	nil	nil	yes	nil	60	30	v2	Twice
17	nil	nil	nil	nil	70	3	nil	Once
18	nil	nil	nil	nil	70	15	nil	Once
19	nil	nil	yes	nil	60	22	v2	Twice
20	nil	nil	nil	nil	65	18	v2	Once
21	nil	nil	yes	nil	65	20	v1	Twice
22	nil	nil	nil	nil	60	25	v2	Once
23	nil	nil	nil	nil	65	18	v2	Twice
24	nil	nil	yes	nil	65	20	v1	Twice
25	nil	nil	yes	nil	60	20	v2	Once
26	nil	nil	yes	nil	65	18	v3	Once
27	nil	nil	yes	nil	65	25	v2	Once
28	nil	nil	yes	nil	60	20	v2	Once
29	nil	nil	nil	nil	60	25	v2	Once
30	nil	yes	yes	nil	65	25	v2	Once