EFFECT OF SEIZURE VIEWING ON PSYCHOLOGICAL OUTCOME AMONG PATIENTS WITH PSYCHOGENIC NON EPILEPTIC SEIZURES (PNES)

DR LAKSHMI PRIYA

DM NEUROLOGY THESIS

2020 - 2022

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY
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THESIS SUBMITTED BY

DR LAKSHMI PRIYA

To

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM

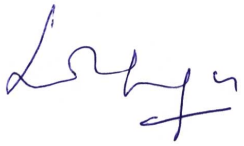
IN PARTIAL FULFILMENT
OF THE REQUIREMENTS FOR THE AWARD OF

DM NEUROLOGY
2020 - 2022

DECLARATION BY THE STUDENT

CERTIFICATE

I, *Dr Lakshmi Priya*, hereby certify that I had personally carried out the work depicted in the thesis titled, "EFFECT OF SEIZURE VIEWING ON PSYCHOLOGICAL OUTCOME AMONG PATIENTS WITH PSYCHOGENIC NON EPILEPTIC SEIZURES (PNES)". No part in this thesis has been submitted for the award of any other degree or diploma prior to this date.



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The thesis entitled, ***"EFFECT OF SEIZURE VIEWING ON PSYCHOLOGICAL OUTCOME AMONG PATIENTS WITH PSYCHOGENIC NON EPILEPTIC SEIZURES (PNES)"*** was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma prior to this date.

Clearance was obtained from Institutional Ethics committee for carrying out this study.

(Dr. Ashalatha R)

Date : 12.8.2022

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APPROVAL OF THE THESIS

The thesis entitled

"EFFECT OF SEIZURE VIEWING ON PSYCHOLOGICAL OUTCOME AMONG PATIENTS WITH PSYCHOGENIC NON EPILEPTIC SEIZURES (PNES)"

Submitted by

Dr. Lakshmi Priya

For the degree of

DM Neurology

Of

Sree Chitra Tirunal Institute for Medical Sciences and Technology,

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Is evaluated and approved by

.....	.....
Signature and name of the Guide	**Signature and name of Examiner**

FORWARDED

This is to certify that thesis entitled "EFFECT OF SEIZURE VIEWING ON PSYCHOLOGICAL OUTCOME AMONG PATIENTS WITH PSYCHOGENIC NON EPILEPTIC SEIZURES (PNES)" was done by Dr. Lakshmi Priya, as a part of partial fulfilment of the requirement for DM Neurology degree

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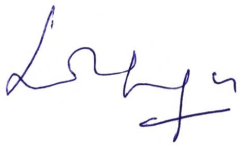

(Dr. Lakshmi Priya)

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LIST OF ABBREVIATIONS

S No	Abbreviation	Full Form
1	ASMs	Anti Seizure Medications
2	EEG	Electroencephalogram
3	ILAE	International League Against Epilepsy
4	PNEE	Psychogenic Non epileptic Events
5	QoL	Quality of Life
6	VEEG	Vidoe Electro Encephalogram
7	DSM	Diagnostic and Statistical Manual of Mental Disorders
8	QOLIE - 31	Quality of Life in Epilepsy - 31 inventory
9	HADS	Hospital Anxiety Depression Scale
10	EMU	Epilepsy Monitoring Unit
11	CT	Computed Tomography
12	MRI	Magnetic Resonance Imaging
13	CBT	Cognitive Behavioural Therapy

SYNOPSIS

EFFECT OF SEIZURE VIEWING ON PSYCHOLOGICAL OUTCOME AMONG PATIENTS WITH PSYCHOGENIC NON EPILEPTIC SEIZURES (PNES)

Synopsis by

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For

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SYNOPSIS

OBJECTIVE

Psychogenic Nonepileptic event (PNEE) is one of the common disorders encountered which feigns a true epilepsy. Inspite of being described from Hippocrates times in 13th century, there are no treatment guidelines after establishing the diagnosis. This study as aimed to study the effect of viewing one's own event on psychological status and event frequency.

METHODS

This study was a single centre randomised controlled trial, where all the patient were given standard psychotherapy, while intervention arm was shown their own habitual event recorded in epilepsy monitoring unit in addition. The baseline and followup psychological status was objectively measured using standard questionnaires (HADS and QoLIE - 31). The event frequency and change in questionnaire scores was compared at baseline and followup at 3 months. Statistical analysis was made using SPSS 2.0 software

RESULTS

A total of 65 patients were included in the study, of which 31 belonged to intervention arm and 34 to non intervention arm. The mean baseline event frequency was 9.9 / week and 11.7/week in intervention and non intervention arm respectively, which reduced significantly in both groups without any statistical difference between both groups. HADS - A and HADS - D scores improved in both groups during follow up. Of the QoLIE - 31 scores, seizure worry component was significantly improved in intervention group ($p=0.008$) as compared to non intervention arm ($p=0.814$).

CONCLUSION

Psychotherapy in addition to event viewing improves psychological status in PNEE especially with regard to seizure worry, perhaps by improving self - acceptance of the diagnosis and increasing the engagement and adherence to psychotherapy.

INTRODUCTION

INTRODUCTION

Psychogenic Non Epileptic Events (PNEE) are episodes of paroxysmal impairment of self control, which are associated with varied motor, sensory and mental manifestations and represent an experimental or behavioural response to distress.(1) The diagnosis is often focussed on exclusion of epilepsy and consequently PNEE becomes a non-disease and leading the patient marginalized between Neurology and Psychiatry with neither profession taking ownership of patient care.(2) The International League Against Epilepsy(ILAE) has identified PNEE as one of the 10 key neuropsychiatric issues associated with epilepsy.(3) PNEE represents 5-10% of outpatients in epilepsy clinics and 20-40% of inpatients in epilepsy monitoring units.(3) The prevalence of PNEE is between 2 and 33 per 1,00,000 making it a significant neuropsychiatric condition. (4) When there is no electrical brain activity correlate during a seizure episode, the events are considered as a psychological manifestation.

Currently, there is good evidence for bio psychosocial model of PNEE, involving increased levels of physiological arousal at rest and abnormal preconscious mental processing characterised by hypervigilance and avoidance of adverse stimuli(1). Bowman and Markand propose four pathways to the development of PNEE, namely a history of childhood physical or sexual abuse, multiple life stresses that compromises coping abilities and panic attacks which may be mistaken for PNEE.(6) This implies that the specificity of any treatment protocol for PNEE

patients can only be moderate and that treatment programs need to be individualized. (6)

Our study attempts to assess the effect of event viewing on psychological outcome and event frequency among patients with PNEE. The major factors which perpetuate the underlying psychological distress is the unawareness of one's own disease and the stigma associated with mere physical changes (viz. change in facial expression, stiffening of limbs, jerks of body, falls, frothing) which occur during the event, especially after hearing the description of the "event" from a caretaker or onlooker from the early days of onset of illness. This gradually causes an abnormal preconscious mental processing, adding to the preexisting anxiety or depression and leads to loss of self esteem and easy vulnerability, causing poor adjustment in society. This negativity in self perception has a negative impact on the overall Quality of Life (QoL). The hypothesis is viewing and perceiving one's own illness in contrast to hearing weird descriptions from a relative; followed by counselling as to how to approach it in a pragmatic way would alter their psychological status and hence improve the QoL.

REVIEW OF LITERATURE

2.1. THE MIND VERSUS THE BODY

Conversion disorder is a psychological disorder where the voluntary motor or sensory function is not explained by neurological or underlying general medical disorder. These events are usually associated with underlying psychological factors like stress or conflicts. The word *conversion* refers to substitution of a somatic symptom for a remotely repressed idea. A psychological conflict brings about subconscious alteration in the body and presents as either a motor or sensory or experiential phenomenon. "The occurrence of certain symptoms not explained by organic diseases reflects unconscious conflict" - Sigmund Freud

The common manifestations of conversion disorder includes blindness, paralysis, dystonia, swallowing difficulties, motor tics, gait disturbances and seizure-like episodes. (13). The externally manifested features are not malingering as they are very real and occur without one's own will. The mental conflicts together with insecurities and insufficient coping abilities brings about out a mental distress in the form of true neurological disorder but without an identifiable organic cause.

There are various theories to explain the association and dissociation of the mind and body, to bring about the non organic manifestations.

2.1.1. Theory of Hysteria by Hippocrates (15)

Hysteria is a term that was first used by Hippocrates to denote an illness in which the uterus dries up and wanders the body in search of moisture. This theory has formed the source for the current name of uterus, from Greek cognate, hystera.

Currently, this term is also used to denote non organic disorders, which are common in women.

2.1.2. Rene Descartes theory of mind-body dualism (16)

Mind and body are two distinct entities that cannot remain in unity, as the body is subjected to mechanical laws but the mind is not. Thus, a reductionist medical model has been developed with dualistic outlook, which has an impact on the management of symptoms.

2.1.3. Freud's psychodynamic theory (17)

This theory states that the unconscious conflict and effective motive are transformed into bodily complaints and this idea has paved the way to the current concept of conversion disorder.

2.1.4. DSM - 5 criteria for conversion disorder (14)

However, the current diagnostic criteria proposed by Diagnostic and Statistical Manual of Mental Disorders (DSM - 5) for conversion disorder is characterised by the following :

- One or more symptoms of altered voluntary sensory or motor function
- Clinical findings that show evidence of incompatibility between the symptoms and recognised neurological or medical condition
- Symptoms or deficit that are not better explained by another medical or mental disorders

- Symptoms or deficit that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning or warrants medical evaluation.

2.2. PNEE

Eponymous terms

- Psychogenic seizures
- Pseudoseizures
- Hysterical seizures
- Psychogenic non epileptic spells
- Psychogenic non epileptic attacks
- Psychogenic non epileptic events
- Functional neurologic disorder

2.2.1. Definition

The events that clinically resemble true epileptic seizures, but occur without the excessive synchronous cortical electroencephalographic activity. (18).

2.2.2. ILAE definition - PNEE

Events that are paroxysmal time-limited, alterations in motor, sensory, autonomic and/or cognitive signs and symptoms, but unlike epilepsy, PNES are not caused by octal epileptiform abnormality. (25).

2.2.3 Burden on self and society

- About 20-40% of the patients admitted in EMUs (Epilepsy Monitoring Units) are diagnosed with PNEE (18)

- About 10% of individuals with GTCS considered as refractory to benzodiazepines (20)
- People who convert their emotional problems into physical symptoms are likely to spend about 9 times the cost for health care as those who do not
- About 82% of adults stop working due to conversion disorder and face the social and economic adversities (21)
- A recent study has found that the annual bill for conversion disorder in western countries accounts for about 20 billion US dollars (21)
- Estimated prevalence of PNEE in US is 33/1,00,000 population (19). However, studies from India are lacking on this regard currently.
- About 80% are women with a mean age of onset at around 31 $\pm$ 15 years (19)
- Majority of individuals at diagnosis are unemployed and about 46% have a coexistent diagnosed psychiatric comorbidity, while about 57% have atleast one associated medically unexplained symptom complex. (19)
- The mean duration from onset to diagnosis is 7.3 months (23)
- In a study by Razvi et al, about 28 newly diagnosed patients with PNEE were responsible for 14 general practitioner home visits, 31 ambulance calls, 34 emergency department visits, 21 hospital admission with 66 inpatient days, 8 MRI scans, 24 CT scans, 2 standard EEGs, 28 short term Video EEGs and 5 ambulatory EEG recordings prior to the diagnosis in a span of just 7.3 months. (23)

2.3. ETIOLOGY AND PRECIPITANTS

2.3.1. BACKGROUND FACTORS

- Age group between 20-30s
- Female sex
- Prior history of seizures
- Other psychogenic disorder
- Antecedants - sexual / physical abuse
- Mental health problems
- Psychosocial problems

2.3.2. PATTERN AND TRIGGERING OF EVENTS

- Higher frequency
- Recurrent hospitalisations
- Recurrent status reported in an alert patient
- Triggered by stressful situation
- Triggered by surgery (including epilepsy surgery)
- Partial or transient response to ASMs
- Physical triggers - lighting conditions / physical activities

2.4. DIAGNOSIS OF PNEE

2.4.1. Semiology

Seizures are classified into 3 categories - True epileptic seizures, PNES and physiologic non epileptic seizures. The suspicion of PNEE shall be made from a detailed history and examination, which helps in early diagnosis. There are various

pointers which denote PNEE, true seizures and intermediate signs from the history on semiology of the events. (24). However, of the various signs suggesting PNEE, the only feature to suggest from epileptic seizure with high specificity is side-to-side head or body movements. Inspite of all the signs and symptoms analysed to indicate PNEE and true seizure, there can never be a single sign or symptom to make the diagnosis and hence it is highly dependant on neurologic and psychiatric internal consistency.

Table1. Semiology clues to identify PNEE and true seizure

PNEE	TRUE SEIZURE	INTERMEDIATE SIGNS
Long duration*	Occurrence in sleep	Gradual onset
Fluctuating course	Post ictal confusion	Non stereotyped events
Pelvic thrusting	Stertorous breathing	Flailing or thrashing movements **
Asynchronous movements		Opisthotonus
Side - to - side head or body movements		Tongue biting
Forced eye closure		Urinary incontinence
Ictal crying		
Memory recall		
Swoon, catatonic, pseudo syncope		
Coordinated agonist - antagonist activity (eg tremors)		
Signs of emotional distress		
Vocalisation during or after the event associated with affective content and complex		

* Duration longer than 2 minutes - possibility of PNEE should be considered and >10 minutes - strongly suggests PNEE

** In PNEE - Frequency remains same through out the event with variable amplitude, while in true seizure, the frequency gradually reduces and amplitude increases

*** Swoon - lasting for more than a minute should raise suspicion of PNEE

2.4.2. Role of EEG

2.4.2.1. Electrical data

Video EEG recording for a habitual event showing no electrical correlate for the particular event is considered gold standard for diagnosis of PNEE with high level of certainty and higher inter rater reliability. (19). When the events have low frequency, it would be impractical to rely on VEEG for clinching the diagnosis. When the events are recorded simultaneously on EEG and video, and there is no ictal EEG correlate found before, during and after the event, it is confirmatory for the diagnosis.

2.4.2.2. Event recording

The events recorded must be witnessed by a family member and should be the same semiology of habitual events. The recorded event must not obscure the electrical data with movement artefacts to be sure of the diagnosis. However, when the clinical history is suggestive of frontal lobe epilepsy of simple partial seizure, the diagnosis of PNEE cannot be made. The majority of patients with PNEE bring about the event within first few hours of VEEG monitoring. However, the techniques such

as verbal suggestions, placebo wipes and saline injection may be helpful in bring out the event. In some cases, the routine activation procedures like hyperventilation, photic stimulation or mental arithmetic tests may bring out these events.

2.4.2.3. Role of Electrocardiography

ECG recording during VEEG is also essential and the ictal tachycardia in true seizure is more than that compared to tachycardia in PNEE, where the heart rate is usually commensurate with the physical activity involved.

2.4.2.4. Role of ambulatory EEG

When the events are not recorded after prolonged stay in monitoring units, ambulatory EEG may be helpful, provided a caretaker who can provide the event description or is able to capture the event completely can be another option for aiding the diagnosis. The caution to be taken in such a setting is that the initial part of the event would usually be missed in video capture and the recorded part of events may just be a behavioural disturbance which simulates PNEE, but is actually not.

2.4.3. DSM - IV - TR / DSM - 5 / ICD - 10 CRITERIA FOR DIAGNOSIS

PNEE are considered as a mental disorder in contrast to malingering, which is not considered so. The Diagnostic and Statistical Manual of Mental Disorders IV - Text Review has proposed a two - stage diagnostic process, where at the first stage, an explanatory medical cause for the illness must be excluded and in the second stage, these medically unexplainable seizures must be allocated to conversion disorder or in some cases into anxiety or dissociative disorder. The conversion disorder criteria in DSM - 5 makes a diagnosis based on symptom presentation and

by relegating a psychological stressor, aligning the DSM system with ICD - 10. The classification of PNES as conversion disorder in DSM - 5 remains the same as in the previous version.

2.4.4. DIAGNOSTIC SUPPLEMENTS

2.4.4.1. PHYSIOLOGIC MEASURES

Serum prolactin is elevated in post ictal state of true seizure and differentiates from pseudo seizure with a mean sensitivity of 89%. Blood drawn 10-20 minutes after the onset of ictus and a value twice above the normal or baseline level is a useful adjunct in identifying true seizure from pseudoseizure. False positive values may be seen with dopamine antagonists, tricyclic antidepressants, syncope and breast stimulation. False negative values are seen with dopamine agonists, status epilepticus and frontal lobe epilepsy. (27)

Serum cortisol level and DST (dexamethasone suppression test) was evaluated in patients with PNEE and was found that those with sexual trauma have an elevated baseline cortisol level and reduced heart rate variability at baseline, suggesting greater sympathetic activity. (26)

Increase in peripheral white blood count, cortisol, creatine kinase and neutron specific enolase, capillary oxygen saturation and brain derived neurotrophic factor have been studied to differentiate true seizure and pseudo seizure, but requires larger studies before clinical use.

2.4.4.2. NEUROIMAGING

Most of the brain imaging in patients with PNEE is normal. There are recent evidences that there are abnormalities in functional connectivity between emotional, cognitive and motor regions. However, epilepsy patients may also have normal imaging at first presentation.

2.4.4.3. COGNITION AND PERSONALITY

Patients with PNEE are generally found to have higher IQ than those with true epilepsy. Detailed neuropsychological evaluation have found that PNEE patients have impairment is some of the domains. There are various personality traits acquired in patients with PNEE based on the emotional or social stressors experienced, but these personality testing may not help in diagnosis but helps to give better and tailored behavioural therapy.

2.4.4.4. HYPNOSIS

Hypnosis technique would invariably precipitate psychogenic event, but the studies have used hypnosis to recall seizure amnesia, which would be possible with PNEE but not with true seizure, with a sensitivity of 85% and specificity of 100%. Hypnotic Induction Profile score is found to be higher with PNEE as compared to true seizures. (28)

2.4.4.5. CONVERSATION ANALYSIS

The history from patient with PNEE shall have the following characteristics in general:

- Focus on situations on which the events occurred and the consequences of those events
- Subjective seizure experience may be underplayed
- When questions are asked specifically, there is usually focussing resistance
- Catastrophism towards the seizure - like event

2.4.4.6. ILAE DIAGNOSTIC CERTAINTY FOR PNEE

The diagnostic certainty of PNEE depends on various combinations encountered in clinical practice and includes the following four levels.

Table 2. Diagnostic certainty for PNEE (ILAE)

CERTAINTY OF DIAGNOSIS	HISTORY	WITNESSED EVENT	EEG
Possible	Consistent with PNEE	By witness or self - report	Normal interictal EEG
Probable	Consistent with PNEE	By clinician who witnessed the video or the event typical of PNEE	Normal interictal EEG
Clinically established	Consistent with PNEE	By clinician experienced in making seizure diagnosis	Normal ambulatory ictal EEG
Documented	Consistent with PNEE	By clinician experienced in making seizure diagnosis while undergoing VEEG	No epileptiform abnormality before, during or after the event

2.5. MANAGEMENT OF PNEE

These events are invariably treated with anti seizure medications at the outset, which has no role or benefit in this entity and adds to the psychological distress addition.

Presenting the diagnosis (29,30)

The first and foremost step in management of PNEE is effective conveyance of the diagnosis in a sensitive manner, which includes the following steps:

- The diagnosis must not be told at the beginning of the conversation
- The fact that the symptoms are real despite an underling definite organic disease identified
- The patient must not get the impression that nothing is wrong in him/her
- Examples of socially acceptable diseases (eg. hypertension) and situations (eg. stage fear) that are stress - related must be quoted
- The subconscious alteration in behaviour must be conveyed (eg. nail bitting, foot tapping)
- "Although the body is not functioning properly, improvement is definitely possible because there is nothing structurally wrong" must be emphasised
- Explaining that understanding and accepting the diagnosis leads to improvement and proper engagement with rehabilitation rather than being stuck worrying and wondering about what is wrong!

The facts to be emphasised while presenting the diagnosis are that "Providers believe that symptoms are real, the disease has a psychogenic nature and mental health treatment is mandatory".

PHASES OF PSYCHOLOGICAL COUNSELLING

A. Engagement

The primary aims of this phase of treatment includes:

- Understanding the diagnosis
- Stop seeking further diagnostic evaluations
- Establish contact with a mental health provider
- Start actively participating in the therapy
- Engagement in other more adaptive strategies to manage stressful situations

However, there are no predictors to identify the adherence to engagement, except one study which has shown that the relationship status (married or a live-in partner) is associated by better and longer engagement. (29). Engagement can also be improved by combining with motivation interviewing to help them adhere with psychotherapy. Motivational interviewing helps them to engage, focusing, evoking and planning the treatment need and course.

B. Acute treatment

Psychotherapeutic

COGNITIVE BEHAVIOURAL THERAPY

It was first proposed by Goldstein et al, as a 12 outpatient sessions emphasising on the following components:

- Treatment engagement
- Reinforcement of independence
- Distraction, relaxation and refocusing techniques

- Graded exposure to avoided situations
- Cognitive restructuring
- Relapse prevention

MINDFULNESS PRINCIPLE

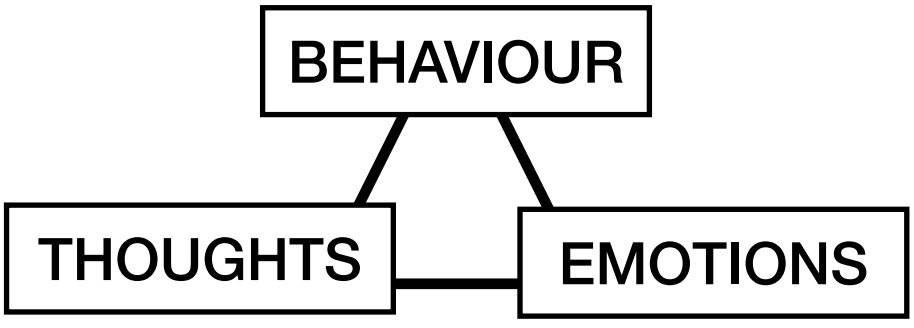
Mindfulness is defined as "paying attention in a particular way: on purpose, in the present moment and non-judgementally". It is primary intervention component in acceptance and commitment therapy, stress therapy and cognitive therapy. This principle can be used in behavioural therapy for PNEE as it addresses psychopathological vulnerabilities like poor recognition or non acceptance of emotional states.

COPING STRATEGIES

- Identifying the precursor, precipitant and perpetuating factors
- Identifying and modifying the cognitive distortions and environmental triggers
- Communicating distress verbally

COGNITIVE TRIANGLE

- It states that an individual's behaviour, thoughts and emotions are inter related and each one influences the other.



REATTRIBUTION THEORY

- Feeling understood
- Changing the agenda
- Making the link

PSYCHOPHARMACOLOGICAL MEASURES

There have been trials of sertraline, venlafaxine

C. Long term follow up

For those who remain symptomatic even after the phase of acute treatment

Risk factors - Recurrent depression, chronic trauma or borderline personality disorder, unable to recognise a stressor at onset

2.6. PSYCHOLOGICAL ASSESSMENT

QUALITY OF LIFE IN EPILEPSY (QOLIE 31)

QOLIE 31 inventory contains 7 multi-item scales that looks into the following domains : emotional well being, fatigue/energy, social functioning, cognitive functioning, seizure worry, seizure worry, medication effect and overall quality of life. Apart from the quality of life assessed by the health status, an overall QOLIE 31 score is drawn from all the components. Of the 31 items in this inventory, 15 were taken from existing sources and 16 were developed de novo by this inventory development group, as shown in Table 3. The questions in QOLIE 31 were drawn from original questionnaire which consisted of 98 items and was filled by 304 patients with epilepsy across 24 centres in US.

Table 3. Components of QOLIE 31 and its adaptations

Component of QOLIE 31	Total questions	Developed denovo	Adapted from existing sources	Source
Emotional well-being	5	0	5	RAND 36-item health survey 1.0
Energy / fatigue	4	0	4	RAND 36-item health survey 1.0
Cognitive function	6	4	2	Medical Outcomes study Epilepsy surgery Inventory - 55
Social functioning	5	4	1	Medical Outcomes study
Overall quality of life	2	0	2	Study of patient preferences (Hadron and Hays, 1991) Daartmouth COOP chart (Nelson et al, 1990)
Seizure worry	5	4	1	Epilepsy surgery Inventory - 55
Medication effects	3	3	0	
Overall health	1		1	Visual analogue scale

Scoring QOLIE 31

Each item is scored on a scale to indicate favourable or unfavourable state of health by precoded numbers. As the scale is not uniform, the precoded numbers are first converted to a scale of 0-100, with higher numbers always indicating better quality of health. The sub scores from each of the component are then added and divided by the total components attended by the patient, which give the overall QOLIE 31 score. Higher score indicates better quality of life. Internal consistencies and reliability for the multi-item scales range from 0.77-0.85, exceeding 0.70

standard for group-level comparison. Pearson correlation co efficient (r) exceeding 0.7 for all the components except medication effects, which was 0.64.

2.7. PROGNOSIS

Poor prognostic factors for treatment response are: co-morbid epilepsy or various psychiatric diagnosis, personality disorder, history of trauma, violent seizure semiology, emergency department visits at baseline, interpersonal difficulties and receiving social security benefits. (31,32). Longer duration of illness has not found to be a poor prognostic factor in contrast to other disorders. (31).

2.8. RECENT CONCEPTS

PNEE has typically been considered as a presentation of conversion disorder. However, there has been recent evidence that it occurs due to functional and structural network abnormality. (34)

LESIONAL ABNORMALITIES

Structural abnormality has been studied in both macroscopic(structural epileptogenic focus) and sub macroscopic abnormalities (atrophy, differences in cortical thickness, integrity of white matter tracts). (35). Structural abnormalities on non dominant hemisphere associated with tendency to development of PNEE which is supported by the fact that most emotions are localised to non dominant hemisphere. (36). A recent study has shown that right sided asymmetry of uncinate fasciculus is associated with higher anxiety and depression levels in this population. (39).

Another study has shown that decreased cortical thickness on right hemisphere is associated with depression in patients with PNEE, however, the comparison with controls was not done. (37). There are also studies which have stated the correlation between left medial orbito frontal cortical thickness and left anterior insula thickness with PNEE. (40).

There has been a novel study which has found an inverse association between left insular volume and functional neurological disorder with childhood abuse in women and PTSD in men. (38).

DIFFUSION TENSOR IMAGING

Studies have shown abnormalities in left hemispheric white matter tract connecting uncinate fasciculus, left superior temporal gyrus and left subcortical structures. (41). One study has shown the the concept of small worldness in patients with PNEE, which is an organised network specifically with attention, sensorimotor, subcortical and default mode network. (42). A meta analysis has shown that the regions of brain involved in PNEE are semi-consistent in studies and an evidence towards multifocal localisation has been raising. (43)

NEURO METABOLIC STUDIES

Various ictal and interictal SPECT studies have shown focal hypoperfusion when compared to patients with true epilepsy, but until recently there has not been any specific focus identified to be associated with PNEE. (44). There are recent studies which have compared SPECT in PNEE and normal subjects and have found that hypo metabolism in right inferior parietal and central region in addition to

bilateral anterior cingulate are found in patients with PNEE. (45). The fact underscored is that emotional processing and motor control are altered in PNEE.

2.9. UNMET NEEDS WITH REGARD TO PNEE

- Reducing the delay in diagnosis
- Comprehensive interdisciplinary care
- Presentation of the diagnosis
- Identifying predictors of treatment response and treatment resistance

OBJECTIVES OF THE STUDY

OBJECTIVES

1. To assess the effect of seizure viewing on psychological status in psychogenic non epileptic events and compare it with a control group
2. To assess the effect of psychological counselling on psychological status in patients with PNEE
3. To assess effect of seizure viewing on event frequency in patients with PNEE and compare it with a control group

MATERIALS AND METHODS

METHODOLOGY

TRIAL DESIGN

This was a randomised controlled trial with parallel design, where the study participants were allocated into intervention and non intervention arm based on random allocation sequences in blocks. The allocation was made in a ratio of 1:1 with blocks made in sequences of 10. Both the groups were followed up and outcomes were compared between both groups at baseline and follow up. The trial was approved by the Institutional Review Board, Sree Chitra Tirunal Institute for medical sciences and technology (SCT/IEC/1596 /NOVEMBER-2020) and was prospectively registered in Clinical Trials Registry - India in April 2021 (CTRI/ 2021/04/033220), following which, the study participants were recruited prospectively for a period of 1 year duration.

PARTICIPANTS

The participants were recruited from a single comprehensive centre for epilepsy care in Trivandrum, India. We consecutively recruited patients from our Video EEG unit / epilepsy monitoring unit centre who had atleast one event recorded in hospital and were diagnosed with Psychogenic non epileptic event as per International League Against Epilepsy criteria. Those individuals above 18 years with habitual seizure like events clinically suggestive of non epileptic events and having no evidence of epileptiform discharges during the recorded habitual event were included in the study after obtaining written informed consent. Patient with true seizures in remission and concurrent active non epileptic events were also

included in the study. Individuals lesser than 18 years, already diagnosed with psychiatric illness, pregnant and those unwilling to view their own event were excluded.

INTERVENTIONS

In the intervention arm, their own event recorded during evaluation was shown to them. However, counselling and motivational therapy was given to all the participants in intervention and nonintervention arm. Psychological status was assessed with standard questionnaires in both groups at baseline and all the participants were followed up after 12 weeks to reassess the psychological status using the same questionnaires.

OUTCOMES

We collected information on demographics, probable precipitating factors for non epileptic events, baseline seizure frequency and psychological status by means of standard questionnaires. Hospital Anxiety Depression Scale (HADS) and QOLIE - 31 was administered for all the patients at baseline. At 12 weeks, all the patients were followed up either in person or telephonically in a blinded fashion and information on seizure frequency and psychological status was collected using the same questionnaires administered at baseline. The primary outcome was a measure of change in scores in questionnaires as compared to the baseline and secondary outcome was change in event frequency.

SAMPLE SIZE

As similar studies were not available previously for comparison, formal statistics could not be applied for calculating sample size. Based on previous hospital records, expecting a similar trend of admission, the sample size is calculated for the planned study period.

RANDOMISATION

Randomisation allocation table was created before the study began at blocks of 10s and allocation of the study subjects into one of the study arms (event viewing vs no event viewing) was made using sequentially numbered opaque envelopes to conceal allocation until after baseline assessment was completed. The randomisation allocation sequence was created by statistician and patients were enrolled by principal investigator, who assessed the baseline status of the patient and was blinded to the randomisation. In addition, the counselling session and motivation therapy was given by neuropsychologist, who was also blinded. The concealed envelopes were handled by co-principal investigator, who carried out the intervention based on the allocation sequence. During followup, the patients were assessed by the principal investigator and neuropsychologist, who was again blinded to the allocation.

TREATMENT

All the patients were given psychotherapy by a trained neuropsychologist for a period of atleast 30 minutes. There was a prompt attempt to identify precipitants of non epileptic events and psychotherapy was focused in the following spheres : 1) engaging 2) focusing 3) evoking 4) planning 5) suggestions to overcome stressors.

Psychotherapy was given at baseline with special adherence to mindfulness principle and later at followup further sessions were given at the request of the patient.

STATISTICAL ANALYSIS

The data shall be analysed with the help of computer software MS Excel and SPSS version. The data shall be presented as percentages or mean +/- standard deviation as defined appropriate for qualitative and quantitative variables respectively. Univariate analysis shall be undertaken to examine relationship of various factors. Crude odds ratio with 95% confidence interval shall be reported. Chi square test/ Fisher's exact test shall be applied to evaluate statistical significance. Multivariate analysis/ logistic regression shall be used to evaluate the independent and joint effect of the variable of interest on the outcome. A p value of <0.05 shall considered statistically significant. All p value shall be two tailed.

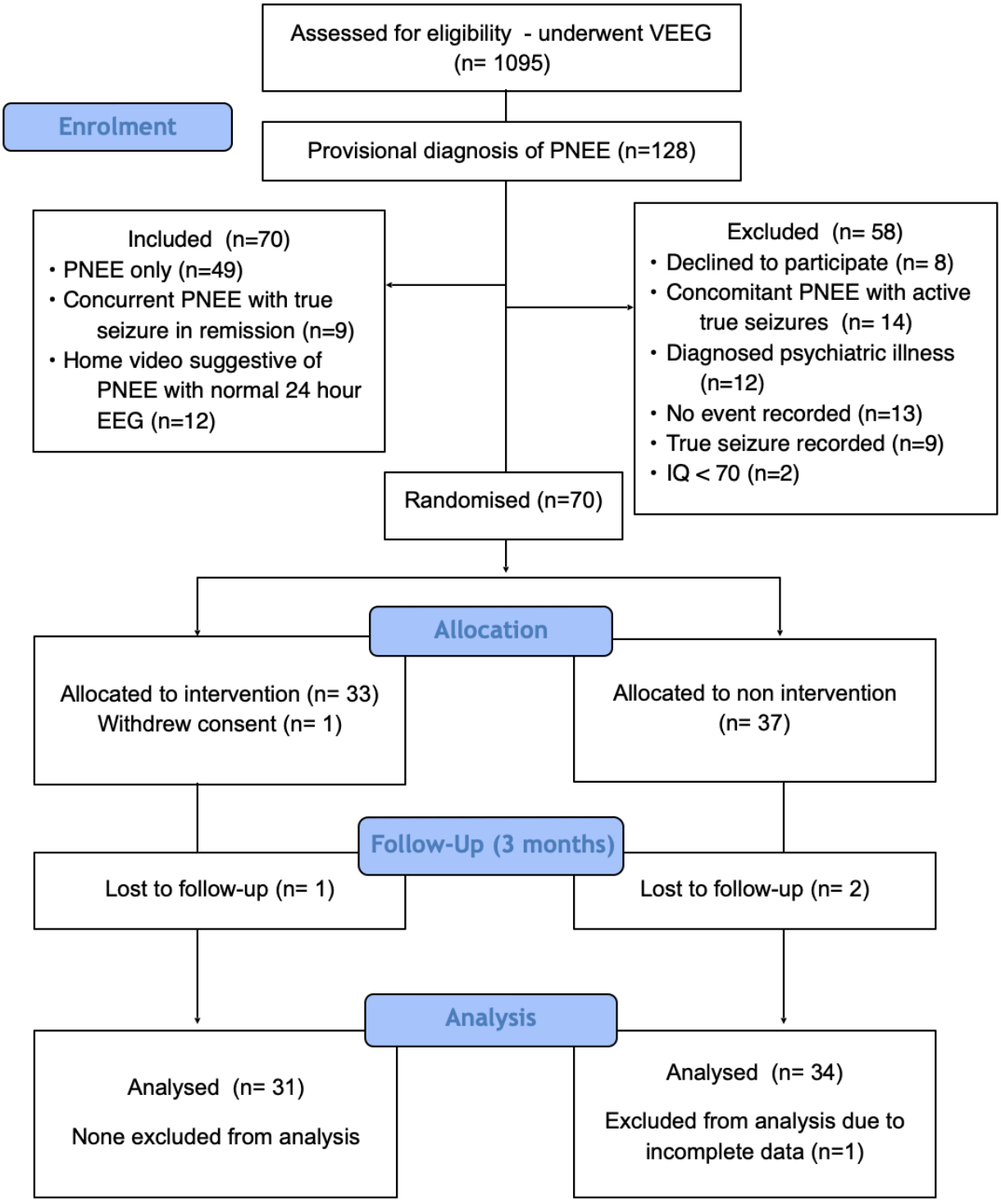


Fig.1. CONSORT flow diagram showing enrolment, randomisation and followup of patients in this study (IQ - Intelligence Quotient)

RESULTS

DEMOGRAPHICS

A total of 65 patients were included in the study, of which 31 patients were in intervention arm and 34 patients were in non intervention arm. In both the groups, females were predominant, with about 84% in intervention group and 71% in non intervention group, as shown in Fig 5.1. However, there was no statistically significant difference between both the groups. The mean age of individuals was slightly lower in non intervention group (29.29 $\pm$ 9.23 years) than intervention group (32.39 $\pm$ 12.83 years).

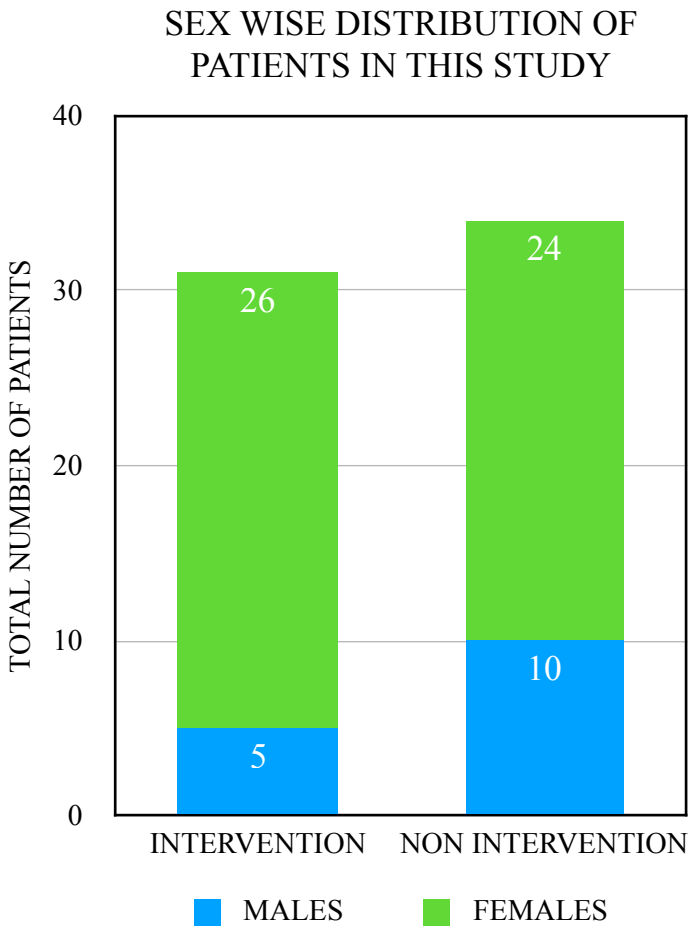


Fig. 5.1. Sex wise distribution of patients in the study

SOCIOECONOMIC STATUS

It is proven in prior studies that lower socioeconomic status is one of the social factors predisposing to the development of PNEE. In this study, Modified Kuppusamy scale was used for stratification of socioeconomic status. (33). Patients belonging to upper and upper middle class were taken as higher socioeconomic strata and those belonging to lower middle, upper lower and lower class were taken as lower socioeconomic strata and the distribution in both groups were as shown in the figure 5.2. There was no statistically significant difference between both the groups, though higher SES group individuals were the predominant population.

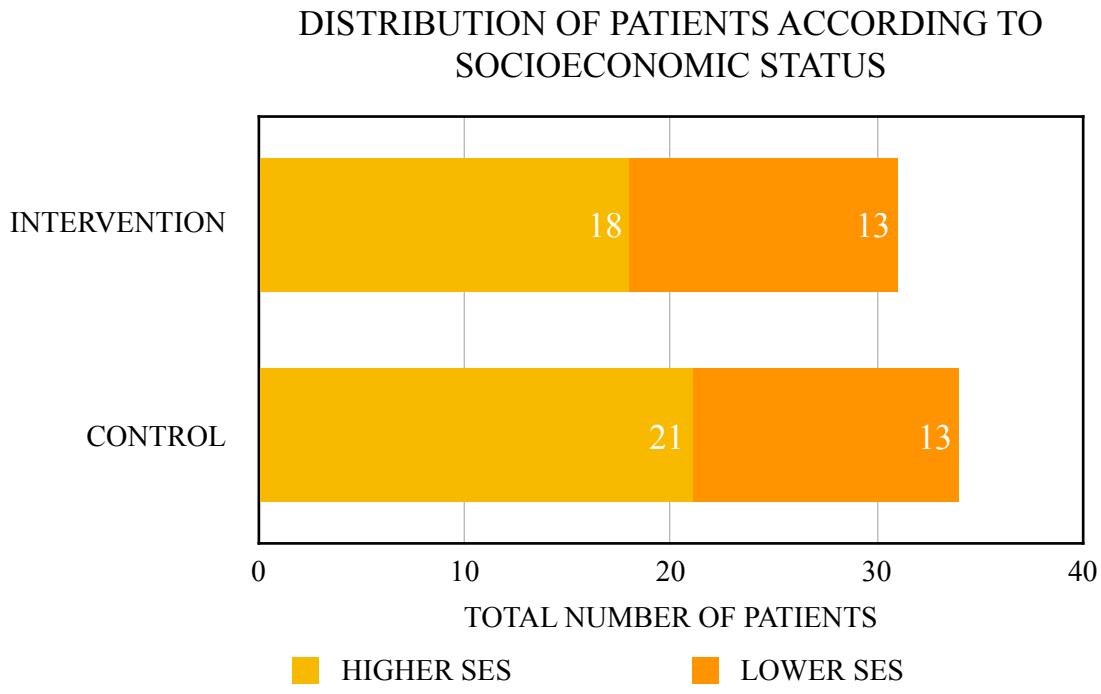


Fig. 5.2. Bar diagram showing the socioeconomic status in both groups

EDUCATIONAL STATUS

The entire study population were grouped into four educational strata as primary school, higher secondary, pre degree and degree or higher. In both intervention and non intervention group, the individuals qualified above pre-degree were the majority and there was no statistically significant difference between groups in any of the subset of education.

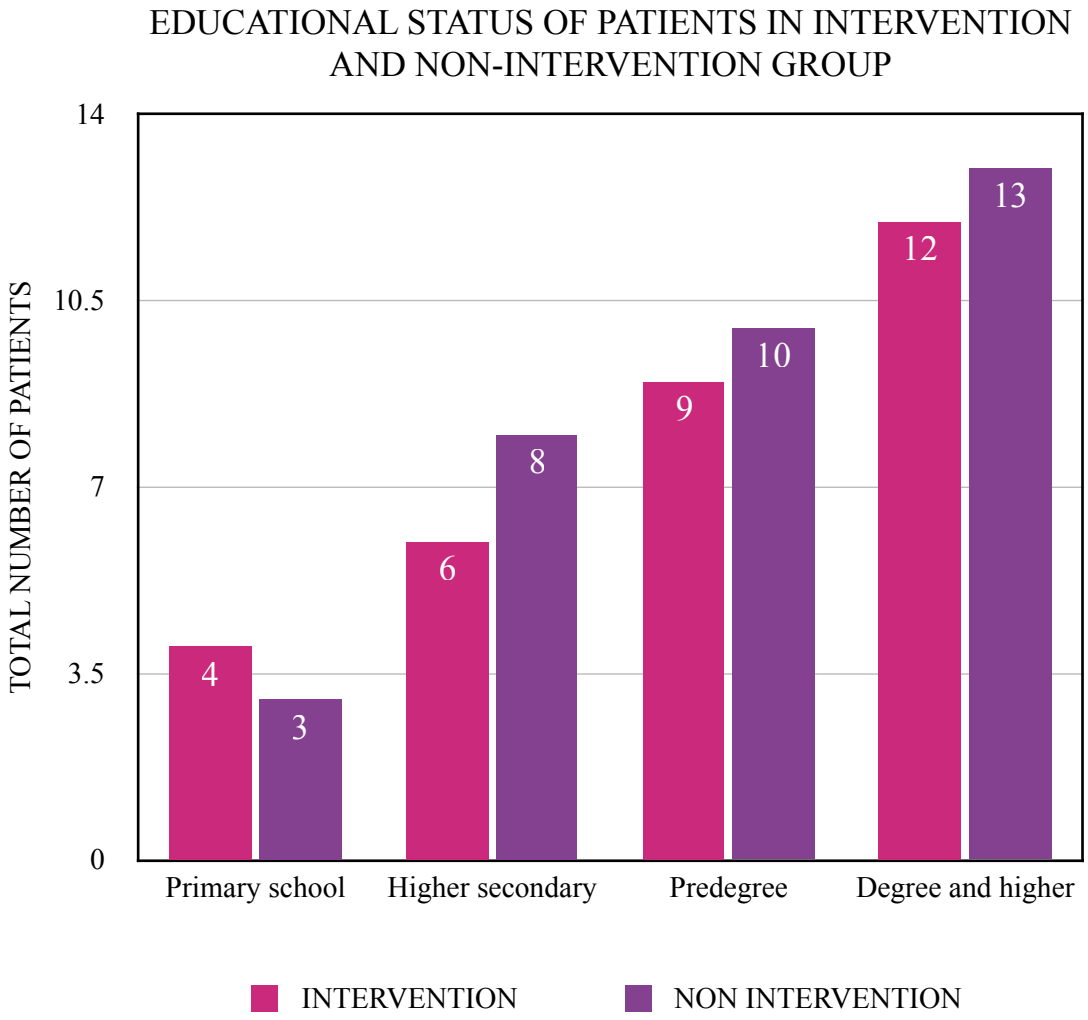


Fig. 5.3. Educational status of patients in each group

OCCUPATION

The occupational status of an individual forms a major factor in terms of being a precipitant for psychogenic event or a relieving factor for home-precipitated psychogenic events. The majority of patients in intervention group were working, while that in control group were house wives. There was only a small proportion of unemployed patients in both groups, but considering the mean age of population in each group, this unemployed proportion forms a major lacunae in the productive group of the society.

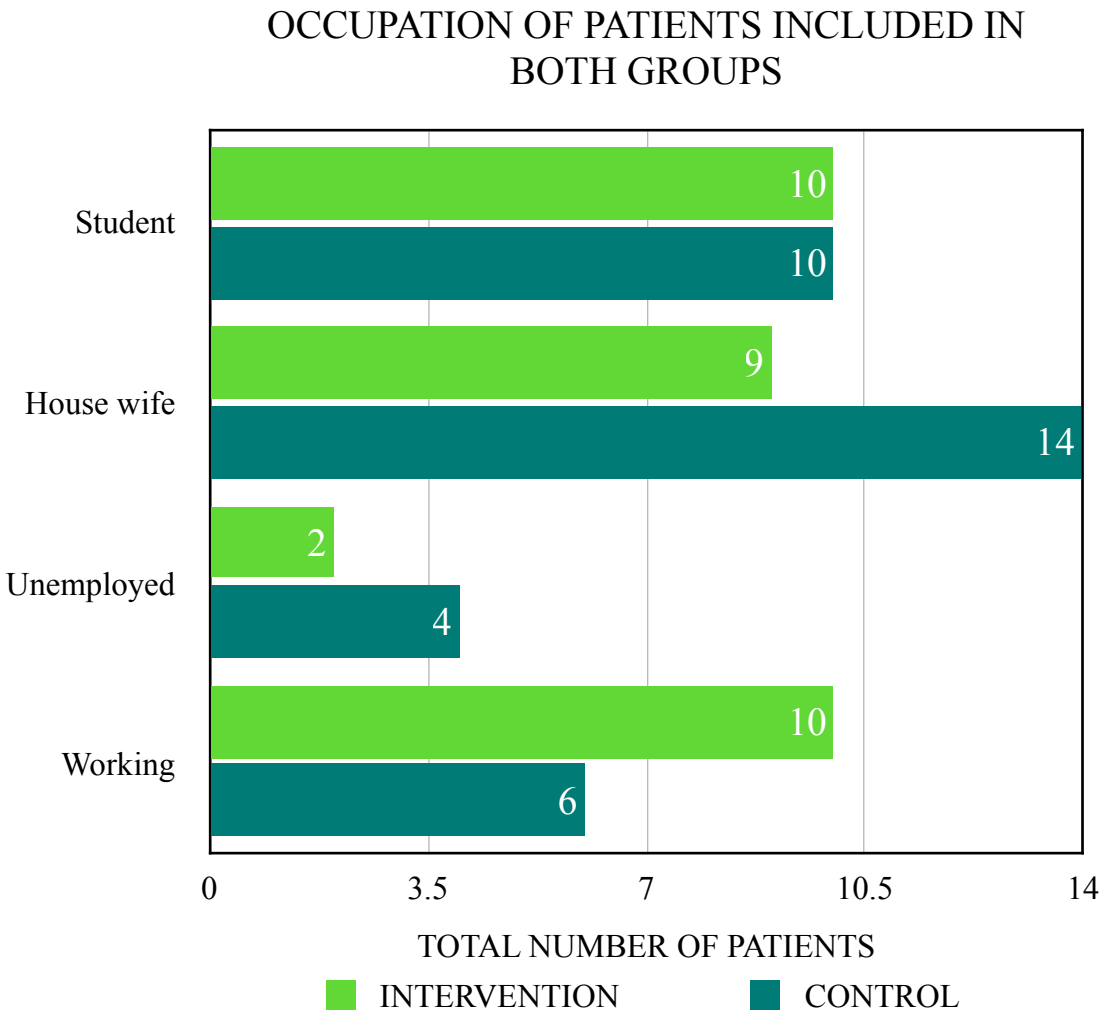


Fig. 5.4. Distribution of occupational status in both groups

MARITAL STATUS

As the psychogenic events are common to occur among the age group of 20-30s, marital status has important influence on mood disorders and conversion disorder as shown by previous studies. In this study, the majority of individuals belonged to unmarried / divorced group in intervention arm, while those in control group were almost equally distributed. However, there was no statistical significance between both groups.

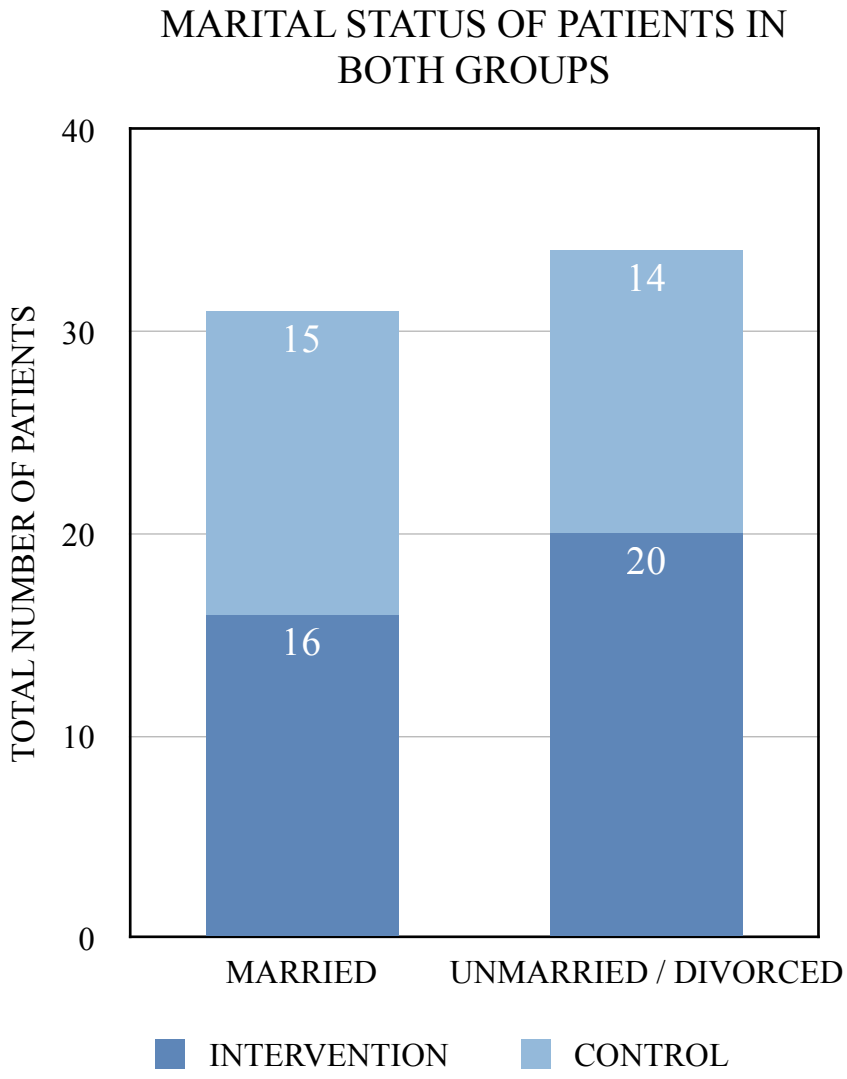


Fig. 5.5. Distribution of patients with regard to marital status

Table. 5.1. Demographic details of patients in both groups

	Intervention group (n=31)	Nonintervention group (n=34)	P value
Mean age	32.39 (±12.83)	29.29 (± 9.23)	p=0.266
Age at onset of PNEE	30.13 (±12.28)	27.88 (±9.16)	p=0.404
Number of family members	4.03 (± 0.93)	4.26 (± 0.89)	p=0.339
Sex			
Male	5 (16.1%)	10(29.4%)	
Female	26 (83.9%)	24 (70.6%)	p=0.204
Domicile			
Kerala	23 (74.2%)	23 (67.6%)	
Other state	8 (25.8%)	11 (32.4%)	p=0.564
Socioeconomic status			
Higher	18 (58.1%)	21 (61.8%)	
Lower	13 (41.9%)	13 (38.2%)	p=0.761
Education			
Primary school	4 (12.9%)	3 (8.8%)	
Higher secondary	6 (19.4%)	8(23.5%)	
Pre degree	9 (29%)	10 (29.4%)	
Degree and higher	12 (38.7%)	13 (38.2%)	p=0.944
Occupation			
Student	10 (32.3%)	10 (29.4%)	
House wife	9 (29%)	14 (41.2%)	
Unemployed	2 (6.5%)	4 (11.8%)	
Working	10 (32.3%)	6 (17.6%)	p=0.454
Marital status			
Married	16 (51.6%)	20 (58.8%)	
Unmarried / divorced	15 (48.4%)	14 (41.2%)	p=0.559

PRECIPITANTS OF PNEE

In addition to the psychological status being evaluated by standard questionnaires, obvious precipitants for PNEE were elicited directly or indirectly from the patients themselves. Of the control group, the most common precipitant was interpersonal issues followed by stressors at home and stressors outside home. However, the pattern was similar with intervention group also. The only statistically significant precipitant was unemployment.

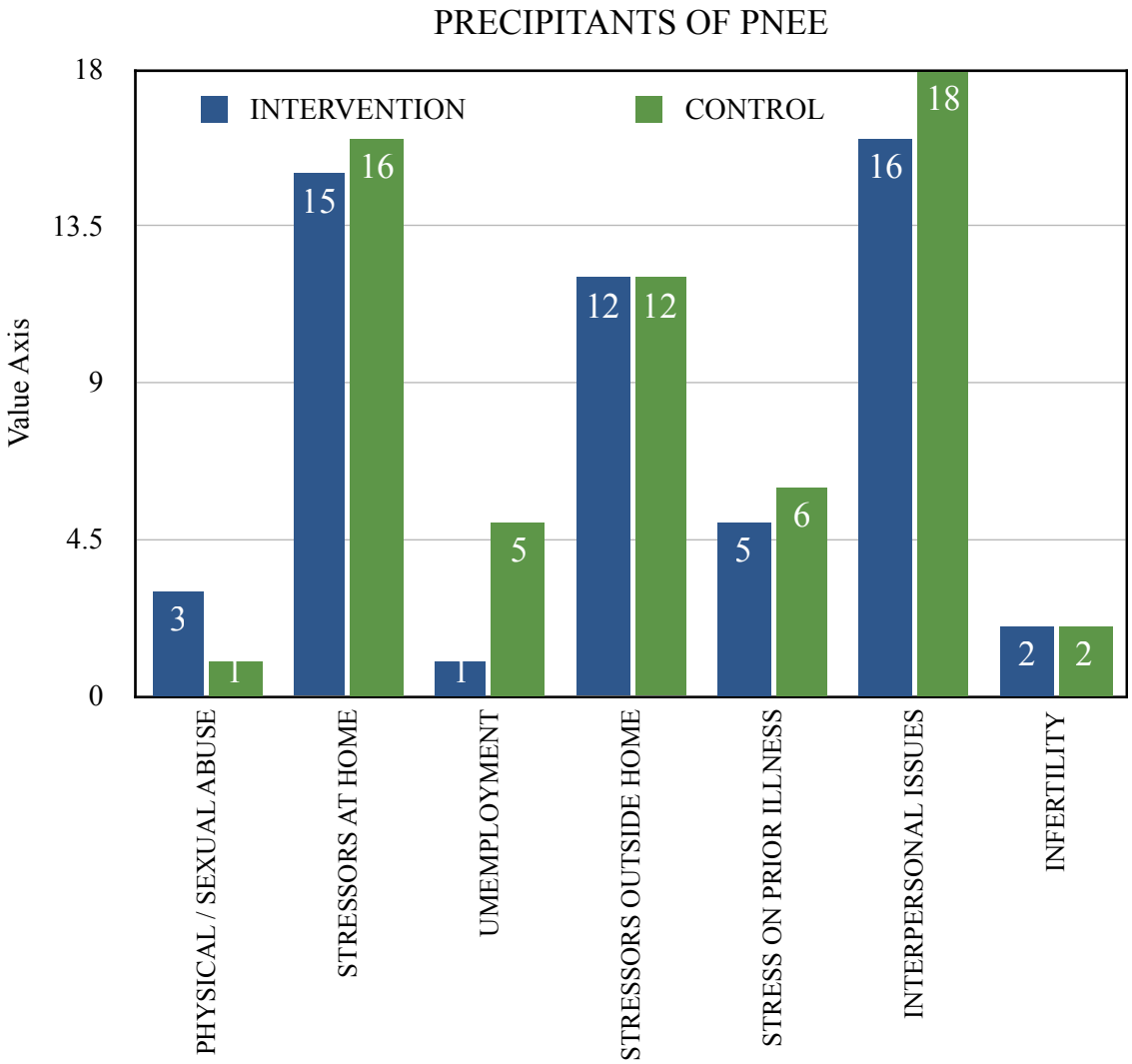


Fig. 5. 6. Precipitants of PNEE

INDIRECT PRECIPITANTS OF PNEE

IMPACT OF COVID 19

The impact of external or remote factors were analysed hence, the impact of COVID 19 scenario and change in lifestyle both within and outside home was taken into account. The subjective feeling on the existing illness as either being worsened or not was analysed, and it was found that 15% of the total 65 patients included in the study had an adverse impact following COVID-19 outbreak.

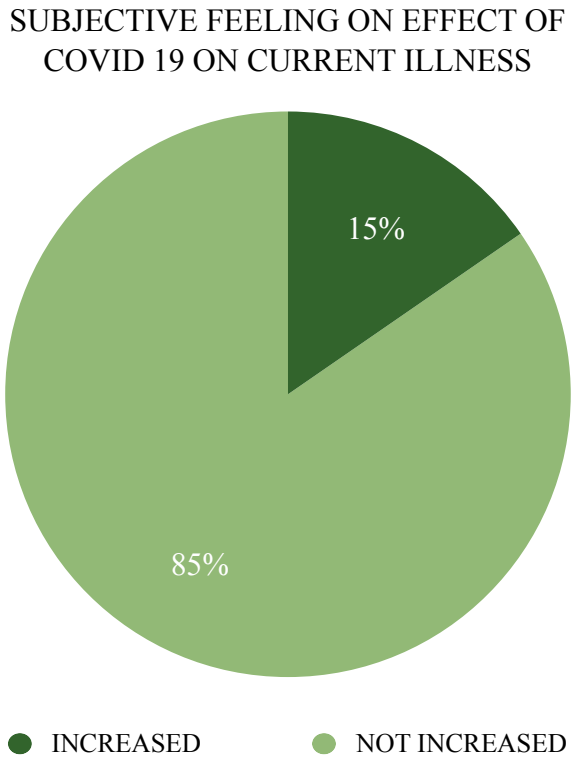


Fig. 5.7. Impact of COVID 19 on PNEE

BURDEN OF COVID 19 ON PNEE PATIENTS

The total number of patients being affected by COVID 19 was analysed to assess its effect on PNEE. In addition, when the family members are also affected by COVID 19, the impact on PNEE may vary due to various psychosocial factors. Among the intervention arm, the majority of the patients had COVID in family, while in the control arm, majority had COVID afflicted to themselves. However, this difference carried no statistical significance.

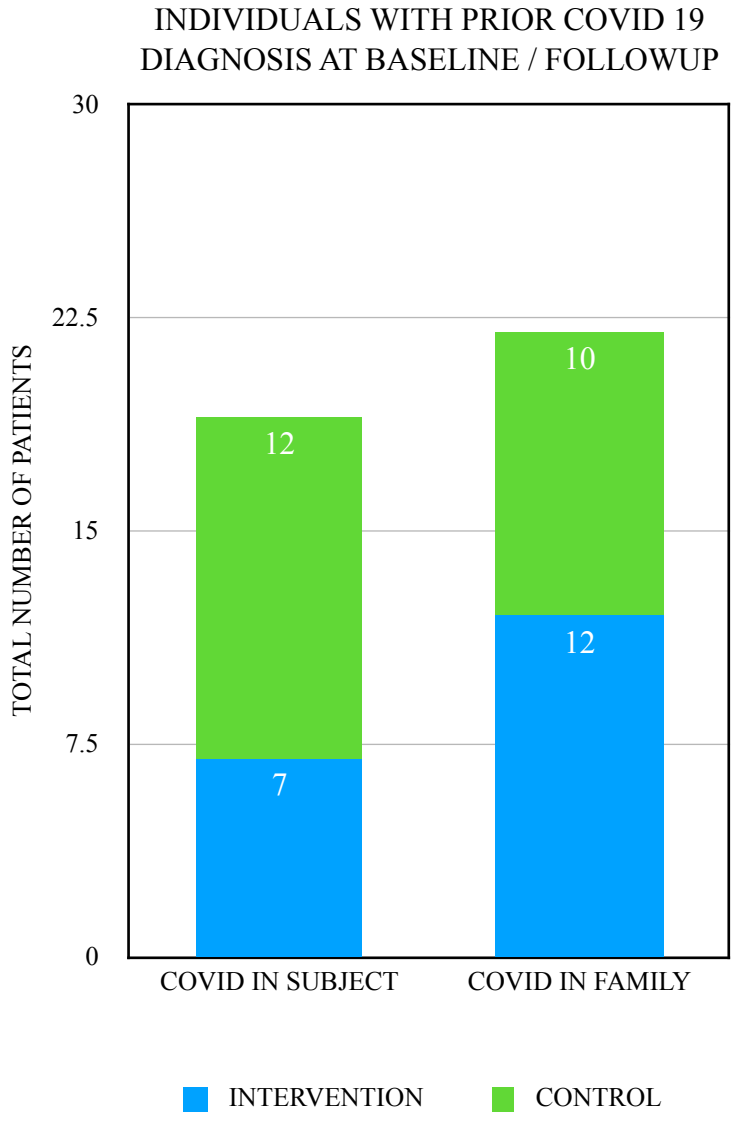


Fig. 5.8. Burden of COVID 19 in PNEE patients

OTHER INDIRECT PNEE PRECIPITANTS

In addition to the impact of COVID 19, there were various other remote factors which would have probably precipitated PNEE attacks indirectly. Among which are the history of true seizures in family members or relatives, single parent, death in family, negative feeling on appearance and medical illness other than seizures. There was statistically significant difference between both groups with regard to history of death in family only.

Table 5.2. Other indirect precipitants of PNEE

PRECIPITANTS	Intervention group (n=31)	Non intervention group (n=34)	P value
Negative feeling on appearance	2 (6.5%)	2 (5.9%)	p=0.999
History of true seizures in family / relatives	7 (22.6%)	4 (11.8%)	p=0.245
Single parent	4 (12.9%)	2 (5.9%)	p=0.298
Death in family	4 (12.9%)	0	p=0.046
Medical illness other than seizures	7 (25.9%)	12 (37.5%)	p=0.343

SEMIOLOGY OF EVENTS

There are various classifications for semiology of event presentation in PNEE. There was similar trend noted in both the groups with the commonest being alteration in consciousness, bizarre body movements followed by somatic complaints, hyperventilation and speech disturbances as shown in Fig. 5.9. However, the only statistically significant different semiology was noted in both groups with regard to speech disturbance (p=0.045). The assumption that the event which is readily visible like bizarre body movements, hyperventilation and speech disturbances have an impact when the event is shown to the patients as compared to silent semiology like alteration in consciousness or somatic complaints.

Table 5.3. Semiology of events in both groups

Semiology	Intervention group (n=31)	Non intervention group (n=34)	P value
HV	8 (25.8%)	4 (11.8%)	P=0.145
Alteration of consciousness	14 (45.2%)	22 (64.7%)	p=0.113
Bizarre body movements	19 (61.3%)	21 (61.8%)	p=0.969
Somatic complaints	16 (51.6%)	15 (44.1%)	p=0.546
Speech	10 (32.3%)	4 (11.8%)	p=0.045

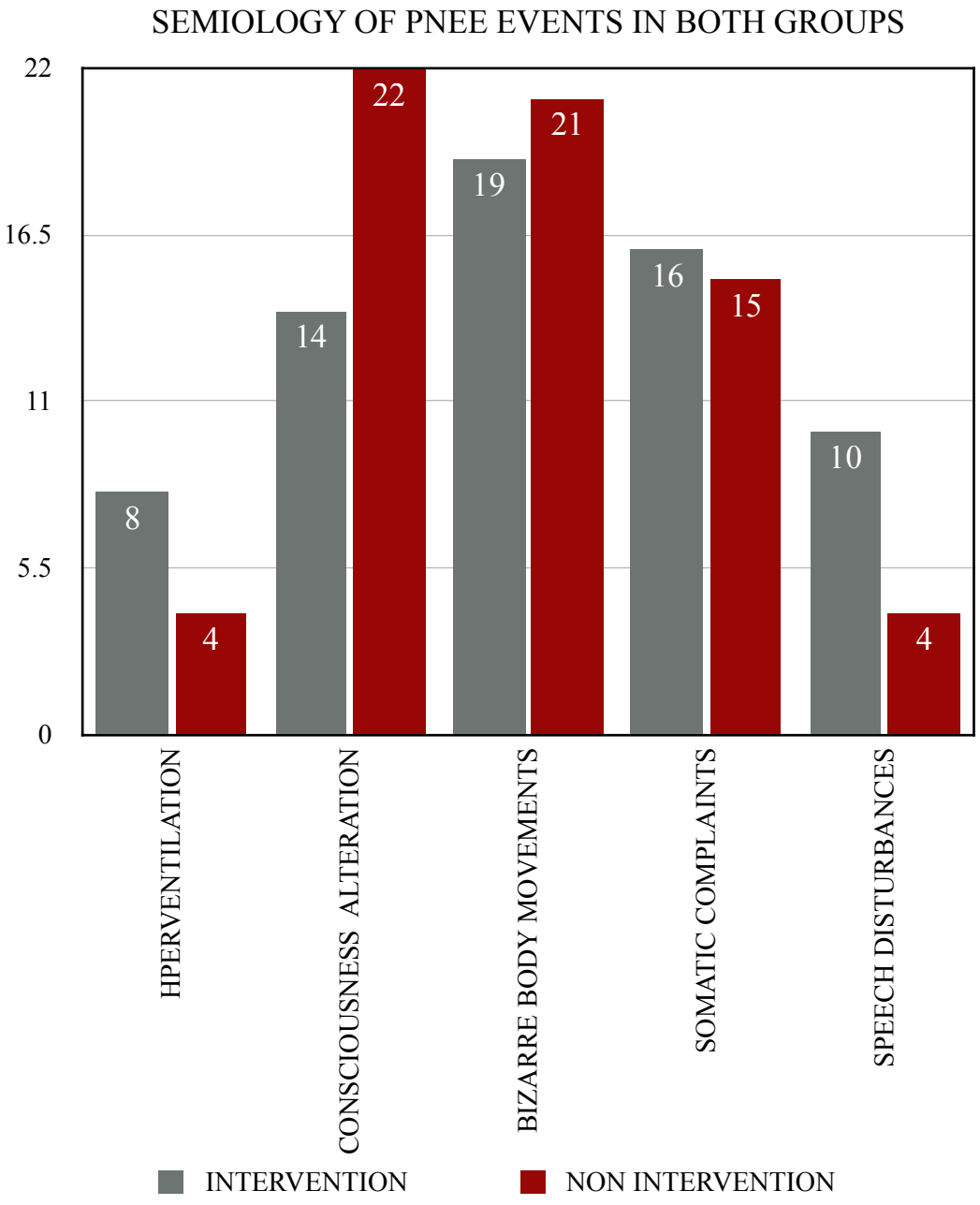


Fig. 5.9. Semiology of PNEE attacks and comparison between both groups

EVENTS RECORDED IN EPILEPSY MONITORING UNIT

All the patients undergoing VEEG monitoring in our centre were monitored for 24 hours or until an habitual event is recorded. The maximum duration of recording was made until about 3 days in anticipation of event occurring in monitoring unit. However, the mean number of events recorded in intervention group was 2.17 ± 1.6 and in the non intervention group it was 1.76 ± 1.56. There was no statistically significant difference in both the groups (p=0.309)

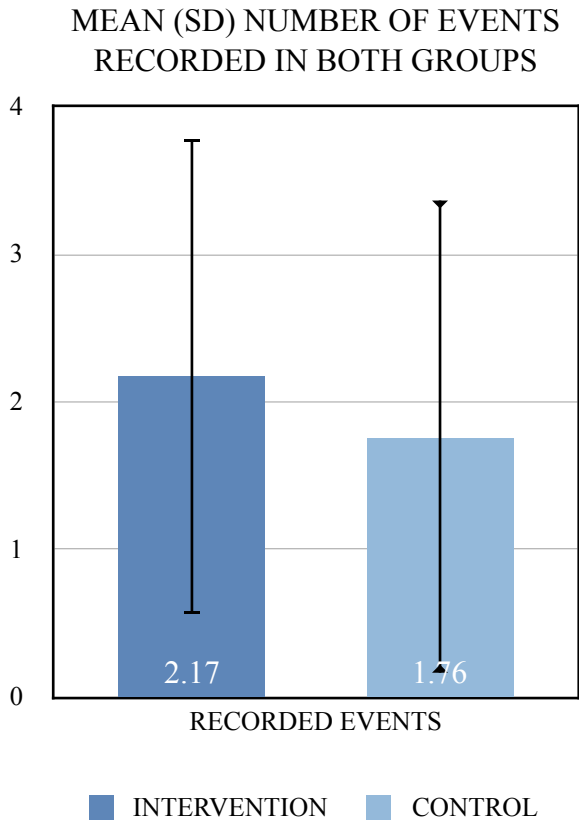


Fig. 5.10. Mean number of events recorded in the study subjects

SECONDARY OUTCOME - EVENT FREQUENCY

The mean event frequency in intervention group was 9.93 ± 16.79 per week while in the non intervention group it was 11.78 ± 25.33 per week. There was a reduction in event frequency in both groups on followup to about 2.58 ± 4.65 per week in intervention group while it was 1.58 ± 3.04 per week in non intervention group. There was no difference between groups neither during baseline (p=0.731) nor during follow up (p=0.311). However, there was statistically significance reduction in event frequency during follow up in both non intervention group (p=0.023) and in intervention group (p=0.007)

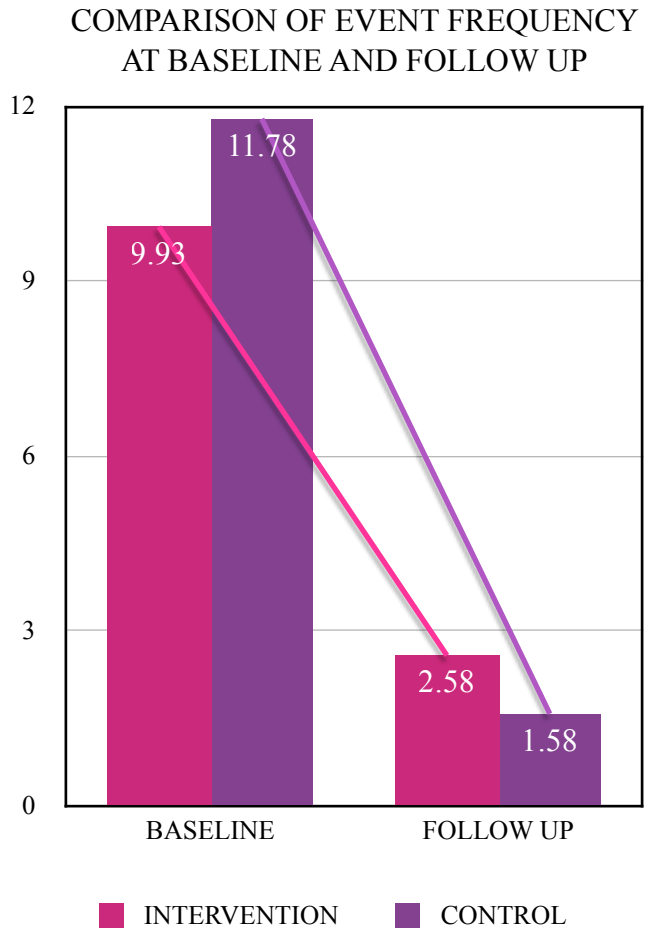


Fig. 5.11. Comparison of event frequency in both groups

PRIMARY OUTCOME - HADS - A

Hospital Anxiety Depression Scale - Anxiety (HADS - A) score at baseline was 9.65 ± 2.88 in intervention group and 9.29 ± 3.02 in non intervention group, with no statistical significance (p=0.634), as shown in Figure 5.12. At 3 months follow up, the mean score in intervention group was 7.81 ± 2.20, while in the non intervention group it was 6.79 ± 2.51, as shown in Table 5.4. However, the p value between both groups was 0.090, which was not statistically significant, but slightly lower in non intervention group as compared to intervention group. When the scores were compared between baseline and follow up using paired t test, there was significant difference in both the groups (p<0.001). Hence, anxiety levels would decrease irrespective of seizure viewing when psychological therapy is given.

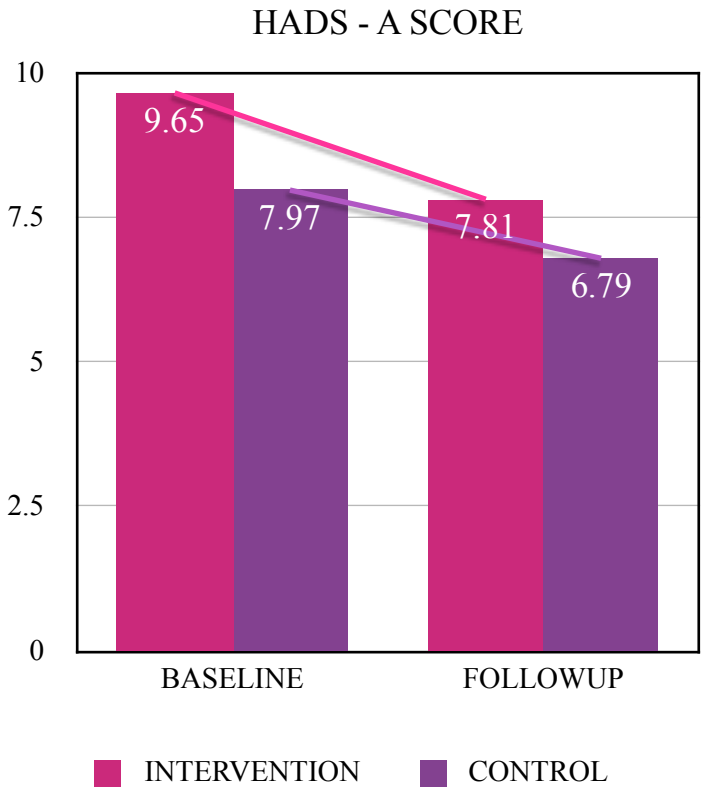


Fig 5.12.a. Comparison of HADS - A score

PRIMARY OUTCOME - HADS - D

The depression scores in the study population had a similar trend as anxiety scores with higher scores at baseline and marginal reduction during follow up though there was no statistical significance as shown in Figure 5.13. When paired t test was applied to both the groups to compare the fall in depression scores during follow up, there was statistical significance in both groups, but was higher for non intervention ($p<0.001$) group as compared to intervention group($p=0.043$), as shown in Table 5.4. Thus, with regard to the depression scores, the effect of seizure viewing has not contributed to a benefit that is lesser than conventional psychotherapy.

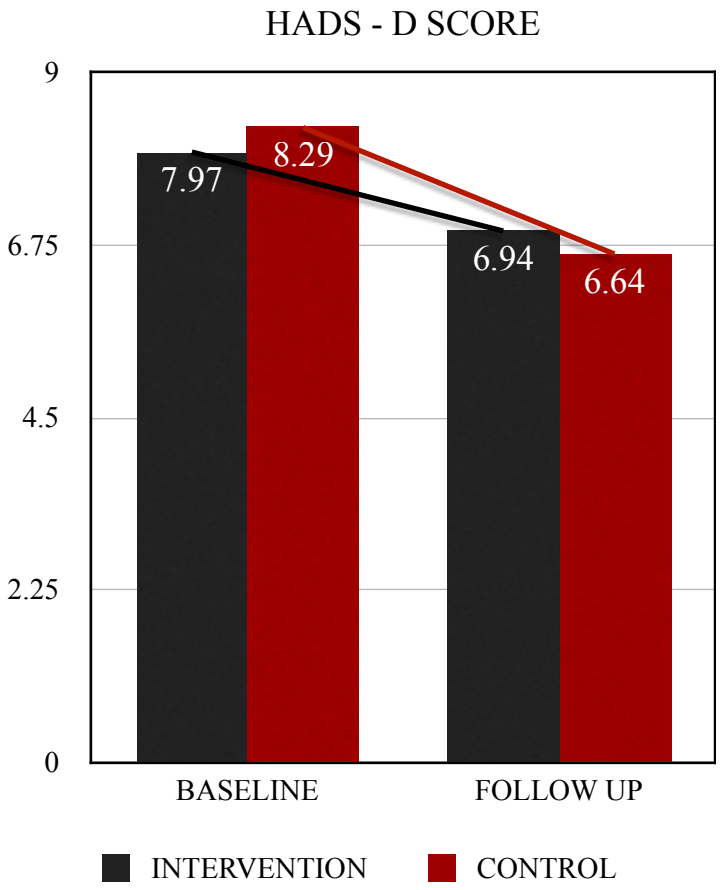


Fig. 5.12.b. Comparison of HADS - D scores

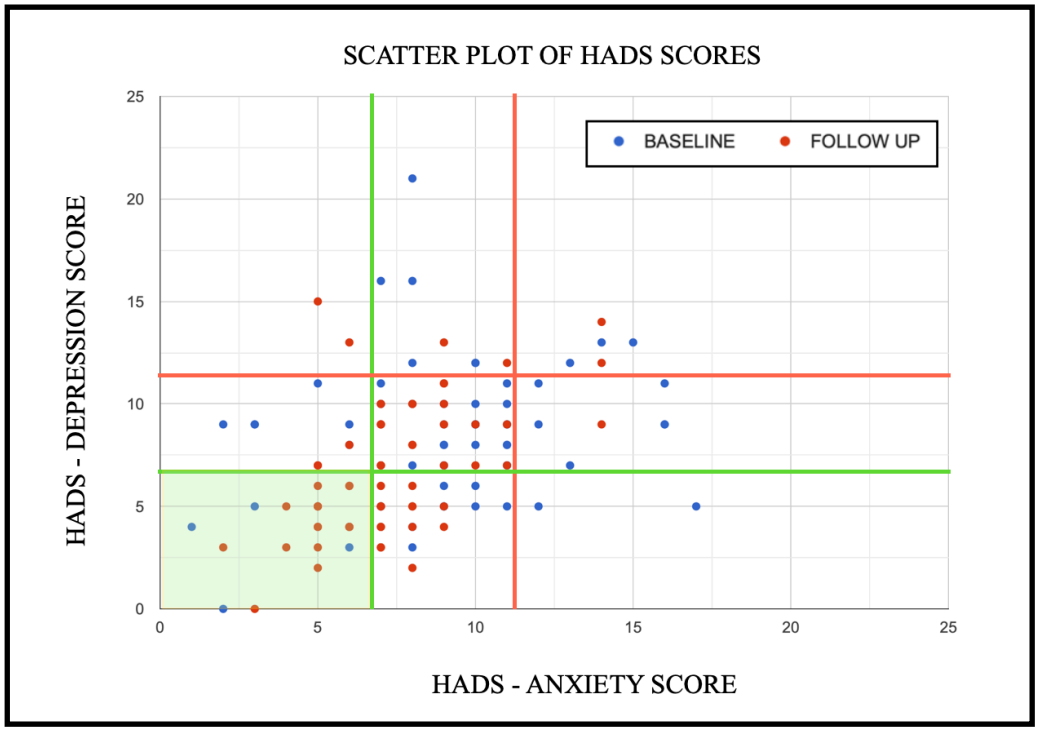


Fig. 5.13. Scatter plot showing the distribution HADS score

Table 5.4. Primary outcome (HADS - A and HADS -D score)

HADS - A	Intervention group (n=31)	Non intervention group (n=34)	P value
Baseline	9.65 (2.88)	9.29 (3.02)	p=0.634
Follow up	7.81 (2.20)	6.79 (2.51)	P=0.090
HADS - D	**Intervention group (n=31)**	**Non intervention group (n=34)**	**P value**
Baseline	7.97 (3.55)	8.29 (4.10)	p=0.733
Follow up	6.94 (2.93)	6.64 (3.49)	P=0.713
Paired t test	**Non intervention group (p value)**	**Intervention group (p value)**	
HADS - A	p<0.001	p<0.001	
HADS - D	p<0.001	p=0.043	

Table. 5.5. QOLIE 31 Scores at baseline

QoLIE component	Intervention group (n=31)	Non intervention group (n=34)	P value
QOLIE 31 overall score	52.90 (8.44)	49.18 (10.05)	p=0.113
Seizure worry	41.58 (14.48)	44.37 (13.60)	p=0.426
Overall QoL	49.68 (16.78)	51.10 (29.16)	p=0.771
Emotional well being	51.58 (9.74)	51.50 (11.88)	p=0.976
Energy / Fatigue	54.19 (11.70)	55.88 (15.64)	p=0.626
Cognitive	52.77 (11.71)	47.96(18.76)	p=0.225
Medication effects	57.43 (19.18)	46.55 (23.46)	p=0.046
Social effects	49.65 (20.68)	42.41 (17.51)	p=0.122

Table. 5.6. QOLIE 31 Scores at 3 months follow up

QOLIE component	Intervention group (n=31)	Non intervention group (n=34)	P value
QOLIE 31 overall score	51.76 (4.61)	51.59 (7.96)	P=0.916
Seizure worry	52.33 (15.14)	45.32 (16.05)	p=0.075
Overall QoL	61.77 (15.17)	63.72 (14.61)	P=0.606
Emotional well being	59.1 (11.90)	57.24 (10.97)	p=0.514
Energy / Fatigue	51.68 (9.52)	59.91 (11.62)	P=0.508
Cognitive	51.61 (9.16)	47.65 (10.72)	P=0.116
Medication effects	57.73 (13.84)	59.03 (13.78)	P=0.706
Social effects	47.16 (11.84)	51.06 (14.53)	P=0.243

Table 5.7. Comparison of QoLIE 31 at baseline and follow up (Paired t test)

QoLIE 31 component	Non intervention group (p value)	Intervention group (p value)
QOLIE - 31	p=0.282	p=0.559
Seizure worry	p=0.814	p=0.008
Overall QoL	p=0.003	p<0.001
Emotional well being	p=0.103	p=0.003
Energy	p=0.121	p=0.387
Cognitive	p=0.934	p=0.687
Medication effects	p<0.001	p=0.936
Social	p=0.016	p=0.588
Event frequency	p=0.023	p=0.007

PRIMARY OUTCOME - QOLIE 31

OVERALL QOLIE 31 SCORE

The overall QOLIE 31 score in had been lesser in non intervention arm, but has improved during followup though the score has marginally fallen down in intervention arm. However, there has been no statistically significant difference when baseline and follow up score comparison was done. The paired t test from non intervention arm was 0.282 while that of intervention arm was 0.559. There has been no conclusive evidence for seizure viewing benefit when compared to conventional psychotherapy with regard to overall QOLIE 31 score.

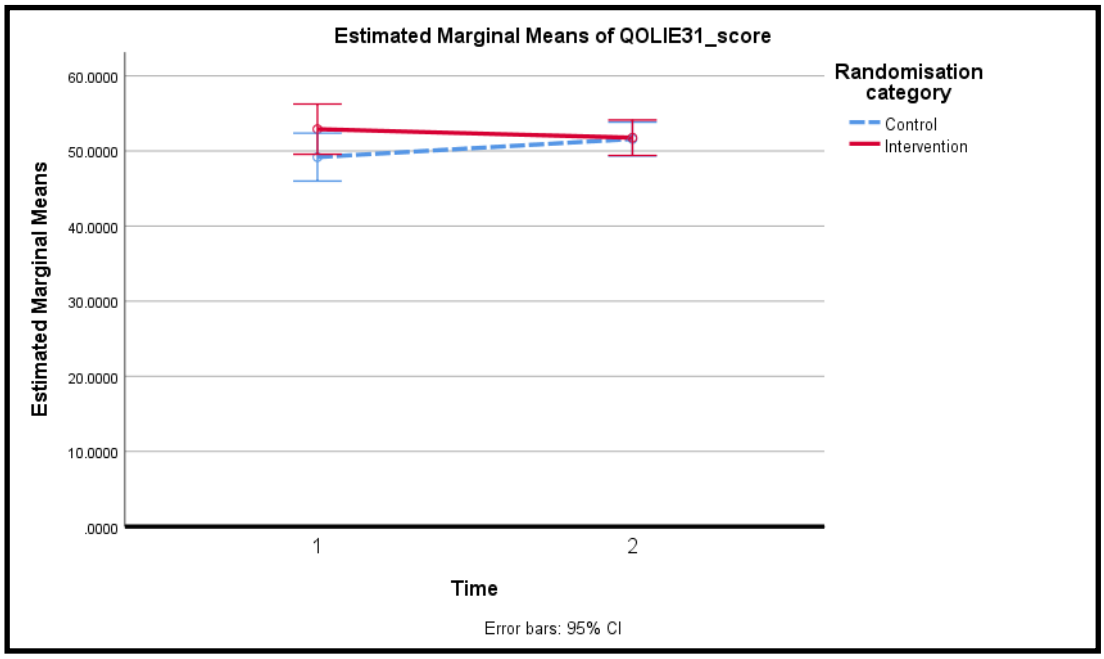


Fig. 5.14. Repeated measure graph showing overall QOLIE 31 score

SEIZURE WORRY

The score on seizure worry is calculated by using 5 subsections of the main questionnaire. It was lower in intervention group at baseline and there was statistically significant increase in this score at follow up, which implies that there is a definite role for seizure viewing in patients with PNEE. However, there has been an increase in the score in control arm as well, but has been very minimal. The followup values was 52.33 $\pm$ 15.14 in intervention group and 45.32 $\pm$ 16.05 in the control group (p=0.075) and the baseline score is shown in Table 5.6. The paired t test for intervention arm was p=0.008, which shows definite significance on the seizure viewing intervention.

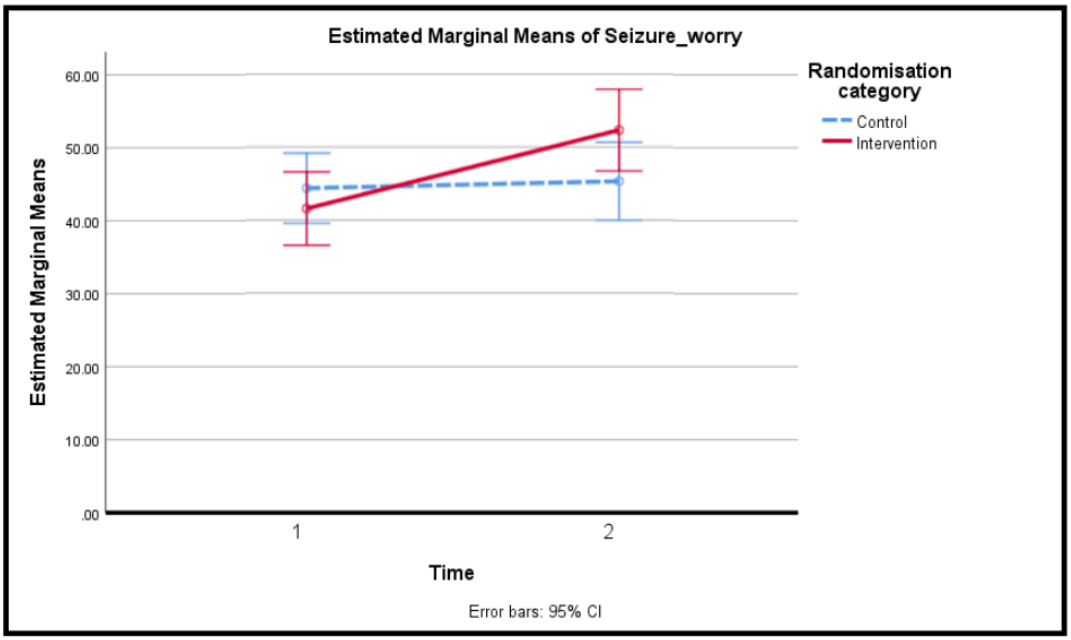


Fig. 5.15. Repeated measure curve on seizure worry

OVERALL QUALITY OF LIFE

A measure of overall quality of life is the individual's own perception was calculated using 2 questions which allowed self rating across a scale of 0-100. The baseline value was close to each other in both groups without any statistical significance (p=0.771), while the follow up score also had a similar trend when compared between both the groups (p=0.606). However, when the baseline and follow up scores were compared, paired t test showed statistical significance in both the arms, as shown in Table 5.7.

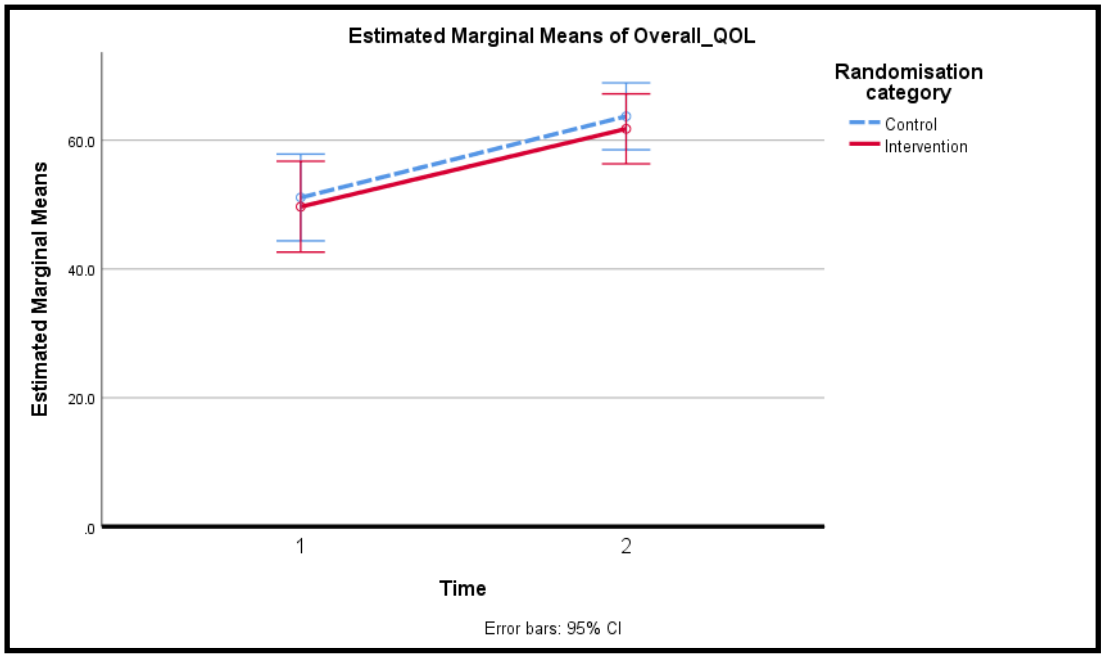


Fig. 5.16. Repeated measure curve on Overall quality of life

EMOTIONAL WELL BEING

There were 5 questions in the standard questionnaire that enquired about the individuals emotional status in the prior 4 weeks. The baseline score in both groups was around 51, which had increased to 59 and 58 in intervention and non intervention arm respectively, as shown in Table 5.6 and 5.7. The paired t test showed a statistical significance ($p<0.003$) in the intervention arm. Thus viewing one's own event has a an impact on emotional well being state of the individual when combined with psychotherapy. Though the score has been increased in control arm it is not statistically significant.

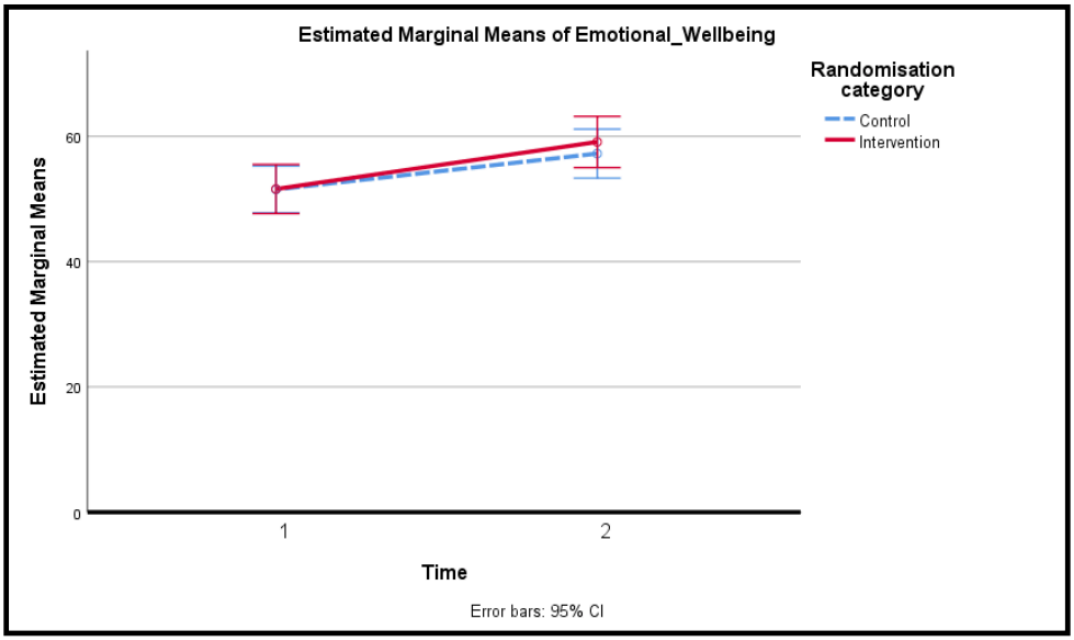


Fig. 5.17. Repeated measure curve showing Emotional well being

ENERGY / FATIGUE

This component was measured by 4 items in the questionnaire. The mean energy/fatigue score at baseline was 54 in intervention arm and 55 in non intervention arm. The mean score at followup in intervention arm was 51, while it was 59 in non intervention arm. The score at baseline was slightly higher than follow up score, but had no statistical significance on paired t test, as shown in Table. 5.7. However, the scores at baseline and follow up remained the same in non intervention arm.

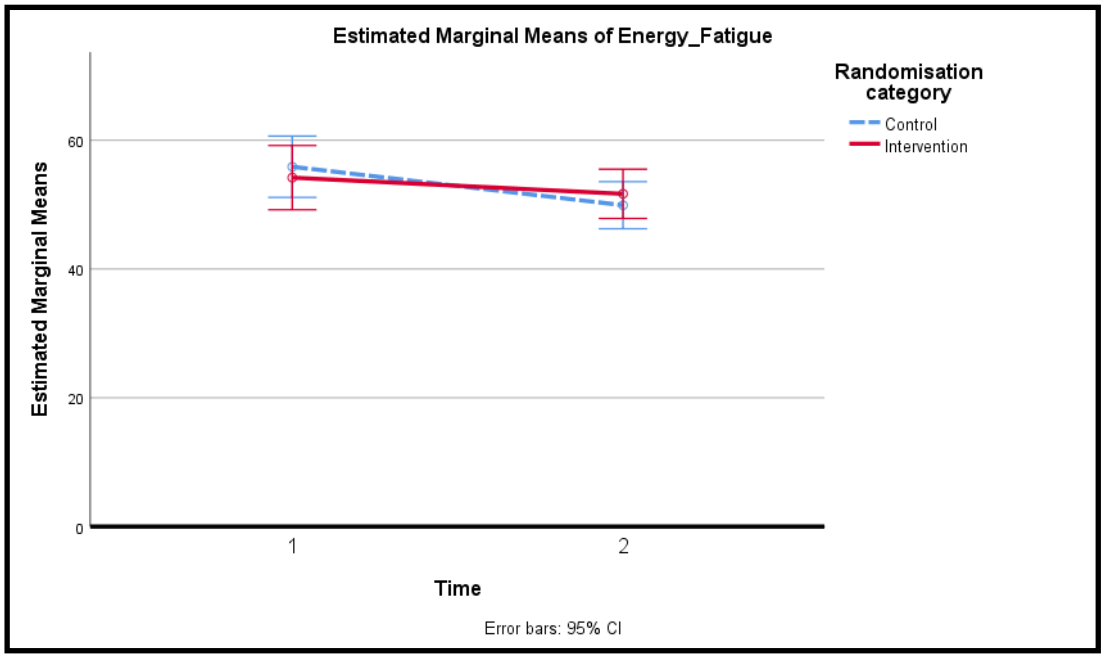


Fig. 5.18. Repeated measure curve on Energy/Fatigue

COGNITIVE EFFECTS

The scores on baseline in intervention and nonintervention arm was 52.77 ± 11.71 and 47.96 ± 18.76 respectively. The followup score was 51.61 ± 9.16 and 47.65 ± 10.72 in intervention and control arm respectively without any statistical significance as shown in Table 5.5 and 5.6. There was no statistical significance between both groups at both baseline and followup. However, paired t test also showed no statistical significance in either groups. Thus neither the event viewing not psychotherapy has effect on cognitive domain of the quality of life in epilepsy inventory.

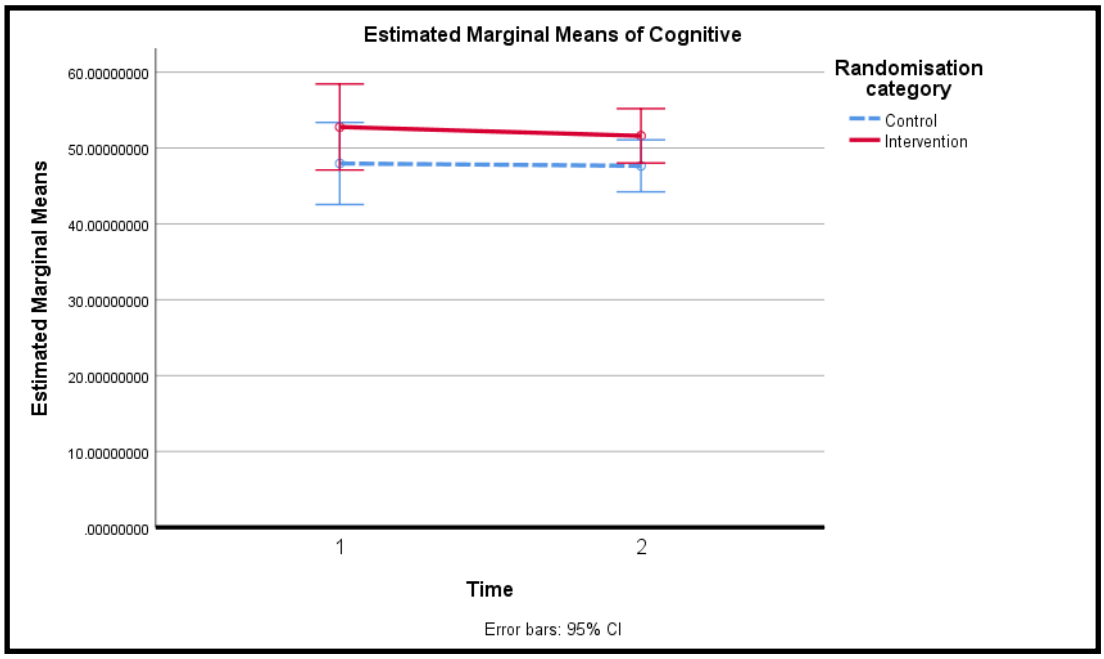


Fig. 5.19. Repeated measure curve on cognitive domain

MEDICATION EFFECT

The worry and psychological status with the intake of long term medications were analysed and the scores were higher in intervention group (57.43± 19.18) as compared to the non intervention group (46.55 ± 23.46). There was a statistically significant difference between both the groups (p=0.046). On followup, the score had almost remained the same in intervention group (57.73 ± 13.84), but had significantly raised in the non intervention group to about 59.03 ± 13.78, with no difference between both groups at followup (p=0.706), but significant difference on paired t test in non intervention group. Thus, there is a better psychological status with regard to medication effect worry in psychotherapy group. However, there has not been an adverse effect in intervention arm.

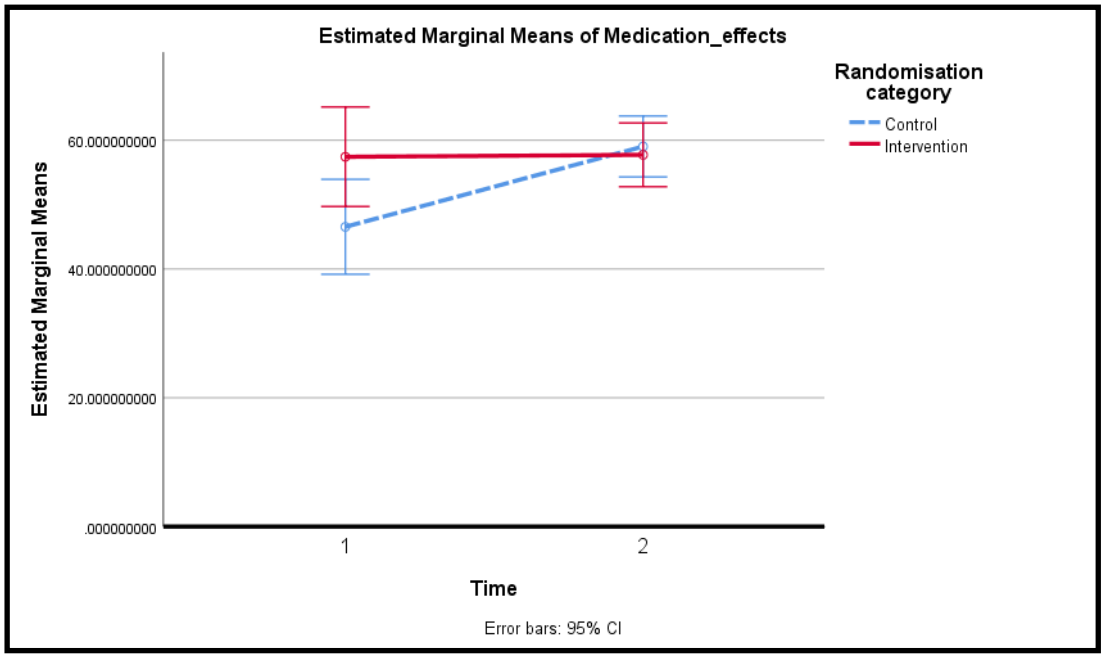


Fig. 5.20. Repeated measure curve on medication effect

SOCIAL EFFECTS

The social effects included functioning of an individual socially in the way similar to their peers or similar to oneself prior to the onset of illness. The scores on baseline in both groups were no statistically significant at baseline (p=0.122), while on the followup, the score had slightly fallen in intervention arm but there was a rise in non intervention arm. However, there was no statistical significance between both the groups neither at baseline nor on follow up. The paired t test showed better results with social functioning in psychotherapy group as compared to intervention arm (p=0.016 vs p=0.588). Thus social functioning may be one of the limitations that occurs following one's own event viewing.

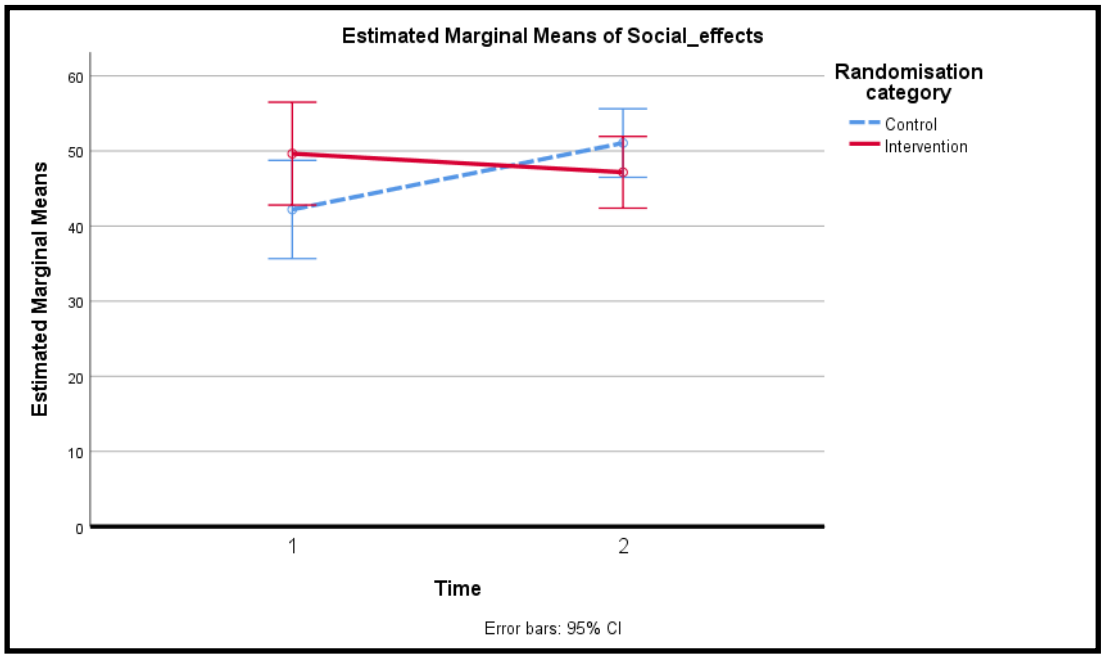


Fig. 5.21. Repeated measure curve on social effect

DISCUSSION

DISCUSSION

Patients with psychogenic non epileptic events are often considered to belong to no man's island, with frequent shuttling between neurologist, internist, psychologist and psychiatrist. The fact that these events are unvoluntary and arise from a disrupted network under a strong emotional disturbance makes this entity to be dealt with a multidisciplinary approach. Among the patients with PNEE, depression is found to be the most common psychiatric disorder with an average prevalence of 31% and lifetime rate ranging from 36% to 80%, which in turn is found to be a significant predictor of poor quality of life. (46, 47). A higher level of education has not found to be a protective shield against development of psychogenic events, but ironically leads to earlier age of onset. (48). The general characteristics like socioeconomic status, employment, marital status and disputes, academic performance and interpersonal issues have been found to influence the state of mind and hence with the initiation or maintenance of PNEE attacks. (48-51).

To the best of our knowledge, this study is first of its kind to introduce a novel method of intervention to approach psychogenic events. With the well proven fact that psychogenic events are subconscious, though it can be partially suppressible, viewing one's own event may change the internal milieu and alleviate the distress associated with one's own illness, which would otherwise add-on with the preexisting psychological comorbidities, which needs to be addressed by individualised psychotherapy. Thus, helping these patients to raise their own views

and reviews of their behaviour and strengthen their commitment to change themselves and improvise their coping strategies.

This study has well randomised the population and a substantial individuals have been followed up and assessed. There was no difference in the baseline characteristics of individuals included in both the groups. In our study, there was a lag of around 2 years from the age of onset of PNEE to age at presentation for being referred to our centre, whilst the average duration from onset to diagnosis in a study with 313 population was surprisingly found to be about 7.2 years. (52). The majority of individuals in our cohort were females, educated to degree or higher, belonged to higher socioeconomic status, employed and married.

The patients with psychogenic events were studied for previous significant life events and were found to have more events in 12 months prior to the onset of initial symptoms as compared to controls. (52). The major precipitants in patients with PNEE were found to be able to get categorised to one of the three: significantly negative events, unexpected and difficult to adjust. (53). Similarly in our study, the majority of individuals had reported negative events or difficulties in adjustments at work place or home followed by interpersonal issues, while there were only few patients with significant prior stressors in the form of unemployment, worry on alternate illness, physical and sexual abuse.

The effective conveyance of this sensitive diagnosis is the cornerstone for success of the treatment. (54). There has been various studies which have shown the abrupt reduction in event frequency after communicating the diagnosis effectively,

however, our study has gone a step ahead to study the psychological status alteration in addition to event frequency. (55). The strategy to convey the diagnosis should include: (a) Acceptance that the events are genuine, but have a psychological background (b) Assurance that all the investigations were within normal limits and (c)Suggestions on coping strategies. (56).

The most common psychiatric comorbidity associated with both true seizures and pseudo seizures is depression. (57). However, our study cohort had higher scores with regard to anxiety as compared to depression and was almost similar in both intervention and non intervention group. Inspite of which, there was neither adverse events reported nor worsening of event frequency or psychological status after viewing the event.

Quality of life in epilepsy - 31 (QOLIE 31) questionnaire gives an overall score in addition to seven components that influence once psychological status predominantly in 4 weeks prior to the assessment, which includes seizure worry, overall quality of life, emotional well being, energy/fatigue, cognitive, medication effects and social effects, while in every sphere, a higher score would indicate a better state of health (58). The baseline scores in our study cohort was not different between groups in any sphere except medication effects, which could be explained by the fact that individuals would be already on various ASMs combinations prior to entering this trial. However, after the diagnosis of PNEE was made, some patients were retained with some ASMs for mood stabilising property and a gradual taper was made for those on polypharmacy, and the decision was highly individualised.

There was significant improvement in seizure worry, emotional well being and quality of life components in intervention group. Assuming the fact that the thought on "What illness do I have?", would alter the other components of cognitive triangle (behaviour and emotions), viewing one's event has perhaps reduced their own worry on seizure and has altered the cognitive triangle positively, causing betterment of emotional well being and quality of life as well, as seen in this study.

The scores in control group show significant improvement with regard to medication effects, social effects and overall quality of life. With higher scores in baseline, the comparison at 12 weeks follow up would be an earlier time point to draw conclusion on its effect and hence a long term follow is required to interpret the influence of event viewing, perhaps when all the patients in this cohort are free of medications. The social effects are partially confounded by the COVID scenario faced by all the patients during this study period. The betterment of overall quality of life proves the efficacy of cognitive behavioural therapy once again.

The strengths of this study are: a) novel intervention to approach psychogenic events b) inexpensive and easy technique to be added along with existing CBT c) randomised trial with good follow up rate d) there were no major harms noticed in this trial except the resurgence of true epilepsy after being in remission, which cannot be solely attributed to the intervention made. However, in the patients with pure PNEE, event viewing appears to be a safe strategy in this trial.

The limitations of this study included that being a single centre study and heterogeneity of psychotherapy received by all the patients and the quality of life

assessed in this study should be exploratory rather than confirmatory. The other limitation being a small sample size though the proportion of patients lost to followup was meagre. Internal validity of the study is being limited by subjective measurement of event frequency which allows for recall bias. This study also supports the existing evidence that psychotherapy and motivational therapy may significantly improve the outcomes in functional disorders like chronic fatigue syndrome and fibromyalgia. Addressing the precipitants and coping strategies in psychotherapy has been the cornerstone aims in psychotherapy given to these patients.

SUMMARY AND CONCLUSIONS

CONCLUSION

In conclusion, this study supports viewing one's own event in psychogenic non epileptic events in addition to psychotherapy in order to reduce the event frequency and reduce seizure worry, improve emotional well being and thereby improving the overall quality of life. Perhaps, further followup and long duration psychotherapy may show promising benefits in event frequency and objective scoring parameters in these patients.

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ANNEXURES

Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week.
Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

Scoring:
Total score: Depression (D) _____ Anxiety (A) _____
0-7 = Normal
8-10 = Borderline abnormal (borderline case)
11-21 = Abnormal (case)

These questions are about how you **FEEL** and how things have been for you during the **past 4 weeks**. For each question, please indicate the one answer that comes closest to the way you have been feeling.

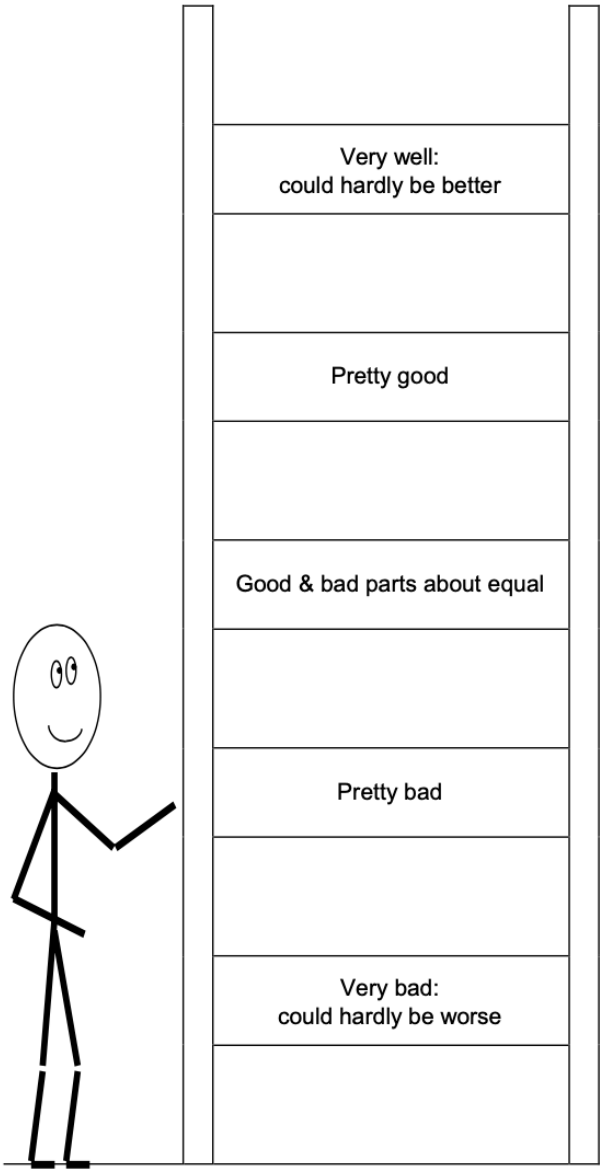
How much of the time during the **past 4 weeks...**

(Circle one number on each line)

		All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
2.	Did you feel full of pep?	1	2	3	4	5	6
3.	Have you been a very nervous person?	1	2	3	4	5	6
4.	Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
5.	Have you felt calm and peaceful?	1	2	3	4	5	6
6.	Did you have a lot of energy?	1	2	3	4	5	6
7.	Have you felt downhearted and blue?	1	2	3	4	5	6
8.	Did you feel worn out?	1	2	3	4	5	6
9.	Have you been a happy person?	1	2	3	4	5	6
10.	Did you feel tired?	1	2	3	4	5	6
11.	Have you worried about having another seizure?	1	2	3	4	5	6
12.	Did you have difficulty reasoning and solving problems (such as making plans, making decisions, learning new things)?	1	2	3	4	5	6
13.	Has your health limited your social activities (such as visiting with friends or close relatives)?	1	2	3	4	5	6

14. How has the **QUALITY OF YOUR LIFE** been during the **past 4 weeks** (that is, how have things been going for you)?

(Circle one number)



The following question is about **MEMORY**.

(Circle one number)

		Yes, a great deal	Yes, somewhat	Only a little	No, not at all
15.	In the past 4 weeks, have you had any trouble with your memory?	1	2	3	4

Circle one number for **how often** in the **past 4 weeks** you have had trouble *remembering* or **how often** this memory problem has interfered with your normal work or living.

		All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
16.	Trouble remembering things people tell you	1	2	3	4	5	6

The following questions are about **CONCENTRATION** problems you may have. Circle one number for **how often** in the **past 4 weeks** you had trouble concentrating or **how often** these problems interfered with your normal work or living.

		All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
17.	Trouble concentrating on reading	1	2	3	4	5	6
18.	Trouble concentrating on doing one thing at a time	1	2	3	4	5	6

The following questions are about problems you may have with certain **ACTIVITIES**. Circle one number for **how much** during the **past 4 weeks** your epilepsy or antiepileptic medication has caused trouble with...

		A great deal	A lot	Somewh at	Only a little	Not at all
19.	Leisure time (such as hobbies, going out)	1	2	3	4	5
20.	Driving	1	2	3	4	5

The following questions relate to the way you **FEEL** about your **seizures.**

(Circle one number on each line)

		Very fearful	Somewhat fearful	Not very fearful	Not fearful at all
21.	How fearful are you of having a seizure during the next month?	1	2	3	4

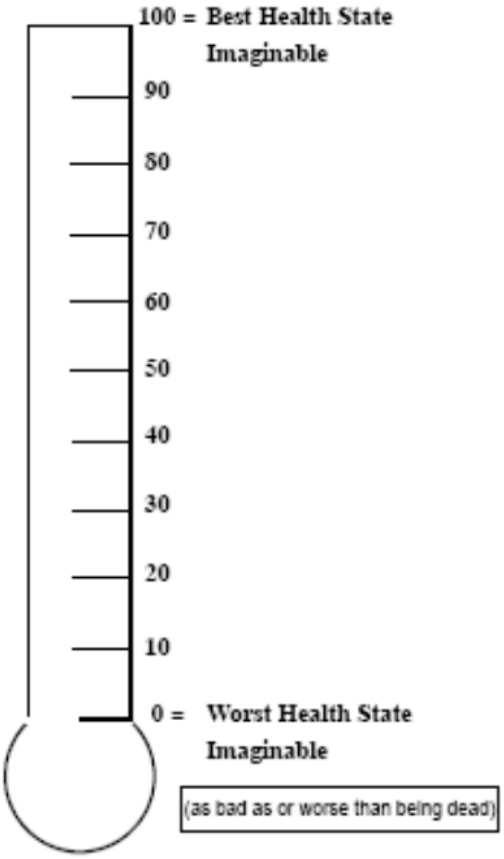
		Worry a lot	Occasionally worry	Don't worry at all
22.	Do you worry about hurting yourself during a seizure?	1	2	3

		Very worried	Somewhat worried	Not very worried	Not at all worried
23.	How worried are you about embarrassment or other social problems resulting from having a seizure during the next month?	1	2	3	4
24.	How worried are you that medications you are taking will be bad for you if taken for a long time?	1	2	3	4

For each of these **PROBLEMS**, circle one number for **how much they bother you** on a scale of 1 to 5 where 1 = Not at all bothersome, and 5 = Extremely bothersome.

		Not at all bothersome				Extremely bothersome
25.	Seizures	1	2	3	4	5
26.	Memory difficulties	1	2	3	4	5
27.	Work limitations	1	2	3	4	5
28.	Social limitations	1	2	3	4	5
29.	Physical effects of antiepileptic medication	1	2	3	4	5
30.	Mental effects of antiepileptic medication	1	2	3	4	5

31. How good or bad do you think your health is? On the thermometer scale below, the best imaginable state of health is 100 and the worst imaginable state is 0. Please indicate how you feel about your health by circling one number on the scale. **Please consider your epilepsy as part of your health when you answer this question**.



श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेंद्रम - 695 011, केरल, भारत
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY
TRIVANDRUM - 695 011, KERALA, INDIA
(एक राष्ट्रीय महत्व का संस्थान, विज्ञान एवं प्रौद्योगिकी विभाग, भारत सरकार)
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Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1596 /NOVEMBER-2020 30.12.2020

Dr. Lakshmi Priya
Senior Resident
Department of Neurology
SCTIMST, Thiruvananthapuram

Dear Dr. Lakshmi Priya,

Thank you for submitting documents related to your proposal titled "(**EFFECT OF SEIZURE VIEWING ON PSYCHOLOGICAL OUTCOME AMONG PATIENTS WITH PSYCHOGENIC NONEPILEPTIC SEIZURES (PNES).**IEC/1596)" to the IEC for review.

The following documents were reviewed:

1. *Check list*
2. *Project Proposal*
3. *IEC Application Form*
4. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 09.09.2020 by the HOD*
5. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 09.09.2020 by the Co-PI*
6. *Proforma*
7. *TAC Approval Letter*
8. *Patient Information Sheet in English*
9. *Patient Information Sheet in Malayalam*
10. *Patient Consent Form in English*
11. *Patient Consent Form in Malayalam*
12. *CV of Dr. Lakshmi Priya with TNMC number*
13. *CV of Dr. Ashalatha Radhakrishnan TCMC number*
14. *CV of Aley Alaxander*
15. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 19.09.2020 by the PI*

The following members of the Students Sub-Committee of the Institutional Ethics Committee participated in the discussions held between August 23-October 29, 2020 at the offices and residences of the members

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
3.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
4.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
5.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
6.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
7.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

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

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

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

Sincerely,

Mala Ramanathan
Member Secretary, IEC

PLAGIARISM CHECK REPORT

RE-2022-43944-plag-report

ORIGINALITY REPORT

2%	1%	2%	0%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

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