

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Stress - Its Role and Consequences In Epilepsy.

Lalitha Devi Seerla^{1*}, Syed Abdul Jaweed², and R Vijayaraghavan³.

¹Research Scholar, Saveetha University, Thandalam, Chennai, Tamil Nadu, India.

²Department of Biochemistry, Professor and Head, Bidar Institute of Medical Sciences, Govt. Medical College, Bidar, Karnataka, India.

³Department of Research and Development, Research Director, Saveetha University, Thandalam, Chennai, Tamil Nadu, India.

ABSTRACT

The aim of the study was to determine stress was the factor which triggers further seizures in epilepsy. A total of 100 Epileptic participants who were diagnosed as epileptic by neurologists were recruited. The participants consists of Group-I (GTCS) n=50, Group-II (JME) n=50. Patient selection and diagnosis was based on the criteria of the commission and terminology of the international league against epilepsy. All epileptic participants taken in the study were on treatment with Anti Epileptic Drugs (AED).The present study results shows that the percentages of participants affected by stress in Group-I (GTCS) females (63.6%) are under more stress compared to Males. In Group-II (JME) males (54.5%) were under more stress compared to females. But, when compare between two groups GTCS and JME Group-I epileptic participants were under more stress (62%) compared to Group-II (52%). Stress can be considered as one of the precipitating factor for repeated seizures in epilepsy and the different mechanisms of stress hormones which can activate major pathways like inflammatory, immune and free radical generation can lead to further complications and might be the causes for frequent seizures observed in epilepsy.

Keywords: Generalized tonic-clonic seizures (GTCS), Juvenile Myoclonic epilepsy (JME), hypothalamic pituitary adrenal (HPA) axis, adrenocorticotrophic hormones (ACTH).

**Corresponding author*

INTRODUCTION

Epilepsy is a disorder of brain dysfunction stressing the role of heredity in the disease. It is a condition or state in which recurrent spontaneous unprovoked seizures occur, which are convulsive or non-convulsive episodes. Stress is a condition of emotional strain and tension where in some epilepsy people can lead to increased trigger on seizure generation. It is a non-specific response of the body to any noxious stimulus [1]. Most of the participants of epilepsy reported stress induced seizures but, the proper relation between these two factors was not clear. The objective measures of stress and other factors like sleep deprivation, fever, Irritability, Poor concentration, Poor memory, Sweating, Lack of appetite, Headaches, Depression or feeling low, Feeling tired, smoking and excess alcohol consumption can be considered. If the stress was identified as isolated factors that increase seizure frequency and duration it can be considered as an alternative treatment to reduce a variety of stress reduction modalities [2, 3].

Under stress conditions brain regulate the stress response by the adrenal glands to release 'stress hormones' which maintain the body ready to take action called 'fight or flight' response a normal condition and stress hormones return to normal but, when these hormones remain longer period is harmful [4]. Stress leads to activation of sympathetic nervous system and hypothalamic pituitary adrenal (HPA) axis leads to release of catecholamines adrenaline and noradrenaline, which maintain heart, liver, muscles, and other organs ready to take action a short term response [5]. A long term response of stress hormones can cause changes in the neuronal functioning system and in brain structure and function which may lead to neuronal excitability might be the reason for stress induced seizures noticed in Epilepsy. Moreover, chronic stress condition might be one of the reasons for most of the **chronic neurological disorders**, psychiatric disorders [6]. Nevertheless animal studies also showed that stress can increase vulnerability to seizures through alterations of brain structure, electrophysiology, neurotransmitter, and neuroendocrine functions promote to development of epilepsy [7]. With this background the present study was taken to study whether stress was the precipitating factor for repeated seizures in epilepsy. So, that stress reducing measures can be taken as an alternative treatment to overcome the seizure frequency.

MATERIAL AND METHODS

A total of 100 Epileptic participants who were diagnosed as epileptic by neurologists were recruited from Girija Neuro centre Vijayawada, Andhra Pradesh and Bidar Govt. Hospital, Bidar, Karnataka.

Patient selection and diagnosis was based on the criteria of the commission and terminology of the international league against epilepsy. Participants were categorized into two groups. In Group-I, 50 participants (Age: 5-40 yrs) with Generalized Tonic Clonic seizures (GTCS), and in Group- II, 50 participants (Age: 5-30 yrs) with Juvenile Myoclonic Epilepsy (JME) (Myoclonic seizures). All epileptic participants taken in the study were on treatment with Anti Epileptic Drugs (AED). Epileptic participants who were seizure free after AED treatment, those with chronic Psychiatric disorders, brain syndrome due to some cause other than epilepsy or usage of stress hormone medication or oral contraceptives were excluded from the study. The study protocol was approved by the institutional ethical review board and informed consent was obtained from participants and for children from their parents.

Questionnaire

A questionnaire with details was obtained from participants with epilepsy and for Children from their parents was taken to obtain information on the relation between stress and epileptic seizures if yes, what factors were influence to stress were collected from the participants. Further clinical data such as type of seizure, time period of seizure, age of onset of epilepsy were also collected. The data was tabulated in the excel sheet and analyzed for total number of participants experiencing the seizures on stress and their percentage was calculated. Categorical variables were arranged as frequency distribution and analysed either by chi square test. A probability of 0.05 or less is taken as statistically significant. The statistical analysis were carried out by sigma plot (sys stat software USA)

RESULTS

Table 1: Age distribution in study Groups

Age in years	Group I (GTCS)		Group II (JME)	
	No	%	No	%
<10	3	6.0	5	10
11-20	11	22.0	28	56
21-30	23	46.0	17	34
31-40	13	26.0	0	0.0
Total	50	100.0	50	100.0
Mean ± SEM	24.88±1.42		19.06±1.29	

Table 2: Shows Gender distribution in study Groups.

Gender	Group I		Group II	
	No	%	No	%
Female	22	44.0	28	56.0
Male	28	56.0	22	44.0
Total	50	100.0	50	100.0

Table 3: Shows Effect of stress in Epileptic participant groups.

Groups	Gender	No. of patients	No. of patients affected by stress	No. of patients not affected by stress
GTCS group-I	Male	28	17(60.7)	11(39.2)
	Female	22	14(63.6)	08(57.1)
	Total	50	31(62)	19(38)
X ² - value	0.007			
P- value	0.935			
JME group-II	Male	22	12(54.5)	10(45.4)
	Female	28	14(50.0)	14(50.0)
	Total	50	26(52)	24(48)
X ² - value	0.001			
P- value	0.973			

Figures in percentiles are percentages

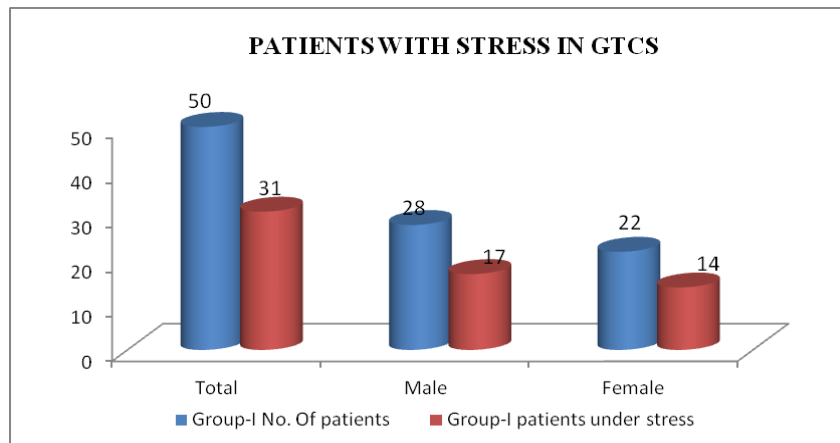


Figure 1: Shows number of participants affected by stress in GTCS

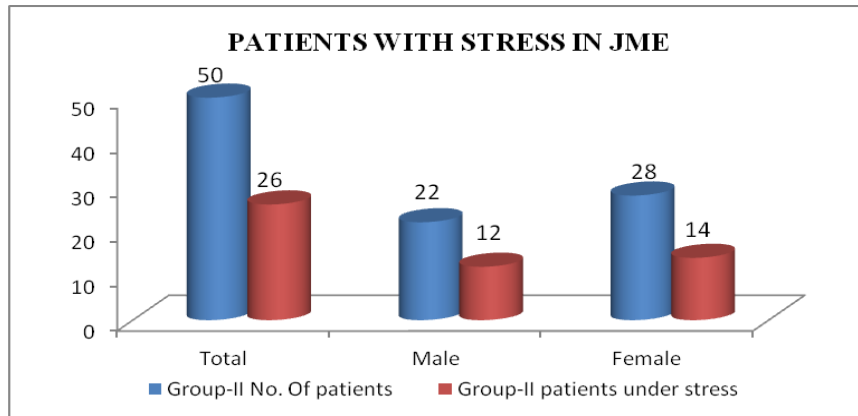


Figure 2: Shows number of participants affected by stress in JME

Table 1: The present study comprises of 100 participants with Group-I (GTCS) 50 and Group-II (JME) 50 representing in Group-I majority of the participants were with an age group of 21-30 (46%) and in Group- II participants were more with an age 11-20 (56%).

Table 2: Represents the gender distribution in study groups. In GTCS Group-I the male participants were more as compared to female. In Group-II Female participants were more in number.

Table 3: Represents the percentages of participants affected by stress in Group-I (GTCS) females (63.6%) are under more stress compared to Males. In Group-II (JME) males (54.5%) were under more stress compared to females. But, when compare between two groups GTCS and JME Group-I epileptic participants were under more stress (62%) compared to Group-II (52%) and chi square test showed insignificant in between male and female P=0.935 participants in GTCS and also between male and female P=0.973 in JME.

DISCUSSION

Excessive stress may leads to psychiatric disorders [25]. Stress influences epilepsy by increase reoccurrence of seizures and also it can influence the development of disease [6]. The results from the present study shows that in Group-I GTCS 62% and in Group-II JME 52% epileptic participants were reported stress as a trigger for seizures. In GTCS females were more with 63.6% compared to males. In JME males were more 54.5% compared to females. Our study was in line with earlier studies [8-10], who proposed that higher levels of stress and anxiety were associated with high risk of seizure frequency. Studies on stress hormone levels showed that increased levels of cortisol and adrenocorticotrophic hormones (ACTH) was noticed after seizure in postictal state observed in GTCS and partial seizures indicating that stress hormones, HPA-axis or neuronal stress hormone receptors plays a role in epilepsy [11-13]. Even animal studies also support the evidence showing that increased levels of stress hormones like adrenocorticotrophic hormone increase the excitability in rodents altering the excitation inhibition balance [14-16]. Stress hormones have reduced negative feedback of HPA- axis in epilepsy participants and the hormones like corticotrophin-releasing hormone have role in stress-precipitation of seizures [4].

Recent studies proposed that early life stress has impact on activating the inflammatory and immune pathways which may lead to neuronal damage in epilepsy [17, 18]. Stress can activate many inflammatory pathways in brain like NF-κB, TNF-α, interleukins, prostaglandins and can also induce generation of free radicals via glucocorticoids and hence can be considered as a major aspect of epileptic seizures [19-22].

The hyperactivity of stress hormones during seizures might be one of the causes of repeated seizures in epilepsy which can cause changes in autonomic nervous system common symptom after GTCS might cause dysfunction of HPA axis and can decrease parasympathetic nervous system tone associated with altered stress appraisal increasing stress vulnerability [23, 24].

In conclusion Stress can be considered as one of the precipitating factor for repeated seizures in epilepsy and the different mechanisms of stress hormones which can activate major pathways like inflammatory, immune and free radical generation can lead to further complications and might be the causes for frequent seizures observed in epilepsy.

REFERENCES

- [1] Chrousos G.P. Nat. Rev. Endocrinol 2009; 5: 374–381.
- [2] Frucht MM, Quigg M, Schwaner C, Fountain NB. Epilepsia 2000; 41:1534–9.
- [3] Mattson RH. Advances in neurology 1991; Vol. 51. New York: Raven Press.
- [4] Jolien S. van Campen, Floor E. Jansen, Milou A. BRAIN 2015; 138: 2234–2248.
- [5] Ulrich-Lai YM, Herman JP. Nat Rev Neuroscience 2009; 10: 397–409.
- [6] Jolien S. van Campen, Floor E. Jansena, Pierre N.E. de Graanb, Kees P.J. Brauna, Marian Joelsb. Epilepsy & Behavior 2013; 2(4):1-12.
- [7] Koe AS, Jones NC, Salzberg MR. Behav Neuroscience 2009; 3:16.
- [8] Haut SR, Hall CB, Masur J, Lipton RB. Neurology 2007; 69:1905–1910.
- [9] Sperling MR, Schilling CA, Glosser D, Tracy JI, Asadi-Pooya AA. Seizure 2008; 17:302–307.
- [10] Thapar A, Kerr M, Harold G. Epilepsy Behav 2009; 14:134–140.
- [11] Rao ML, Stefan H, Bauer J. Neuroendocrinology 1989; 49(1):33–9.
- [12] Aminoff MJ, Simon RP, Wiedemann E. Brain 1984; 107(2):569–78.
- [13] Zhang SW, Liu YX. Neuroscience 2008; 24(2):84–8.
- [14] Aldenhoff JB, Gruol DL, Rivier J, Vale W, Siggins GR. Neuronal Science 1983; 221: 875–7
- [15] Baram TZ, Schultz L. Brain Res Dev Brain Res 1991; 61: 97–101.
- [16] Hollrigel GS, Chen K, Baram TZ, Soltesz I. Neuroscience 1998; 84: 71–9.
- [17] D. L. Bellinger, C. Lubahn, and D. Lorton. Journal of Immunotoxicology 2008; (4): 419–444.
- [18] A.Danese, C.M.Pariante, A.Caspi, A.Taylor, and R.Poulton. Proceedings of the National Academy of Sciences of the United States of America 2007; 104(4):1319–1324.
- [19] K. Dinkel, A. MacPherson, and R. M. Sapolsky. Journal of Neurochemistry 2003; 84(4):705–716.
- [20] S. F. Sorrells, J. R. Caso, C. D. Munhoz, and R. M. Sapolsky. Neuron 2009; 64 (1):33–39.
- [21] J. L. M. Madrigal, O. Hurtado, M. A. Moro. Neuropsychopharmacology 2002; 26 (2)155–163.
- [22] B. Garcia-Bueno, J. L. M. Madrigal, B. G. Perez-Nievas, and J. C. Leza. Endocrinology 2008; 149 (4) : 1969-1978.
- [23] Porges SW. Pediatrics 1992; 90:498–504.
- [24] Moseley B, Bateman L, Millichap JJ, Wirrell E. Epilepsy Behav 2013; 26(3):375–85.
- [25] Mohammed Faraaz Khan. Res J Pharm Biol Chem Sci 2015; 6(6):1310-1313.