Original Article

Dual-Mechanism Antidepressant as a promising Antiepileptic: A Chronic Evaluation of Vilazodone in swiss albino mice

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Abstract

Background: Epilepsy is a long-lasting neurological ailment defined by repeated seizures caused by irregular neuronal excitability. In spite of numerous antiepileptic treatments, a substantial fraction of patients remains unresponsive or encounters negative reactions. New evidence emphasizes the importance of serotonergic regulation in managing seizures. Vilazodone, which functions as a selective serotonin reuptake inhibitor and a partial agonist at 5-HT1A, could have anticonvulsant capabilities. Objectives: To investigate the anticonvulsant properties of vilazodone in chronic seizure models and contrast its effects with sodium valproate in Swiss albino mice. **Material and Methods:** A preclinical experimental study was conducted on 36 Swiss albino mice divided into six groups (n=6). Animals received distilled water (control), sodium valproate (40 mg/kg), or vilazodone (1, 2, 5, and 10 mg/kg) orally for 21 days. Models of pentylenetetrazole (PTZ) and maximum electroshock (MES) were used to produce seizures. Seizure latency (PTZ), seizure duration, and tonic hind limb extension (MES) duration were among the parameters evaluated. Student's t-test was used for statistical analysis; $p<0.05$ was deemed significant. **Results:** Vilazodone significantly reduced the duration of tonic hind limb extension in the MES model across all doses ($p<0.05$), with maximum effect at 10 mg/kg. In the PTZ model, vilazodone significantly decreased seizure duration and increased seizure latency compared to control ($p<0.05$), showing dose-dependent efficacy, particularly at 5 and 10 mg/kg. **Conclusion:** Vilazodone demonstrated significant anticonvulsant activity in both chronic MES and PTZ models, likely mediated through enhanced serotonergic neurotransmission. These findings suggest its potential as a repurposed or adjunct antiepileptic agent, warranting further clinical investigation.

Keywords: Vilazodone, Epilepsy, Anticonvulsant, MES model, PTZ model.

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INTRODUCTION

Recurrent, unprovoked seizures caused by aberrant, excessive neuronal discharges in the brain are the hallmark of epilepsy, a chronic neurological condition. It is among the most prevalent neurological disorders in the world, affecting about 50 million people.[1] Despite the availability of multiple antiepileptic drugs (AEDs), nearly one-third of patients remain refractory to treatment, highlighting the need for novel therapeutic agents with improved efficacy and safety profiles.[2] Existing anticonvulsant therapies are neither uniformly efficacious nor reliably safe, as they are linked to side effects including ataxia, CNS depression, megaloblastic anemia, cardiac arrhythmias, teratogenicity, and hepatic impairment. The underlying mechanisms of epilepsy entail an imbalance in excitatory and inhibitory neurotransmission, chiefly regulated by glutamate and gamma-aminobutyric acid (GABA).[3] In addition to these classical pathways, increasing evidence suggests a significant role of monoaminergic systems, particularly serotonin (5-hydroxytryptamine, 5-HT), in modulating seizure susceptibility.[4] Serotonergic neurotransmission has been shown to exert inhibitory effects on neuronal excitability, and alterations in serotonin levels have been implicated in seizure disorders.[5] Vilazodone is a new class of antidepressants, operating as a selective serotonin reuptake inhibitor (SSRI) and partially activating 5-HT1A receptors. This dual approach augments serotonergic neurotransmission to a greater extent than standard SSRIs.[7] Given the involvement of serotonin in seizure modulation, vilazodone may possess potential anticonvulsant properties. Previous studies have demonstrated that drugs enhancing serotonergic activity can increase seizure threshold and reduce seizure severity in experimental models.[8] Although vilazodone is primarily indicated for the treatment of major depressive disorder, its

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pharmacological profile suggests a possible role in seizure modulation. However, limited data are available regarding its anticonvulsant potential. Therefore, the present study aims to evaluate the anticonvulsant activity of vilazodone in Swiss albino mice using established experimental chronic seizure models. This investigation may provide insights into the potential repurposing of vilazodone as an antiepileptic agent and contribute to the development of novel therapeutic strategies for epilepsy management.

Objectives:-

- To study the anticonvulsant effect of vilazodone in MES mice models
- To study the anticonvulsant effect of vilazodone in PTZ mice models
- To compare the anticonvulsant effect of vilazodone and sodium valproate

Materials and Methods

This preclinical experimental study was carried out in the Department of Pharmacology, Karpagam Faculty of Medical Sciences and Research, Coimbatore. The investigation took place over a six-month timeframe, from August 2019 until January 2020. A total of 36 Swiss albino mice, of both genders and weighing around 25 to 30 grams, were sourced from the central animal house at Karpagam University, Coimbatore. Following CCSEA directives, animals were acclimatized for a duration of one week within the pharmacology department of Karpagam Faculty of Medical Sciences and Research. They were housed properly within clean cages and fed with standard pellet diet and water ad libitum throughout the study. Animals were maintained at 22 – 240 c temperature and 12/12 dark-light cycle.

- The Institute of Animal Ethics Committee of the Karpagam Faculty of Medical Sciences and Research in Coimbatore granted ethical approval. (IAEC No.: KFMSR/MD(PC)/05/2018, dated December 11, 2018)

Drugs and Chemicals: -

1. Vilazodone (1mg/kg, 2mg/kg, 5mg/kg and 10mg/kg BW*)
2. Sodium valproate (40mg/kg BW)
3. Distilled water (10ml/kg BW)
4. Pentylenetetrazole (70mg/kg BW).

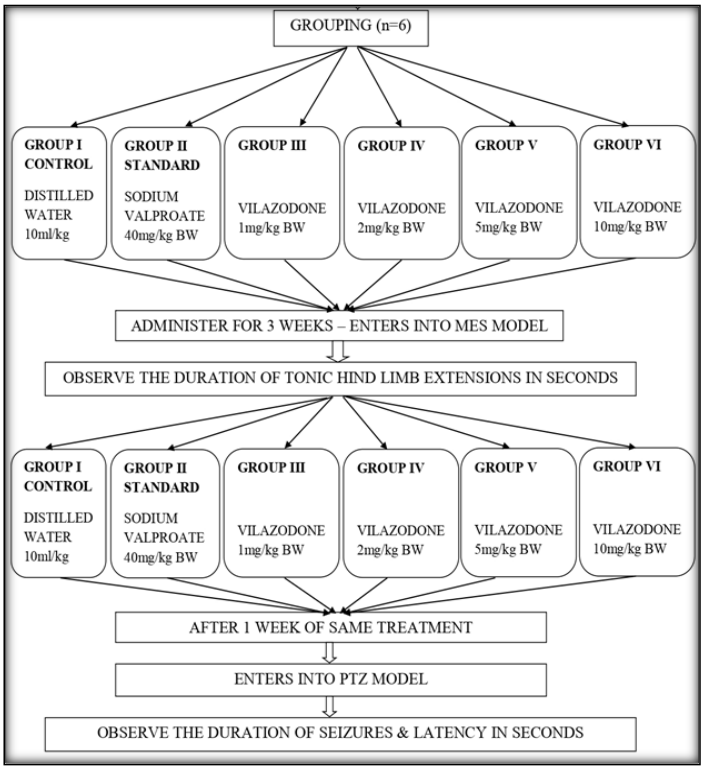

Table 1: Animal Groups: A total of 36 swiss albino mice were divided into 6 group (n=6 in each group)

GROUPS	DRUG & DOSE	ROUTE
I (CONTROL)	Distilled water 10 ml/kg BW	Oral
II (STANDARD)	Sodium valproate 40mg/kg BW	Oral
III	Vilazodone 1mg/kg BW	Oral
IV	Vilazodone 2mg/kg BW	Oral
V	Vilazodone 5mg/kg BW	Oral
VI	Vilazodone 10mg/kg BW	Oral

*BW – Body Weight

Animals from the above mentioned six groups were subjected to Maximal Electroshock (MES) model (electrically induced seizures) and after 1 week animals were used for pentylenetetrazole (PTZ) model (chemically induced seizures).

Mouse models of epilepsy: Control, standard and test drugs were administered for 21 consecutive days (63). On day 22, all the animals were subjected to MES model.

Maximal Electroshock (MES) model:- In this method, an electroconvulsiometer is used to induce the seizure by delivering electrical shock of 50 mA current through a pair of ear clip electrodes for 0.2 seconds in mice. Drugs were administered orally 60 minutes before the seizure induction in mice. Duration of tonic hind limb extension in seconds was noted for each animal.[9]

Pentyleneteterazole (PTZ) model: In this method, seizure is induced by administering 70mg/kg BW of pentylenetetrazole is injected intraperitoneally. Drugs were administered orally 60 minutes before the seizure induction in mice. Duration of seizures and seizure latency in seconds was noted for each animal.[10,11]

Statistical analysis:

- The mean plus standard deviation (S.D.) was used to express the results. SPSS version 23.0 was utilized for statistical analysis using the student-t-test. A P value of less than 0.05 was considered statistically significant.

RESULTS

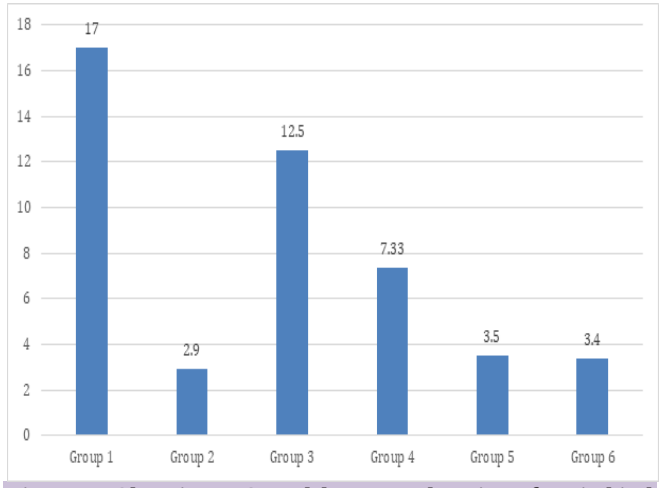

Figure 1: Chronic MES model - Mean duration of tonic hind limb extensions in seconds

Chronic study – Maximal electroshock (MES) model
A statistical analysis of group I (control) against groups II, III, IV, V, and VI indicates a substantial reduction ($P < 0.05$) in the mean duration of tonic hind limb extension expressed in seconds. Every dosage of vilazodone lessened the mean time of tonic hind limb extension, achieving the greatest reduction at 10mg/kg BW [Figure 1].

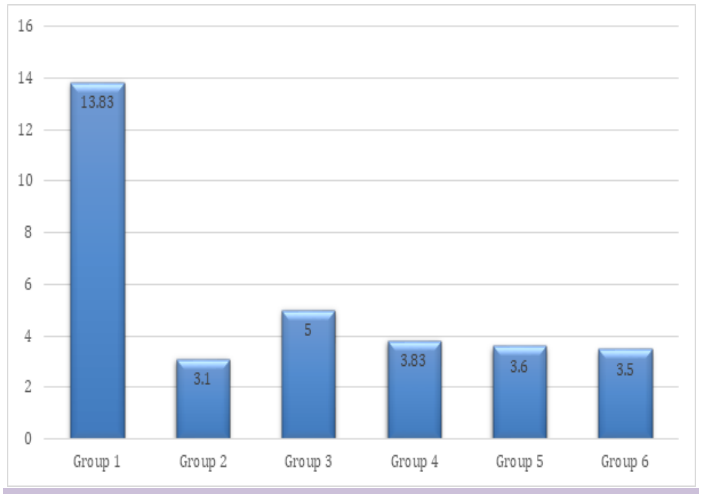

Figure 2: Chronic PTZ model - Mean duration of seizures in seconds.

Table 1: Chronic MES model - Statistical analysis of mean duration of Tonic Hind Limb Extension in seconds

Groups	Control (p value)
GROUP I	-
GROUP II	0.009
GROUP III	0.0001
GROUP IV	0.0001
GROUP V	0.0001
GROUP VI	0.0001

Chronic study – Pentylenetetrazole (PTZ) model:
Effect of mean duration of seizures in seconds
Groups II, III, IV, V, VI groups show statistical significant reduction ($P < 0.05$) in mean duration of seizures in seconds in comparison to control (Group 1).
Reduction in mean duration of seizures was noted across all doses of vilazodone with maximum reduction seen at higher doses (5mg/kg BW and 10mg/kg BW) [Figure 2].

Table 2: Chronic PTZ model - Statistical analysis of duration of seizures in seconds

Groups	Control (p value)
GROUP I	-
GROUP II	0.0001
GROUP III	0.0002
GROUP IV	0.0001
GROUP V	0.0001
GROUP VI	0.0001

Effect of mean duration of seizure latency in seconds:
Groups II, III, IV, V, VI groups show statistical significant increase ($P < 0.05$) in mean duration of seizure latency in seconds in comparison to control (Group 1).
Dose related increase in seizure latency was seen in viladazone groups with maximum increase was noted in 10mg/kg BW of viladazone [Figure 3].

Table 3: Chronic PTZ model - Statistical analysis of duration of seizure latency in seconds

Groups	Control (p value)
GROUP I	-
GROUP II	0.0001
GROUP III	0.0001
GROUP IV	0.0001
GROUP V	0.0001
GROUP VI	0.0001

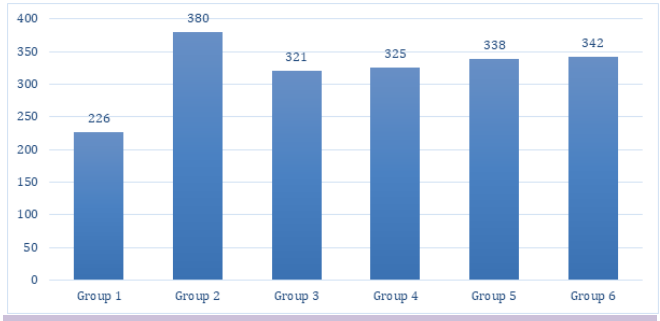

Figure 3: Chronic PTZ model - Mean duration of seizure latency in seconds

Discussion

This study was conducted as per CPCSEA guidelines, and all precautions were taken to reduce errors due to gender related and diurnal variations. Errors due to diurnal variations were minimised by all the experiments were conducted during the same time on each day. A total of 36 swiss albino mice were used in this study to evaluate the anticonvulsant property of vilazodone and compared with sodium valproate.

Vilazodone was used at various doses of 1mg/kg, 2mg/kg, 5mg/kg and 10mg/kg of mice body weight. To screen the anticonvulsant activity, there are large number of models are available. But maximal electroshock model and pentylenetetrazole model remain the gold standard models for antiepileptic drug screening. The observations emanated in this study indicated that duration of tonic hind limb extension phase was significantly decreased in test groups (vilazodone 1mg/kg, 2 mg/kg, 5mg/kg and 10mg/kg) when compared to control group. The decreased duration of these components may be due to the anticonvulsant activities of vilazodone. Statistical examination demonstrated that these experimental groups displayed a substantial anticonvulsant effect in comparison to the control across both MES and PTZ models. According to Barnes et al. (1999), the serotonergic ascending route modulates the balance of excitation and inhibition in cortical and subcortical areas, influencing the management of epileptic activity.[12]. Lu KT et al study supports barnes et al proposals that agents that increases the extracellular serotonin levels, which include 5-HT and 5-HT reuptake blockers, inhibit each focal (limbic) and generalized seizures.[13] Jakus et al & Sarnyai et al also report that selective inhibition of 5-HT1A receptors reduces the seizure activity.[14] We already know that vilazodone has both of these actions such as 5-HT reuptake blocking and 5-HT1A partial agonism. So Vilazodone has the ability to reduce the seizure activity. Our study results also support the same at all doses of Vilazodone (1mg/kg, 2mg/kg, 5mg/kg and 10mg/kg). Wang et al (2013) study showed that acute administration of SSRI like anti-depressant drugs increase the extra neuronal levels of serotonin. However, this increase of serotonin is immediately counteracted by presynaptic 5-HT1A auto receptor mediated negative feedback inhibition.[15] Ashby et al (2013) study showed that chronic stimulation of 5HT1A receptors (via continuous administration) may produce pre-synaptic auto receptor desensitization but this does not happen in postsynaptic receptors. Therefore, the autoreceptor-mediated negative feedback action will be reduced and the serotonin release is normalized and the postsynaptic serotonergic receptors are activated enormously that results in increased serotonin levels in synaptic region.[16] Drevets et al. (1999) discovered a decrease in 5-HT1A receptors and their binding in individuals with depression, while Savic et al. bolsters this hypothesis, and Bagdy et al. verifies that anti-epileptic medications diminish seizure foci, indicating that patients with both epilepsy and depression exhibit reduced activity compared to those with epilepsy alone.[17-19] Additional research is necessary to validate the anticonvulsant properties of vilazodone. Should the anti-epileptic efficacy of vilazodone be established, it could serve as adjunctive treatment alongside first-line anti-epileptic medications for individuals experiencing depression.

Conclusion

Findings demonstrated anticonvulsant efficacy across all administered doses of vilazodone (1mg/kg, 2mg/kg, 5mg/kg, and 10mg/kg BW) in chronic MES and PTZ models involving Swiss albino mice. Additional research is necessary to validate the anticonvulsant properties of vilazodone. Should the anti-epileptic efficacy of vilazodone be established, it could serve as adjunctive treatment alongside first-line anti-epileptic medications for individuals experiencing depression.

References

1. World Health Organization. Epilepsy: A public health imperative. Geneva: WHO; 2019.
2. Löscher W, Schmidt D. Modern antiepileptic drug development has failed to deliver: Ways out of the current dilemma. Epilepsia. 2011;52(4):657–678.
3. Rogawski MA, Löscher W. The neurobiology of antiepileptic drugs. Nat Rev Neurosci. 2004;5(7):553–564.
4. Bagdy G, Kecskemeti V, Riba P, Jakus R. Serotonin and epilepsy. J Neurochem. 2007;100(4):857–873.
5. Dailey JW, Naritoku DK. Serotonin and seizure modulation. Epilepsy Curr. 2004;4(2):37–40.
6. Khan A, Cutler AJ, Kajdasz DK, et al. A randomized, double-blind, placebo-controlled study of vilazodone in major depressive disorder. J Clin Psychiatry. 2011;72(4):441–447.
7. Citrome L. Vilazodone for major depressive disorder: A systematic review of the efficacy and safety profile. Int J Clin Pract. 2012;66(4):356–368.
8. Peroutka SJ. 5-HT1A receptor modulation in neurological disorders. Neuropharmacology. 1998;37(4–5):609–620.
9. Sachan V, Gaur RS, Prakash P, Kori P. Evaluation of antiepileptic activity of ethanolic extract of Tinospora Cordifolia stem using maximal electric shocks induced seizure (MES) method in albino mice.Pharmaceutical sciences.2024;4(2).
10. Bhat JU, Nizami Q, Asiaf A, Parray SA, Ahmad ST et al. Anticonvulsant activity of methanolic and aqueous extracts of Melissa parviflora in experimentally induced swiss albino mice. Excli J.2021;11:1-6.
11. Koutroumanidou E, Kimbaris A, Kortsaris A, Bezirtzoglou E, Polissiou M, et al. Increased seizure latency and decreased severity of Pentylenetetrazol-induced seizures in mice after essential oil administration. Epilepsy Res Treat.2013:532657.
12. Barnes NM, Sharp T.A review of central 5-HT receptors and their function.Neuropharmacology.1999 Aug 1;38(8):1083-152.

13. Lu KT, Gean PW. Endogenous serotonin inhibits epileptiform activity in rat hippocampal CA1 neurons via 5-hydroxytrytamine 1A receptor activation. Neuroscience.1998 Jun 8;86(3):729-37.
14. Jakus R, Graf M, Juhasz G, Gerber K, Levay G, Halasz P, et al. 5-HT2C receptors inhibit and 5 HT1A receptors activate the generation of spike-wave discharges in a genetic rat model of absence epilepsy. Exp Neurol.2003;184(2):964-972.
15. Wang S-M, Han C, Lee S-J, Patkar AA, Masand PS, Pae C-U. A review of current evidence for vilazodone in major depressive disorder. Int J Psychiatry Clin Pract. 2013; 17(3):160-169.
16. Ashby Jr CR, Kehne JH, Bartoszyk GD, Renda MJ, Athanasiou M, Pirez KA, et al. Electrophysiological evidence for rapid 5-HT1A autoreceptor inhibition by vilazodone, a 5-HT1A receptor partial agonist and 5-HT reuptake inhibitor. Eur J Pharmacol.2013;714(1-3):359-365.
17. Drevets WC, Frank E, Price JC, Kupfer DJ,Holt D, Greer PJ et al.PET inamging of serotonin 1 A receptor binding in depression.Biol Psychiatry.1999;46(10):1375-1387.
18. Savic I, Lindstrom P, Gulyas B, Halldin C, Andree B, Farde L.Limbic reductions of 5-HT1A receptor binding in human temporal lobe epilepsy.Neurology.2004 Apr 27;62(8):1343-51.
19. Bagdy G, Kecskemeti V, Ribaa P, Jakus R. Serotonin and epilepsy.Journal of neurochemistry.2007;100:857-873.