Original Research Article

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Effectiveness of Homotaurine in the Management of Cognitive Function Disorders Following Traumatic Brain Injury

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Abstract

Introductions:- The traumatic Brain injury (TBI) is an important and large clinical problem worldwide which can lead to severe sequel like cognitive deficits and movement obstacles etc. Cognitive function disorders (CFDS) are group of disorders characterized by one or more of the cognitive domains. CFDs are major Neuro cognitive disorders, which includes three group of disorders[1]. All these three are characterized by an important cognition (as in memory, language or attention) 2 Overall these functions are of paramount importance and are essential for carrying out day to day activities. Homotaurine is a close structural analogue of the natural amino acid gamma-aminobutyrid acid (GABA) an endogenous neurotransmitter present within the central nervous system. This new compound is used in present study, showing improvement is post TBI cognitive functions related to memory, arousal and aggression. *Material and methods*:- This study was conducted in the neurosurgery unit of Gandhi Medical College & Associated Hamidia Hospital Bhopal from April 2017 to April 2019, A total number of 76 patients included in the study who had post TBI cognitive functions disturbance. *Aim and Objects*: To evaluate the effectiveness and safety of Homoturine in the patients suffering from cognitive function disturbance following Traumatic Brain injury. *Result*:- Homotaurine 100mg TDS for 4 weeks and 50mg TDS for 8 weeks and 50mg BD for 12 weeks appears to be an effective and safe for improving the memory and reducing the irritability and aggression among patients with TBI. Further none of the available treatment option for cognitive disorders affords definitive resolution of symptoms.*Conclusion*: Our study concludes that the usage of Homotaurine therapy can be safe and useful in traumatic Brain injury in terms of post TBI cognitive and functional outcome with beter recovery though the sympathetic and supporting role of family and friends help in Quick recovery.

Keyword: Cognitive function disorders; Traumatic Brain injury; TBI Homotaurine; Memory; Aggression.

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Introduction

Cognitive Function disorders (CFDS) are group of disorders which are characterized by disruption in one or more of the cognitive domains. There are three major groups of cognitive/executive disorders Delirium, Dementia, Amnestic disorders. All these disorders are characterized by impairment in cognition (memory, language, or attention). Cognitive executive functions are known to have significant implications for a standard quality of life and succeeding at homes in the community and at work. In cognitive function disorders individuals experience progressive loss of memory and executive functions as well as aphasia, agnosia and difficulties with the activities of daily living, these loses might be related to synaptic damage and neuronal loss in the hippocampus, cerebral cortex and these are as of Brain loss and atrophy has been associated with cognitive impairment. The neuroprotective effects of Homotaurine, against age related impairments contribute towards maintains neuronal health and protecting brain regions involved to control learning, cognition and executive functions is well documented.

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Preliminary studies have suggested that homotaurine may promote functional recovery in the term of post TBI cognitive function related to arousal, aggression and memory. The post traumatic irritability or aggression needs treatment to minimize the negative impact on their relationship, home life, social interactions, community participation and employment etc.

The Homotaurine generally be started at 100 mg TDS any time from first day to a month's post TBI. The dose and time of therapy should be individualized to each patient.

Homotaurine chemical name is 3 Amino-1-propanesulfonic acid, tramiprosate. Homotaurine is chemically produced synthetic analogue of the naturally occurring compound that is found in the red and green algae species Greate loupia Livida. In mammalian tissues, taurine is an important natural component and most abundant free amino acid in the heart, reline, skeletal muscles and Brain. Homotaurine is intended to protect cognitive and executive functions in healthy adults. It is used to maintain brain cell health and protect the hippocampus (Brain regions involved in learning, cognition and executive functions control) maintain Comprehension ability. Also effective in individuals suffering with excessive sleepiness.

Material and Methods

This study was conducted in the Neurosurgery unit of surgery department of Gandhi Medical College and Associated Hamidia Hospital Bhopal India. Total number of 76 patients included in the study from April 2017 to April 2019

Patients were divided in two groups. Group I (Study Group) includes 38 patients and group II (Control group) also includes 38 patients.

Group I (Study group) was given 100 mg Homotaurine three times a day for 4 weeks, then 50 mg there times for 8 week and two times a day for 12 weeks. Homotauraine is available in India in the name of Tab Viviloref 50mg.

The control group received cholinesterase inhibitors donepezil, Rivastigmine, nicergoline ect and also Piracetam, Citicholine and memantamine.

Aims and Objectives

We have assessed the effectiveness and safety of the Homotauraine in patients with cognitive and behavioral disorders like reduction is irritability and aggression and improvement in the memory among individual more than six months post TBI

Clinical Pharmacology-Homotaurine

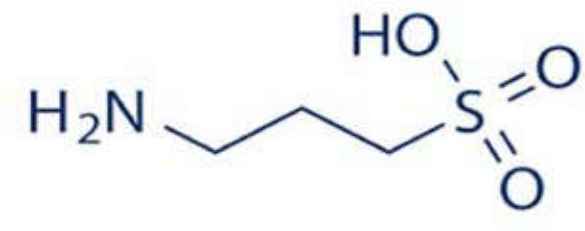
Homotaurine is chemically produced synthetic analogue of the naturally occurring compound. It is a small aminosulfonate compound. Indeed, homotaurine is one of the first natural products to be investigated with an anti-aggregation mechanism, and is a homolog of the amino acid taurine. Molecular structure of homotaurine shares close similarity with that of the natural amino acid taurine.[3,4] Beside, homotaurine is also a close structural analogue of the natural amino acid Gamma-Aminobutyric Acid (GABA), an endogenous neurotransmitter present within the Central Nervous System (CNS).[5,6,7,8]

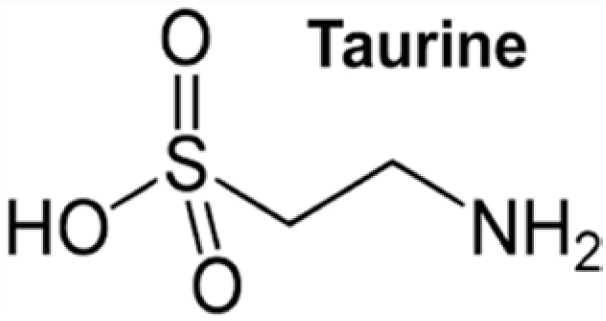
Chemical name: 3-Amino-1-propanesulfonic acid, tramiprosate

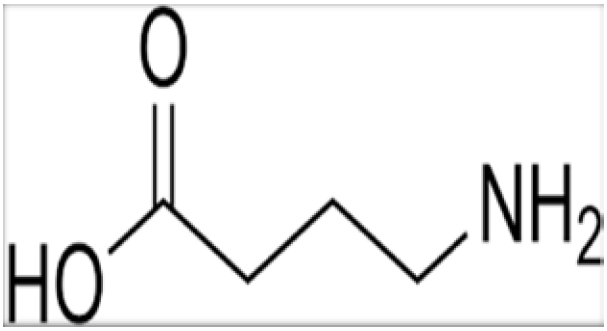
IUPAC name: 3-Aminopropane-1-sulfonic acid

Molecular Formula: C3H9NO3S

Structure: As depicted in fig:1.[9]







Disussion

TBI results in Oedema which results in elevation of intra cranial pressure (ICP) leading subsequent impairment of CBF and metabolism.[10] Cerebral auto regulation can be impaired in moderate and severe TBI and also in mild TBI, which is one factor involved in the pathophysiolosy of TBI and contribute in ischemia and brain damage.[11] Taurine is a neuroprotective agent which reduced the oedema and inflammation, reduces the oxidative stress and depression mitochondrial mediated cell death.[12] Taurine treatment improve the CBF in the ipsilateral and contra lateral injured brain cortex for about 7 days taurine is known for its beneficial effects in hypercogulable steal.[13] Schaffer et al. found that taurine deficiency reduced the biosynthesis of mitochondria encoded proteins ND5 and ND6, which they therefore suggested a novel mechanism that taurine specifically alters complex I through alterations in mitochondrial protein biosynthesis which provides an explanation for the antioxidant activity of taurine (Jong et al, 2012; Schaffer et al, 2014a, b).[14] Taurine significantly increase the activities of mitochondrial respiratory Complexes I and II, which was consistent with the studies of Schaffer et al. The result from Schaffer et al. demonstrated that taurine antioxidant activity is linked to improved mitochondrial function, which diminishes mitochondrial superoxide generation. They also supplied that taurine could regulate mitochondrial protein synthesis, thereby enhancing electron transport chain activity and protecting the mitochondria against excessive superoxide generation (Schaffer et al. 2014a, b; Shimada et al, 2015).[15]

The patients were randomly assigned to receive 12 weeks of Homotaurine at 1 of 3 oral doses (50mg BD& TDS or 100mg TDS). Patients were followed for clinical adverse effects, laboratory, vital sign, electrocardiogram, cognitive, or functional changes, appearance of new symptomatic or asymptomatic hemorrhages and pharmacokinetic parameters. Homotaurine therapy was not associated with any concerning safety issues; nausea and vomiting were the most common untoward effects and were more frequent at high doses.

Result

There was consistent trend towards a more rapid important in post tramatic cognitive functional disorders during the 24 weeks treatment period in the patients group who were getting homotaurine than the control group. Significant improvent on tests of executive functional were observed with homotaurine, the frequency and severity of irritability and aggression were reduced and there was improvement in there memory status among TBI patients. In the Homotaurine group, 78.56% improved at least 3 points on the Neuropsychiatric Inventory irritability (NPI-1) as compared with 46.44% in the group that not received the Homotaurine (p=.0016). Mean change in the NPI-1 was -4.4 in the Homotaurine group and 2.4 in the study group (P=.0086). When excluding individuals with minimal to no baseline aggression, mean change in NPI-A was-4.52 in the Homotaurine group and -2.44 in the study group (P=.048) mean change in NPT-1 and NPI-A distress were not statistically significant between Homotaurine group and study group. Significant improvements on tests of executive function were observed The analysis of PET (Positron Emission Tomography) data demonstrate a significant increase in left pre forntal cortex glucose metabolism. There is also a good positive correlation between executive domain score and left prefrontal glucose metabolism.

Conclusion

The homoturaine therapy producers favorable outcome for patients with TBI and may lead to increased post TBI arousal, memory and cognitive functions. Homoturine appears an effective and safe treatment for reducing frequency and severity of irritability and aggression and improver the memory individuals with past TBI. Homotaurine also appears beneficial in improving the memory particularly from the prospective of the individual with brain injury. Clinical Homotaurine provides a potentially effective and well tolerated option for treating aspects of executive dysfunction following TBI. The data provides evidences to support the hypotheses that taurine exerts protective effect through various pathways. The Effect of Homotaurine are:- 1. Homotauine has been found to maintain neural transmission and protect against non-ß amyloid and ß amyloid- induced cell death partly through GABA-mediated mechanism. 2. The neuroprotective effects of homotaurine contribute towards maintaining neuronal health and protecting brain regions involved in control of learning, cognition and Executive Functions. 3. Homotaurine is shown to exert direct effects also on neuronal activity as a modulator of excitatory neurotransmission, due to its binding affinity for GABA receptors. This modulatory action

strengthens the potential neuroprotective effects of homotaurine. Further studies are needed to detect the effect of homotaurine on cognitive functions disturbances in patients with TBI, using large sample size and different measures like randomized-controlled double-blinded and placebo controlled studies.

References

1. R.O'Hara, DSM 5 Major Changes from DSM IV: Neurocognitive Disorders, 2013, http://sgec.stanford.edu/presentations/Updates-on-Dementia/Presentation/2Updates%20on%20Dementia.
2. B. J. Sadock and V. A. Sadock, Kaplan & Sadock's Synopsis of Psychiatry: Behavioral Sciences/ Clinical Psychiatry, Lippincott Williams & Wilkins, Baltimore, Md, USA, 10th edition, 2007.
3. Williams P, sorribas A, Howes M-jr natural Products as a Source of Alzhemier's Drug Leads. Nat Prod Rep. 2011:28(1):48:77
4. Kocis P. Tolar M, Yu J, et al. Eluciding the AB42 anti-aggregation Mechanism of action of tramiprosate in Alzheimer's Diesease integrating Molecular anatycal Methoed Pharmacokinetic and Clinical Data CNS drugs. 2017:31(6) 495-509.
5. Data on file: Arinna lifeciences.
6. Caltagirone C, Ferrannini l, Marchionni N,et al The Potential Protective effect of tramiprosate (homoturine) against Alzhemer's disease: a rewive Aginig Clin Exp Res. 2012:21(6): 580-7
7. Chung MC, Malatesta P, Bosquesi PL, et al advanes in drug Design Based on the the amino Acid approach: Turine Analogues for the Treatment of CNS Diseases Pharmaceuticals. 2012(10): 1128-1146.
8. Ripps H, Shen W. Review: Taurine: A "Very essential" amino acid Mol Vis 2012:18:26773:2686.
9. Homoturine Available at: https://pubchem.ncbi.nlm.nih.gov/compound/164#section=top. Accessed 0n 06-089-2017.
10. Jaggi JL, Obrist WD, Gennarelli TA, Langfitt TW (1990) Relationship of early cerebral blood flow and metabolism to outcome in acute head injury. J Neurosurg 72:176–182
11. Marion DW, Darby J, Yonas H (1991) Acute regional cerebral blood flow changes caused by severe head injuries. J Neurosurg 74:407–414
12. Aly HA, Khafagy RM (2014) Taurine reverses endosulfan-induced oxidative stress and apoptosis in adult rat testis. Food Chem Toxicol 64:1–9
13. Guan W, Zhao Y, Xu C (2011) A combined treatment with taurine and intra-arterial thrombolysis in an embolic model of stroke in rats: increased neuroprotective efficacy and extended therapeutic time window. Transl Stroke Res 2:80–91
14. Jong CJ, Ito T, Schaffer SW (2015) The ubiquitin – proteasome system and autophagy are defective in the taurine-deficient heart. Amino Acids 47:2609_2622
15. Schaffer SW, Jong CJ, Ito T, Azuma J (2014a) Effect of taurine on ischemia-reperfusion injury. Amino Acids 46:21-30