Original Article

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Neurology Section

The Role of Magnesium Sulphate in Tuberculous Meningitis

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ABSTRACT

Context: Magnesium sulphate (MgSO4) has been studied for its beneficial role in traumatic brain injury (TBI) and ischaemic cerebral infarcts as it decreases the oxidative stress and increases the cerebral perfusion. The present study was done for evaluating its role in tuberculous meningitis (TBM).

Aims: To study the role of intravenous magnesium sulphate in tuberculous meningitis.

Methods and Material: The present study had 40 cases of tuberculous meningitis which comprised of 20 cases of group A(n-20) as contols for the study group B (n-20). The study group (Group B) was given intravenous magnesium sulphate 2 gm six hourly for 7 days additionally than the control group (Group A) which was treated with steroids and anti-tubercular drugs. The outcome was measured by using the Barthel Index (BI) and the Modified Rankin Scale (MRS) on the first day, the seventh day and after six weeks. The cases with arteritis in the two groups were compared separately.

Statistical analysis: The results were analyzed by using the SPSS software and the unpaired t-test with p-values.

Results: The means of the changes in the MRS and the BI of the Groups A and B were not statistically significant. When the means of the changes in the BI and the MRS were compared in the arteritis cases of the two groups separately, they were found to be statistically significant with a p value <0.05.

Conclusions: Magnesium sulphate had a statistically significant role in TBM with tuberculous arteritis and it had a statistically nonsignificant role in TBM without arteritis.

Key Words: Tuberculous Meningitis, Magnesium Sulphate, Barthel Index, Modified Rankin Scale, Arteritis

INTRODUCTION

Magnesium has an important role in the homeostatic regulation of the pathways which are involved in brain injuries [1]. During the normal physiological processes, magnesium acts as a non-competitive inhibitor of the NMDA receptors [2] and it thereby regulates the calcium influx [3]. In TBI, there is a depletion of magnesium and its homeostatic control on the NMDA receptors is lost, leading to a massive influx of calcium, causing neuronal degeneration and cell death [1]. The therapy with magnesium sulphate reduces the oxidative stress after a traumatic brain injury TBI in humans [4]. In subarachnoid haemorrhage patients who underwent temporary cerebral artery occlusion for the clipping of the cerebral aneurysms, the treatment with magnesium sulfate dilated the leptomeningeal arteries and enhanced the collateral blood flow and the tissue oxygenation [5]. Magnesium sulphate is a potent cerebral vasodilator due to calcium channel antagonism in the vascular smooth muscle cells and its effects on the myosin-binding proteins that regulate muscle contraction [6,7]. Consequently, magnesium sulphate typically increases the cerebral perfusion [8,9,10].

Various studies are available on the role of magnesium sulphate in TBI and cerebrovascular accidents, but no study is available on its role in TBM.This study was designed to study the neuroprotective role of magnesium sulphate in TBM.

SUBJECTS AND METHODS

The study was done at a tertiary care centre of north India between 2008-2009 on patients with tubercular meningitis who were admitted in the Department of Medicine or were referred from other departments. This study was approved by the Medical College Ethical Committee. After taking the informed consent of the patients and after explaining about the prognosis and the side effects to the patients and their relatives, the patients were asked for a detailed clinical history.

A diagnosis for definite TBM was made in cases where the CSF smear or culture was positive for AFB or where the PCR was positive for AFB. In the absence of the above criteria, the diagnosis of the most probable TBM was based on the clinical features (history and examination) which was suggestive of meningitis, while the cerebrospinal fluid examination was suggestive of predominant lymphocyte cells, rise in the protein levels with low CSF sugar or ratio of CSF sugar to simultaneously measured blood sugar value less than 60% and head CT scan suggestive of exudates, hydrocephalus and arteritis.

An unmarked, sealed envelope which contained directives for group A and B were prepared in advance and they were drawn at random. Group A (n=20) was given the standard therapy only and Group B (n=20) was given the standard therapy plus intravenous magnesium sulphate (2 gm, 6 hourly which was diluted with 100 ml of normal saline for 7 days). All the patients were followed for a minimum period of 6 weeks and often for longer, whenever it was possible after their discharge. A clinical assessment of the neurological state of the all the patients was done by using the Barthel Index (BI) [11] and the Modified Rankin Score (MRS) [12] on days 1, 7 and 42. The parameters of BI are feeding, bathing, grooming, dressing, bladder and bowel control, toilet use, transfer (bed to chair and back), mobility and stairs. The parameters of MRS include the degree of disability and the level of assistance which the patients need.

RESULTS

The maximum number of cases were in the 2nd to 3rd decades of life [Table/Fig-1]. The common symptoms in both the groups were fever (85%), headache (74%) and vomiting (62%). The presence of infarction was further confirmed by doing a CT scan or MRI of the brain (if the CT scan was inconclusive). There was no significant difference between the groups in the clinical presentation, as the symptoms and signs were found to be equally distributed among the groups [Table/Fig-2]. The means of MRS and BI of the two groups on the 1st, 7th, and the 42nd day signified the progressive clinical improvement in both the groups [Table/Fig-3]. The mean of the MRS change in Group A from day 1 to day 7 and that from day 1 to day 42 was 0.89 ± 0.59 and 1.5 ± 0.69 respectively. Though there was more change of MRS in Group B, the mean fall from days 1–7 was 1.17 ± 0.55 and that from days 1–42 was 1.80 ± 0.70 as compared to Group A, but it was not statistically significant [Table/Fig-4].

The change of MRS in Group B with arteritis was more as compared to that in Group A with arteritis and it was statistically significant [Table/Fig-5]. The mean of the BI change in Group A from the 1st to the 7th day and that from the 1st to the 42nd day was 11 ± 15.44 and 17.25 ± 22.03 respectively. Though there was more change in BI in Group B, the mean of the change from days 1–7 was 13 ± 13.22 and that from days 1–42 was 32 ± 25.31 as compared to Group A, but it was not statistically significant [Table/Fig-6]. The changes of BI in Groups A (n=5) and B (n=7) who had arteritis.were compared and it was found that the change of the Barthel Index in Group B was more as compared to that in Group A. This was statistically significant [Table/Fig-7].

DISCUSSION

The present study showed the significant role of magnesium sulphate (MgSO4) in cases of TBM with vasculitis and it has proved its neuroprotective role. The outcome was measured in terms of BI and MRS. The changes in BI and MRS were not statistically significant in the two study groups. In the cases of TBM with vasculitis among the two groups, the changes in BI and MRS were statistically significant ($p \leq 0.05$), thus establishing the beneficial effect of magnesium sulphate in TBM with arterits. The incidence of cerebral infarction which is secondary to TBM is reportedly 6%–47% [13].

It can lead to a permanent neurological disability in the survivors of TBM. Magnesium sulphate may be a cost effective neuroprotective therapy as it decreases the morbidity which is associated with cerebral infarcts. The limitations of the present study were its small sample size and the non availability of a radiological follow-up with CT/MRI of the brain sequentially. Further studies with larger sample size are needed for establishing the role of MgSO4 in TBM with vasculitis. This study was supported by various animal and human studies which were available, on the role of magnesium sulphate in the central nervous system. A decline in the ionized magnesium concentrations in rat brain was observed after a brain injury, that correlated with the neurological outcome and the behavioural deficits in rats [14]. A significant positive and linear correlation was established between the ionized magnesium levels which were measured at 24 h after the injury and the motor outcome at 1 and 2 weeks [15]. Many studies in rats have shown that the treatment with magnesium after a brain injury had neuron-protective effects on the motor and the behavioural outcome [1,16-18] in a dose-dependent manner [19,20]. The cortical damages were attenuated

Age (years)	Group A			Group B		
	M	F	T	M	F	T
> 12 – 20	4	3	7	2	3	5
21 – 30	5	3	8	7	3	10
31 – 40	3	1	4	2	1	3
41 – 50	0	1	1	1	0	1
> 51	0	0	0	0	1	1
Total	12	8	20	12	8	20

[Table/Fig-1]: Age & Sex Distribution in Two Groups

Symptoms	Group A	Group B	Total
Fever	16	18	34
Headache	15	16	31
Vomiting	13	12	25
Altered Sensorium	6	6	12
Convulsions	2	3	5
Cranial nerve involvement	6	8	14
History of exposure	2	1	3
History of ATT	6	2	8
Neck rigidity	17	19	36
Kernig's sign	17	14	31
Babinski's sign	15	15	30
Hemiplegia	5	7	12

[Table/Fig-2]: Symptoms and Signs in of TBM in Both Groups.

Days	Group A (MRS)		Group B (MRS)		Group A (BI)		Group B (BI)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Day 1	3.7	1.45	3.6	1.7	52	43.54	45	42
Day 7	2.85	1.5	2.5	1.6	63	37	58	33
Day 42	2.2	1.76	1.7	1.26	70	33.12	76	30

[Table/Fig-3]: Mean modified Rankin Score and Barthel Index

Days	Group A		Group B		p-value	t-value
	Mean	SD	Mean	SD		
Day 1–7	0.85	0.59	1.17	0.55	0.17	1.4
Day 1–42	1.5	0.69	1.80	0.70	0.18	1.37

[Table/Fig-4]: Mean of Change of Modified Rankin Score

Days	Group A		Group B		p value
	Mean	SD	Mean	SD	
1 – 7	0.80	0.45	1.43	0.53	0.05
1 – 42	1.2	0.45	2.14	0.69	0.03

[Table/Fig-5]: Comparing MRS in Tuberculous Arteritis

Days	Group A		Group B		p-value	t-value
	Mean	SD	Mean	SD		
Day 1 – 7	11	15.44	13	13.22	0.17	1.3
Day 1 – 42	17.25	22.03	32	25	0.18	1.4

[Table/Fig-6]: Mean of Change of Barthel Index

Days	Group A		Group B		p-value
	Mean	SD	Mean	SD	
1 – 7	9	4.18	20	10	0.02
1 – 42	20	7.91	30	5	0.03

[Table/Fig-7]: Barthel Index in Tuberculous Meningitis with Arteritis after the treatment with magnesium in rats [21]. Magnesium, which was administered at 24 hours, improved the motor outcome and the behavioural parameters in rats with brain injuries [22,23]. Magnesium reversed the persistent motor and cognitive deficits with the reduction of the post-traumatic stress and anxiety after brain injuries in rats.

In conclusion, the present study showed that MgSO4 was beneficial in TBM with vasculitis, but further studies with larger sample sizes are needed for establishing its role.

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