Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Pediatrics

A Comparative Study of Hypertonic Saline V/S Mannitol in Raised Intracranial Pressure in Children Aged Between 02 to 12 Years

Dr. Anil Kumar[1*], Dr. Reshma Chillal[2], Dr. Durugappa H[3]

[1,2]Post Graduate, Vims Ballari Karnataka India
[3]Professor and Head, Dept of Pediatrics, VIMS, Ballari Karnataka India

DOI: 10.36347/sjams.2021.v09i06.027 | **Received:** 07.05.2021 | **Accepted:** 12.06.2021 | **Published:** 21.06.2021

***Corresponding author:** Dr. Anil Kumar

Abstract **Review Article**

Raised intracranial pressure, the most common problem encountered in critical care unit, is often end result of various neurological disorders[1]. It is an important independent prognostic factor[1] Most of the available therapies in the management of raised intracranial pressure in children are like double edged sword. Hence this study was undertaken, to know the efficacy, safety, complications and outcome of Osmotherapies (hypertonic saline v/s Mannitol). This study was carried out in children aged between 02-12 years, admitted to paediatric critical care Unit in the Department of paediatric, at Vijayanagar institute of medical sciences Ballari, from January-16 to December-16 with features of raised ICP. 50 children were randomly given. Hypertonic saline (HTS) and 50 were given mannitol. Following parameters compared n results drawn: symptomatology, GCS, papilledema, pupillary reactions after 72 hrs of administration and effects on serum electrolytes, urea n creatinine, and osmolarity. We found that out of 50 children who were onmannitol therapy, 12 children needed HTS for sustained reduction of ICP beyond 72 hours (p=0.056). Improvement in GCS was better with use of mannitol (p=0.024) during first 72 hours compared to HTS. Increase in serum sodium levels were seen with use of HTS which was statistically significant (p=0.064). But mortality in both groups was similar. Hence, we concluded that mannitol was a better drug to be used in first 72 hrs but for sustained reduction of ICP beyond 72 hrs hts was better option.

Keywords: Hypertonic Saline Intracranial Pressure Osmotherapies.

INTRODUCTION

Cerebral edema is a potentially life threatening complication that can arise from any Acute neurological insult. The Monro-Kelie hypothesis[2] says that the sum of volume of BBC remains constant in a cranial vault. When the brain experiences an injury, the skull cannot allow for the additional volume. If the brain, blood volume or CSF continues to rise, this will increase in intracranial pressure (ICP) and causes the brain to lose the capacity to compensate. Urgent intervention is required to stop the cascade of events to prevent herniation and death especially in children who rapidly succumb. Despite various therapies available for reduction of ICP in children most of them are like a double edged sword. However Osmotherapy remains the cornerstone in the management of raised ICP in children which act by creating osmotic gradient between brain and plasma. The normal serum osmolarityranges from 280-290mOsm/kg and serum osmolarity to cause water removal from brain without much side effects ranges from 300-320mOsm/kg which can be created by hypertonic solutions like HTS and mannitol.

HTS is available in concentrations like, 3%, 5%, 7.5%, 10.0%, 20%, 23.4%. with sodium content of 154meq/l, 291meq/l, 513 meq/l ,856 meq/l, 1283meq/l, 1713meq/l, 3426meq/l, 4004meq/l respectively .5 Most commonly used is 3% hypertonic saline with sodium content of 513meq/l and serum osmolarity of 1026mOsm/L in dose of 1ml/kg qid

Mannitol is an osmotic agent naturally occurring sugar alcohol with a molecular weight of 183kDa, it lowers ICP by 15 to 20 minutes after administration by reducing viscocity, lowering the hematocrit, increasing CBF and oxygen supply 8, 9. Given as 5ml/kg of loading dose and 2ml/kg of maintenance dose. We studied the outcome and adverse effects following use of both drugs and compared.

Aims of study

1. To study the efficacy, safety and adverse effects of hypertonic saline v/s mannitol in the treatment of raised intracranial pressure in children aged between 02 to 12 years.

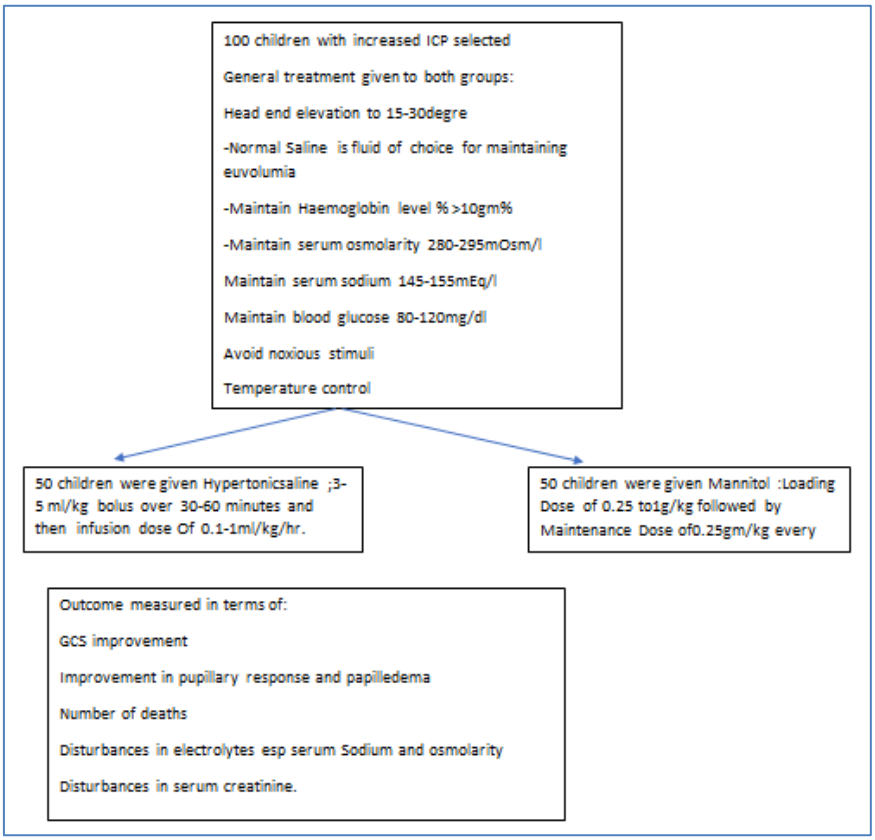

Table-1: The following table shows the age wise distribution of children among Mannitol and HTS group

Age wise distribution of the patients among the two treatment groups					
Age group	**Mannitol**		**Hypertonic saline**		**P value**
	Frequency	**Percent**	**Frequency**	**Percent**	
2 - 5 yrs	20	40.0	27	54.0	0.161
6 - 12 yrs	30	60.0	23	46.0	
Total	50	100.0	50	100.0	
Mean ± SD	6.46 ± 2.90		6.00 ± 2.84		

In both Mannitol and HTS group demographic feature like age was matching. And mean age in mannitol group was 6.462±.90 and HTS group was6.002±.84

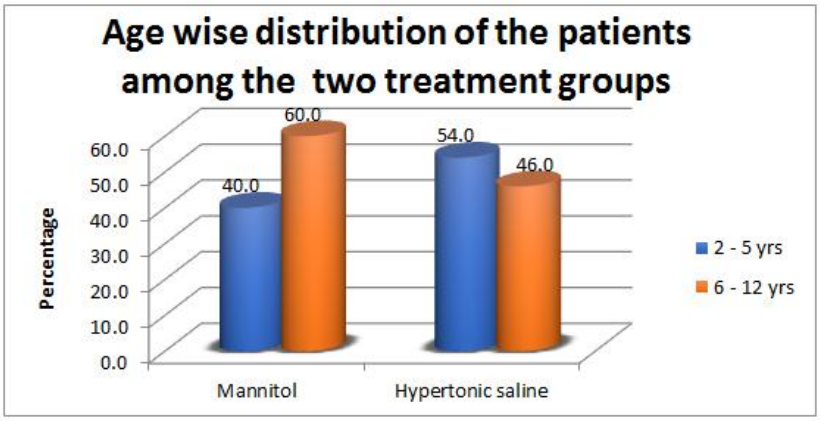

Fig-1: The age wise distribution of children among Mannitol and HTS groups

Table-2: The following table shows the sex wise distribution of children among Mannitol and HTS groups

Sex wise distribution of the patients among the two treatment groups					
Sex	**Mannitol**		**Hypertonic saline**		**P value**
	Frequency	**Percent**	**Frequency**	**Percent**	
Female	22	44.0	22	44.0	1
Male	28	56.0	28	56.0	
Total	50	100.0	50	100.0	

There were 50 children in mannitol group of these 28 (56%) were male and 22(44%) were female. HTS group of 50 children, 28 (56%) male and 22 (44%) female. There was statically no significant difference in both the group in terms of gender (P=1) both the groups matching in terms of gender.

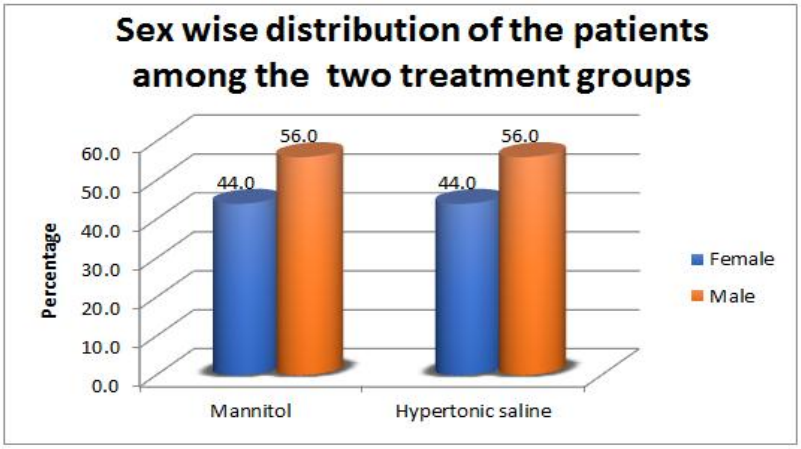

Fig-2: Shows the sex wise distribution of children among Mannitol and HTS groups

Table-3: The following table shows the GCS in children among Mannitol and HTS groups both before and after treatment

Comparison of GCS before and after treatment among the two groups					
GCS[57]	**Mannitol**		**Hypertonic saline**		**P value**
	Before	**After**	**Before**	**After**	
Mild (≥13)	0 (0)	8 (16)	1 (2)	8 (16)	0.006*
Moderate (8-12)	40(80)	11 (22)	25 (50)	23 (46)	
Severe (<8-9)	10(10)	3 (6)	24 (48)	5 (10)	0.024**
Norma l(15)	0 (0)	28 (56)	0 (0)	14 (28)	
Total	50(100)	50 (100)	50 (100)	50 (100)	

*p value before treatment and **p value after treatment

Above table depicts that there was dramatic improvement in the GCS in mannitol group (28, 56%) during first 72 hours compared to HTS group (p=0.024), which was statistically significant.

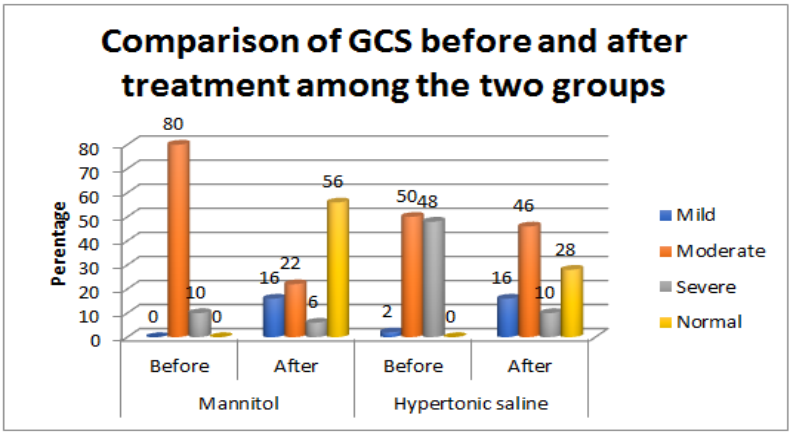

Fig-3: Shows the GCS in children among Mannitol and HTS groups both before and after treatment

Table-4: The following table shows the pupillary reaction in children among Mannitol and HTS groups before and after treatment

Comparison of pupillary reaction before and after treatment among the two groups					
Pupillary reaction	**Mannitol**		**Hypertonic saline**		**P value**
	Before	**After**	**Before**	**After**	
Normal	44 (88)	46 (92)	40 (80)	48 (96)	0.275*
Sluggishly reactive	6 (12)	4 (8)	10 (20)	2 (4)	0.400**
Total	50 (100)	50 (100)	50 (100)	50 (100)	

*p value before treatment and **p value after treatment

Above table shows there was no significant difference in pupillary changes in both the Mannito and HTS groups. (p=0.400).

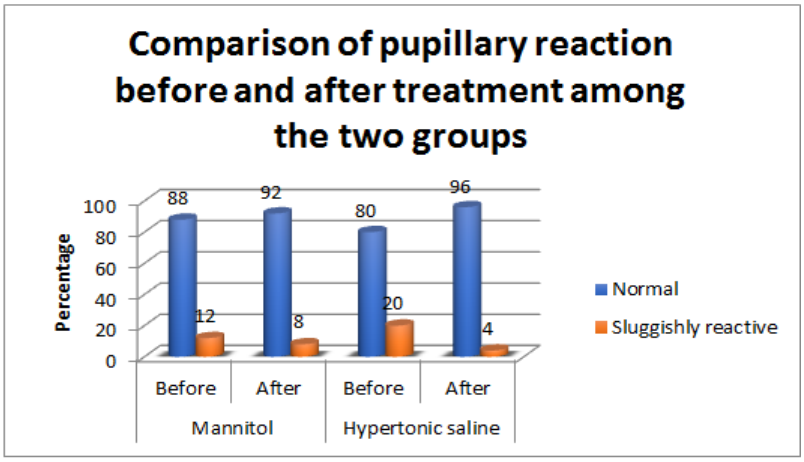

Fig-4

Table-5: The following table shows the Fundal changes in children among Mannitol and HTS groups before and after treatment.

Comparison of fundoscopy before and after treatment among the two groups					
Fundoscopy	**Mannitol**		**Hypertonic saline**		**P value**
	Before	**After**	**Before**	**After**	
Normal	49 (98)	50 (100)	48 (96)	50 (100)	0.558*
Papilloedema	1 (2)	0 (0)	2 (4)	0 (0)	
Total	50 (100)	50 (100)	50 (100)	50 (100)	

Comparison of fundoscopy before and after treatment among the two groups
*p value before treatment and **p value after treatment

In this table fundal changes were not significantly different in both Mannitoland HTS group (p=0.558).

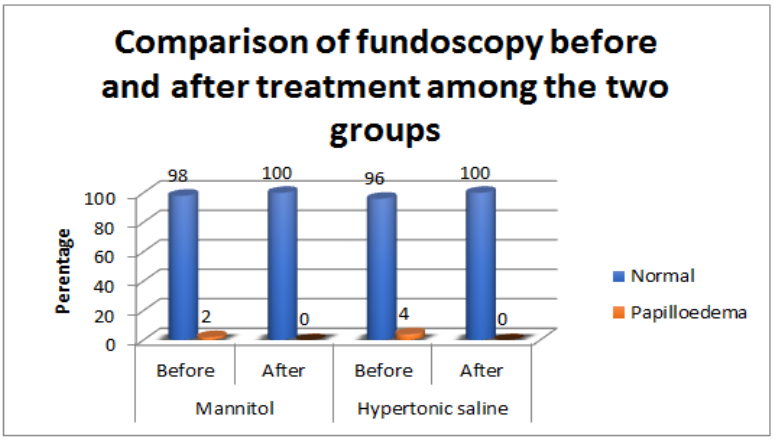

Fig-5

Table-6: The following table shows the comparison of serum creatinine level in children among Mannitol and HTS groups before and after treatment

Comparison of Serum Creatinine levels before and after treatment among the two groups					
S.Creatinine(mg/dl)[58]	**Mannitol**		**Hypertonic saline**		**P value**
	Before	**After**	**Before**	**After**	
Abnormal (l>1.0)	5 (10)	7 (14)	5 (10)	3 (6)	1.00*
Normal (0.5-1)	45 (90)	43 (86)	45 (90)	47 (94)	0.182**
Total	50 (100)	50 (100)	50 (100)	50 (50)	
Mean±SD	0.76±0.21	0.82±0.30	0.75±0.24	0.74±0.17	

*p value before treatment and **p value after treatment

In our study there was marginal increase in mean serum creatinine level in Mannitol group (0.82 ±0.30) compared to HTS (0.740±.17) group. However it was statistically not significant

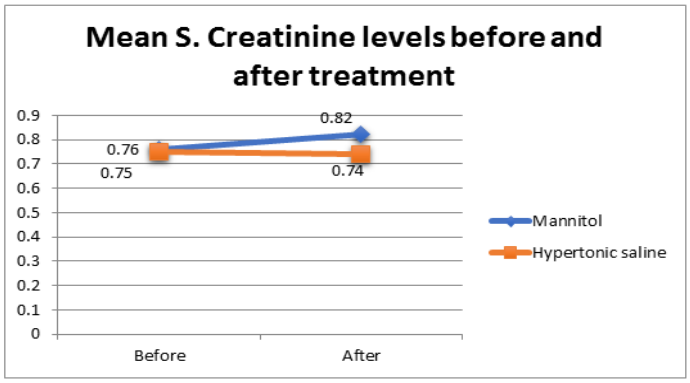

Fig-6

Table-7: The following table shows the Comparison of serum sodium levels in children among Mannitol and HTS groups before and after treatment

Comparison of S. Sodium levels before and after treatment among the two groups					
S. Sodium[58] (Mequ/l)	**Mannitol**		**Hypertonic saline**		**P value**
	Before	**After**	**Before**	**After**	
Abnormal(>145)	7 (14)	5 (10)	10 (20)	13 (26)	0.124
Normal(135-145)	34 (68)	42 (84)	32 (64)	35 (75)	0.127
Subnormal(<135)	9 (18)	3 (6)	8 (16)	2 (4)	
Total	50 (100)	50 (100)	50 (50)	50 (50)	
Mean ± SD	139.395±.86	140.564 ± .67	139.90 ±5.58	143.20 ± 5.09	

*p value before treatment and **p value after treatment

Electrolyte disturbances, like increase in serum sodium levels were seen in HTS (143.90±5.58) group, which was statistically significant compared to mannitol group (140.56±4.67) (p=0.064). However the value remained within acceptable limits

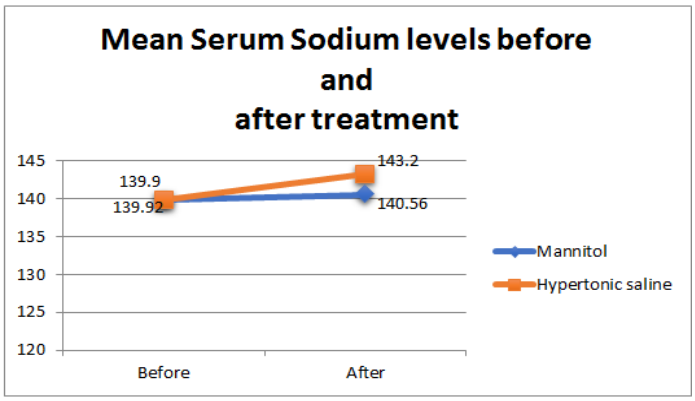

Fig-7

Table-8: The following table shows the Comparison of serum Osmolarity levels in children among Mannitol and HTS groups before and after treatment.

Serum Osmolarity[58] mOsmo/kg	Mannitol		Hypertonic saline		P value
	Before	After	Before	After	
Abnormal(>290)	6(12%)	6 (2%)	9 (18%)	15(30%)	0.619*
Normal (285-290)	30(60%)	36 (12%)	30(60%)	32 (64%)	0.041**
Subnormal(<285)	14 (28%)	8(86%)	11 (22%)	3 (6%)	
Total	50(100%)	50(100%)	50(100%)	50(100%)	
Mean	285.74±11.73	287.36±9.43	285.38±11.56	292.12 ±10.51	

*p value before treatment and **p value after treatment

In mannitolgroup, there was marginal improvement in the serum osmolarity (287.369±9.43), however it was not statistically significant. While in HTS group there was statistically significant improvement in serum osmolarity (292.121±0.51). p=(0.041)

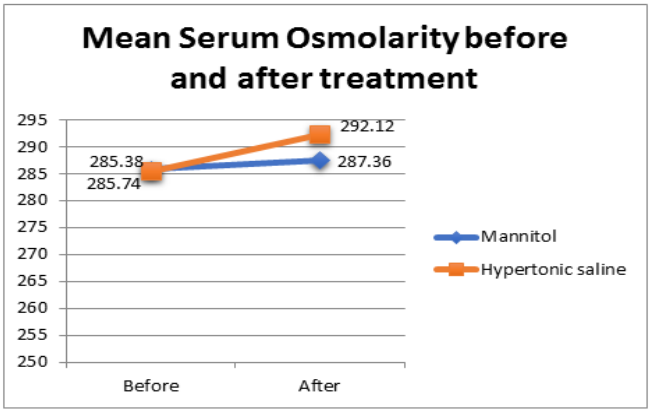

Fig-8

Shows the Survival out come in children among Mannitol and HTS group before and after treatment.

Table-9: The following table shows the Survival out come in children among Mannitol and HTS groups before and after treatment.

Survival of the patients among the two treatment groups					
Outcome	Mannitol		Hypertonic saline		P value
	Frequency	Percent	Frequency	Percent	
Died	3	6.0	4	8.0	0.695
Survived	47	94.0	46	92.0	
Total	50	100.0	50	100.0	

It was observed from above table that there was no statistical survival benefit in both the mannitol (47, 94%) and HTS (46, 93%) groups (P=0.695).

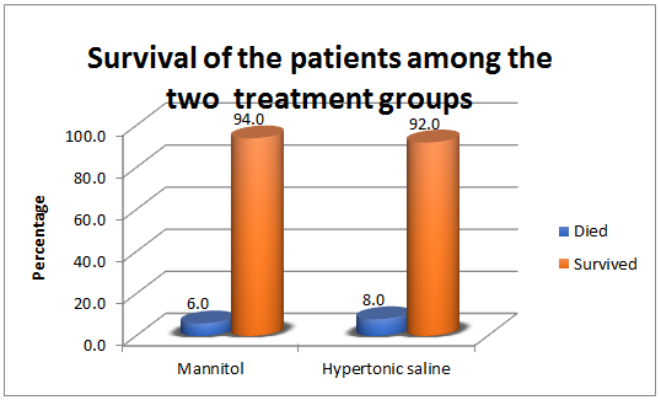

Fig-9

DISCUSSION

In our study there was dramatic improvement of GCS in mannitol group during first 72hours after therapy compared HTS group (p=0.024).And our findings were consistent with the studies done by sarnaik12 (1989) and also by Cruzetal59 (2001, 2002, 2004).

There were no significant pupillary and fundus changes in both groups. And P=0.400 and p=0.558 respectively and similar observations were observed by Kumaraguru Detal.34

In our study there was marginal increase in the serum creatinine and blood urea level in the mannitol group (0.82±0.30), 29.74±8.18 that compared to HTS group (0.74±0.17), (28.86±7.73). However it was statistically not significant .Similar observation were observed by Van Hengel Petal51

There was increase in Serum sodium level 143.20±5.09 (P=0.064) in HTS group. However the values remained within acceptable limits. And similar findings were found in studies conducted by Piyushupadhyayetal30. Also some studies report an inverse relationship between serum sodium concentration and ICP. Similar profile was observered by Qureshietal6 in 27 patients with multiple causes of raised ICP

In our study we observered that, improvement in serum osmolarity was significantly higher in HTS group 292.12±0.51 (p=0.041) compared to mannitol group 287.36 ±9.43.Although the values were within normal limits. This could be probably due to higher osmolarity in HTS (1026mOsm/L) compared mannitol. However it was statistically significant. Our findings are consistent with the Randomized controlled study conducted byPiyushupadyayetal30.

In our study we also found that there was no statistically significant survival benefit in both the groups (p=0.695). In RCT conducted by Kumaraguru Detal.33 showed that there was no significant survival benefit in his study group. Our findings areconsistent with Kumaraguru Detal.33 (p=0.07). and Piyushupadyayetal30. Where as in the study done by Yaldizdasetal22 showed there was statistically significant decreased mortality in HTS compared to mannitol group (p=0.004).

ICP measure could not be conducted in our study, so we continued our treatment considering the serum sodium concentrations and osmolarity till clinical improvement was seen. However potential side effects like ARF, congestive heart failure, pulmonary edema, pontine myelinosis and phlebitis were not observed in any of our patients.

The study is limited by smaller sample size; therefore study needs to be done in larger settings. With measurement of ICP which could not be done in our study.

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