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Original Article:

Hypertonic Saline Versus Mannitol Therapy in Traumatic Brain Injured Patients Guiding by Transcranial Doppler Pulsatile Index in Zagazig University Hospital

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Abstract

Background: Hyperosmolar therapy is the primary medical management strategy for brain edema and raised intracranial pressure. The role of osmotic therapy with either mannitol or hypertonic saline is based on the principle that these agents will help to remove water from brain tissue across an intact blood brain barrier. There is a debatation regarding the efficacy of hypertonic saline (HTS) versus mannitol in traumatic brain injury when are given in equiosmolar doses.

Patients and Methods: An interventional study carried out at trauma and surgical critical care units in Zagazig University Hospital during the period from march 2016 to march 2017. It included ninety patients with different ages, sexes and Glasgow coma scale. The patients were randomly selected from the trauma and surgical critical care units, provided that the patients not received hyperosmolar drug before admission The patients were classified into three groups (thirty patients for each group) as the following: Group A: Included those who are treated with 20% mannitol. Group B: Included those who are treated with 3% hypertonic saline. Group C: Included those who are treated with 3% hypertonic saline alternating with 20% mannitol. Transcranial Doppler parameters especially pulsatility index were observed in the patients before every drug dose and 30 min after giving. Then we observed the change in value of cranial Doppler pulsatility index with subsequently interpretation of values.

Results: There was no significant difference in equiosmolar dose (2ml/kg/6h) between mannitol 20% and hypertonic saline 3% in reducing noninvasive intracranial pressure (nICP) and pulsatility index (PI). Also, there were no significant differences in GCS at the end of treatment and GOS at one month from admission and decrease nICP between the two agents.

Conclusion: This study recommends that in absence of contraindications, no superiority of hypertonic saline 3% over mannitol 20% as hyperosmolar therapy in TBI patients as the both are equally effective in reducing ICP and neurological outcome.

Key Words: *Traumatic brain injury – Transcranial doppler – Pulsatility index and Hyperosmolar Therapy.*

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Introduction

TRAUMATIC Brain Injury is a major cause of death and disability, leading to great personal suffering to victim and relatives, as well as huge direct and indirect costs to society. According to the World Health Organization (WHO), TBI will be the major cause of death and disability by the year 2020 [1].

Several mechanisms are responsible in increasing ICP after TBI. Disruption of blood brain barrier leads to hemorrhage or exudation of plasma into brain tissue that increases plasma portion of cranial tissue. In addition, inflammatory process caused by injured tissue also aggravates the exudation process by inducing vasodilatation. Injured brain parenchyma itself also contributes to increase ICP. Injured cells tend to have dysfunctional transport mechanism within plasma membrane. This leads to sodium and calcium accumulation in cytoplasm that eventually leads to cellular edema [2].

Hyperosmolar treatment is one of the important methods for treating cerebral edema, and has been employed since early 1960. Urea, glycerol and mannitol were used for the treatment of this condition in the early years, but urea and glycerol were soon abandoned because of low efficacy. Mannitol is still used extensively. Side effects such as rebound effect, serum electrolyte imbalance and hypovolemia have led to the continued search for other osmotically active agents. One of them is hypertonic saline [3].

Increasing ICP is associated with decrease cerebral perfusion, brainstem herniation, and death. Hyperosmolar fluid administration, such as mannitol or hypertonic saline, has been proven to be

effective in reducing ICP. While some studies favored hypertonic saline over mannitol, however it is still difficult to prove the superiority between the two fluids because of the heterogeneity of the studies; so, which is more effective remains a matter of debate [2].

This study was conducted to study the efficacy of hypertonic saline in the management of traumatic brain injuries in comparison to mannitol therapy, besides assessment the effect of cerebral dehydrating measures in head trauma patients using the transcranial doppler pulsatility index.

Patients and Methods

After approval of the Ethical Committee, an interventional study carried out at trauma and surgical critical care units in Zagazig University Hospital during the period from march 2016 to march 2017. It included ninety patients with different ages, sexes and Glasgow coma scale. The patients were randomly selected from the trauma and surgical critical care units, provided that the patients not received hyperosmolar drug before admission The patients were classified into three groups (thirty patients for each group) as the following: Group A: Included those who are treated with 20% mannitol. Group B: Included those who are treated with 3% hypertonic saline. Group C: Included those who are treated with 3% hypertonic saline alternating with 20% mannitol. Dose for each drug was 2ml/kg starting on admission and repeated every 6h for 48 hour. Given in central IV line over 30min as osmolarity of mannitol and 3% hypertonic saline are almost the same i.e. 1100mOsm/l and 1098mOsm/l, respectively. Ideal body weight was calculated by using the Devine formula [4]:

- Male IBW = 50 kilograms + 2.3 kilograms* [height (in) – 60].
- Female IBW = 45.5 kilograms + 2.3 kilograms* [height (in) – 60].

Transcranial Doppler parameters especially pulsatility index were observed in the patients before every drug dose and 30min after giving. Then we observed the change in value of cranial Doppler pulsatility index with subsequently interpretation of values. The collecting data includes: Heart rate and Blood pressure: Pre and post every drug dose, Glasgow coma scale (GCS) on admission and after 48h from drug therapy.Glasgow outcome scale (GOS) after one month from drug therapy. Noninvasive intracranial pressure (nICP =10.93* PI – 1.28) on admission and after 48h from drug therapy, [5]. Renal function tests (serum creatinine, blood urea), Arterial blood gases (ABG). Serum electrolytes (k, Na, cl) and Serum osmolarity.

If the patients developed side effects like hypernatremia, hypotension and renal dysfunctions, the drugs should be stopped and the patients managed at once (Dropping cases). Also, the patients who were not suitable to be treated by 3% hypertonic saline or 20% mannitol on admission were recorded.

The Glasgow Outcome Scale (GOS) is a global scale for functional outcome Table (1) that rates patient status into one of five categories [6]. Transcranial doppler pulsatility index is measured by using Siemens Acuson X300 Ultrasound Machine.

Statistical analysis:

The collected data were computerized and statistically analyzed using SPSS program (Statistical Package for Social Science) version 18.0. Qualitative data were represented as frequencies and relative percentages. Chi square test was used to calculate difference between qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). ANOVA F-test test was used to calculate difference between quantitative variables in more than two groups in normally distributed data. Kruskal Wallis test was used to calculate difference between quantitative variables in more than 2 groups in not normally distributed data. Paired *t*-test was used to calculate difference between quantitative variables in the same group at two different times in normally distributed data. Paired Wilcoxon test was used to calculate difference between quantitative variables in the same group at two different times in not normally distributed data. Pearson correlation coefficient used to calculate correlation between quantitative variables. The threshold of significance is fixed at 5% level (p-value): *p-value of >0.05 indicates non-significant results,*p-value of <0.05 indicates significant results and *p-value of <0.01 indicates highly significant results.

Results

As regard demographic data of the studied groups, there were ninety traumatic brain injured patients include 65 males (72.2%) & 25 females (27.8%) divided into three groups, each group was thirty patient. There were no statistical significance differences between the three studied groups in age (Mean ± SD for Group A=33.8±10.23, Group B=35.07±9.15, Group C=32.1 ±9.87) or sex distribution (Table 2).

As regard Pi in the first and 2 nd days of the three studied groups at different times from admission (0h, 6h, 12h.18h, 24, 30h, 36h and 42h), there were no statistical significance differences between the three studied groups. But regarding Pi before and after treatment in each group, there were highly statistical significance decrease in Pi level after treatment in all times as shown in (Table 3) and (Table 4).

There were no statistical significance differences between the three studied groups in Pi on admission and at the end of treatment but there was highly statistical significance decrease in Pi level after treatment (48) in each group as shown in (Fig. 1) (Table 5).

There were no statistical significance differences between the three studied groups in GCS on admission and at the end of treatment; also there were no statistical significance differences in GCS level after treatment (48h) in each group. There was no statistical significance difference between the three studied groups in number of improved cases after treatment (48h) (Table 6).

There was no statistical significance difference between the three studied groups in nICP on admission and at the end of treatment, but there were statistical significance decrease in nICP after treatment (48h) in each group. There was no statistical significance difference between the three studied groups in number of improved cases after treatment (48h) (Table 7).

There were no statistical significance differences between the three studied groups in GOS as shown in (Table 8).

The correlation between the change in Pi, GCS, ICP and GOS among all cases showing that There was +ve significant correlation between change in ICP and change in Pi but There was –ve significant correlation between change in Pi and GOS as shown in (Table 9).

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The correlation between the change in Pi, GCS, ICP and GOS among all cases showing that There were +ve significant correlation between change in ICP and change in Pi but There were –ve significant correlation between change in Pi and GOS.

Table (1): Glasgow outcome scale.

Glasgow outcome scale		
Death	Severe injury or death without recovery of consciousness	1
Persistent vegetative state	Severe damage with prolonged state of unresponsiveness and a lack of higher mental function	2
Severe disability	Severe injury with permanent need for help with daily living	3
Moderate disability	No need for assistance in everyday life. Employment is possible but may require special equipment	4
Low disability	Light damage with minor neurological and physiological deficits	5

Table (2): Comparison of demographic data of the studied groups.

Variable	Group A (n=30)		Group B (n=30)		Group C (n=30)		F	*p*
Age: (years)								
Mean ± SD	33.8±10.23		35.07±9.15		32.1±9.87		0.51	0.6
Range	18-51		19-51		20-51			NS
	No.	%	No.	%	No.	%	χ^2	*p*
Sex:								
Female	8	26.7	10	33.3	7	23.3	0.78	0.68
Male	22	73.3	20	66.7	23	76.7		NS

Table (3): Comparison of Pi of the studied groups at different times in the 1 st day.

Time	Variable	Group A (n=30)	Group B (n=30)	Group C (n=30)	F#	*p*#	LSD
	Pi: (0 h)						0.4 [1]
Before	Mean ± SD	1.6±0.52	1.37±0.2	1.43±0.31	2.39	0.1	0.12 [2]
	Range	1.2-3.6	1.2-1.89	1.2-2.15		NS	0.6 [3]
	Pi: (0 h)						0.16 [1]
After	Mean ± SD	1.35±0.28	1.26±0.12	1.313±0.3	1.04	0.36	0.58 [2]
	Range	0.97-2.05	1.15-1.6	0.97-2.05		NS	0.39 [3]
	p$	0.004**	<0.001**	<0.001 **			
	Pi: (6 h)						0.09 [1]
Before	Mean ± SD	1.39±0.38	1.25±0.11	1.35±0.38	1.58	0.21	0.64 [2]
	Range	0.97-2.5	1.13-1.6	0.97-2.5		NS	0.22 [3]
	Pi: (6 h)						0.27 [1]
After	Mean ± SD	1.27±0.31	1.19±0.13	1.21±0.3	0.66	0.52	0.43 [2]
	Range	0.74-2	1-1.6	0.74-2		NS	0.75 [3]
	p$	<0.001**	<0.001**	<0.001 **			
	Pi: (12 h)						0.09 [1]
Before	Mean ± SD	1.35±0.38	1.21±0.15	1.27±0.35	1.52	0.22	0.29 [2]
	Range	0.85-2.4	0.98-1.52	0.85-2.4		NS	0.5 [3]
	Pi: (12 h)						0.31 [1]
After	Mean ± SD	1.23±0.4	1.15±0.13	1.17±0.37	0.56	0.57	0.46 [2]
	Range	0.6-2.3	0.94-1.49	0.6-2.3		NS	0.78 [3]
	p$	<0.001**	<0.001**	<0.001 **			
	Pi: (18 h)						0.06 [1]
Before	Mean ± SD	1.34±0.43	1.16±0.15	1.25±0.39	1.87	0.16	0.35 [2]
	Range	0.91-2.6	0.82-1.53	0.91-2.6		NS	0.33 [3]
	Pi: (18 h)						0.11 [1]
After	Mean ± SD	1.24±0.4	1.1±0.14	1.19±0.38	1.35	0.27	0.58 [2]
	Range	0.85-2.4	0.8-1.3	0.84-2.4		NS	0.3 [3]
	p$	<0.001**	<0.001**	<0.001 **			

LSD: Least significant post hoc test.
#: One way ANOVA.
$: Paired *t.*

p1: Group A versus Group B.
p2: Group A versus Group C.
p3: Group B versus Group C.

Table (4): Comparison of Pi of the studied groups at different times in the 2nd day.

Time	Variable	Group A (n=30)	Group B (n=30)	Group C (n=30)	F#	*p*#	LSD
	Pi: (24 h)						0.2 [1]
Before	Mean ± SD	1.31±0.44	1.09±0.16	1.2±0.4	2.95	0.06	0.25 [2]
	Range	0.9-2.53	0.81-1.36	0.82-2.53		NS	0.21 [3]
	Pi: (24 h)						0.08 [1]
After	Mean ± SD	1.19±0.43	1.03±0.15	1.08±0.39	1.69	0.19	0.23 [2]
	Range	0.75-2.4	0.79-1.23	0.75-2.4		NS	0.54 [3]
	p$	<0.001**	<0.001 **	<0.001**			
	Pi: (30 h)						0.11 [1]
Before	Mean ± SD	1.22±0.37	1.07±0.15	1.14±0.33	1.31	0.28	0.39 [2]
	Range	0.71-2.6	0.81-1.3	0.71-2.6		NS	0.45 [3]
	Pi: (30 h)						0.19 [1]
After	Mean ± SD	1.12±0.38	0.99±0.13	1.02±0.33	0.96	0.39	0.33 [2]
	Range	0.6-2.5	0.77-1.23	0.6-2.5		NS	0.73 [3]
	p$	<0.001**	<0.001 **	<0.001**			
	Pi: (36 h)						0.12 [1]
Before	Mean ± SD	1.22±0.41	0.98±0.15	1.12±0.37	2.72	0.07	0.35 [2]
	Range	0.75-2.72	0.79-1.26	0.77-2.72		NS	0.17 [3]
	Pi: (36 h)						0.06 [1]
After	Mean ± SD	1.1±0.29	0.9±0.14	0.98±0.32	1.93	0.15	0.23 [2]
	Range	0.72-2.6	0.74-1.19	0.72-2.6		NS	0.45 [3]
	p$	<0.001**	<0.001 **	<0.001**			
	Pi: (42 h)						0.06 [1]
Before	Mean ± SD	1.15±0.34	0.96±0.16	1.02±0.31	2.83	0.07	0.12 [2]
	Range	0.73-2.3	0.71-1.26	0.7-2		NS	0.44 [3]
	Pi: (42 h)						0.08 [1]
After	Mean ± SD	0.93±0.31	0.81±0.16	0.87±0.24	2.13	0.12	0.23 [2]
	Range	0.6-1.5	0.6-1.2	0.6-1.5			0.56 [3]
	p$	<0.001**	<0.001 **	<0.001**			

LSD: Least significant post hoc test.
#: One way ANOVA.
$: Paired *t.*
p1: Group A versus Group B.
p2: Group A versus Group C.
p3: Group B versus Group C.

Table (5): Comparison of Pi of the studied groups before (on admission) and at the end of treatment.

Time	Variable	Group A (n=30)	Group B (n=30)	Group C (n=30)	F#	*p*#	LSD
	Pi: (0 h)						0.4 [1]
Before ttt	Mean ± SD	1.6±0.52	1.37±0.2	1.43±0.31	2.39	0.1	0.12 [2]
	Range	1.2-3.6	1.2-1.89	1.2-2.15		NS	0.6 [3]
	Pi: (42 h)						0.08 [1]
End of ttt	Mean ± SD	0.93±0.31	0.81±0.16	0.87±0.24	2.13	0.12	0.23 [2]
	Range	0.6-1.5	0.6-1.2	0.6-1.5			0.56 [3]
	p	<0.001**	<0.001**	<0.001**			

Table (6): Comparison of GCS of the studied groups before (on admission) and at end of treatment.

Time	Variable	Group A (n=30)	Group B (n=30)	Group C (n=30)	K	*p*^	LSD
Before ttt	*GCS:*						0.51 [1]
	Mean ± SD	7.67±2.67	7.2±2.71	7.53±2.85	0.23	0.8	0.85 [2]
	Range	4-12	3-12	3-12		NS	0.64 [3]
After ttt	*GCS:*						0.53 [1]
	Mean ± SD	8.17±3.69	7.47±3.76	8.1±3.49	0.24	0.78	0.94 [2]
	Range	3-14	3-13	3-13		NS	0.57 [3]
	p [1]	0.12	0.25	0.07			

Improvement:	No.	%	No.	%	No.	%	χ^2	*p*
No	18	60	19	63.3	20	66.7	0.29	0.87
Yes	12	40	11	36.7	10	33.3		NS

Table (7): Comparison of ICP of the studied groups before (on admission) and at end of treatment.

Time	Variable	Group A (n=30)	Group B (n=30)	Group C (n=30)	Test	*p*#	LSD
Before ttt	*ICP:*						0.06 [1]
	Mean ± SD	16.45±4.64	13.87±3.12	14.69±3.24	F	#	0.32 [2]
	Range	11.83-38.06	11.94-39.3	11.8-38.06	2.32	0.06 NS	0.74 [3]
End of ttt	*ICP:*						0.16 [1]
	Mean ± SD	10.74±6.43	7.67± 1.55	8.43±2.49	K	^	0.58 [2]
	Range	6.26-29.32	6.15-11.83	6.15-15.05	0.22	0.90 NS	0.39 [3]
	p	<0.001*	<0.001**	<0.001**			

Improvement:	No.	%	No.	%	No.	%	χ^2	*p*
No	2	6.7	1	3.3	0	0	2.07	0.36
Yes	28	93.3	29	96.7	30	100		NS

Table (8): Comparison of GOS of the studied groups at one month from drug therapy.

Variable	Group A (n=30)	Group B (n=30)	Group C (n=30)	K	*p*^	LSD
GOS:						0.03 [1]
Mean ± SD	**2.73±1.55**	2.6± 1.73	2.6± 1.61	0.07	0.94	0.13 [2]
Range	**1-5**	1-5	1-5		NS	0.48 [3]

Table (9): Correlation between Pi, GCS, ICP and GOS among all cases.

Variable	% of Change in Pi	% of Change in GCS	% of Change in ICP	GOS
% of Change in Pi:				
r	–	−0.12	0.95	−0.22
p	–	0.25	<0.001**	0.04*
% of Change in GCS:				
r	−0.12	–	−0.09	0.73
p	0.25	–	0.40	<0.001**
% of Change in ICP:				
r	0.95	−0.09	–	−0.18
p	<0.001**	0.40	–	0.09
GOS:				
r	−0.22	0.73	−0.18	–
p	0.04*	<0.001**	0.09	–

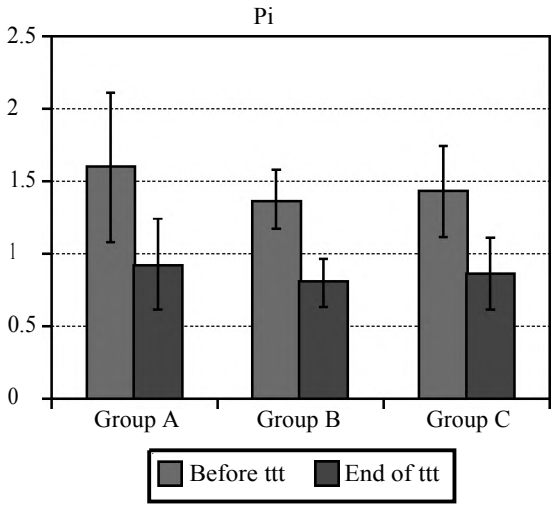

Fig. (1): Comparison of Pi of the studied groups before (on admission) and at the end of treatment.

Discussion

In the present study, the mean age of TBI in the three studied groups (Mean ± SD for Group A=33.8± 10.23, Group B=35.07±9.15, Group C=32.1±9.87). This is consistent with worldwide studies concerning TBI that quote mean ages between 28 and 44 years [7].

Helmy et al., reported a mean age of 31.6 years in an epidemiological study of 970 TBI patients admitted to Alexandria Main University Hospital [1].

Bouguetof et al., and Gura et al., observed the strong correlation between ICP and PI through the management period of TBI patients. Therefore, we used TCD ultrasonography derived PI as a guide to assess the effectiveness of management in the current study [8,9].

The insertion of ICP monitors is an invasive procedure with inherent risks and is contraindicated in case of severe coagulopathy. The transcranial doppler pulsatility index has emerged as a surrogate marker for ICP [10].

De Riva et al., reported that TCD pulsatility index can be easily and quickly assessed. The mathematical model presents a complex relationship between PI and multiple haemodynamic variables [11]. Bellner et al., Calculated noninvasive ICP (nICP) as nICP = (10.93 x PI) – 1.28 or nICP = (11.1 x PI) – 1.43, which could determine an ICP via the PI within ±4.2mmHg of the actual ICP, which is reasonably accurate [5].

In the present study, we used PI and noninvasive ICP to compare between the efficacy of mannitol and hypertonic saline in reducing ICP in traumatic brain injured patients while the previous studies compare between them by using invasive ICP, CBF measurement by positron emission tomography or clinical improvement by GCS. Al-Jehani et al., 2012 used PI as a guide for optimal dosing of hyperosmolar therapy during the management of high ICP.

In the current study, there was no significant difference in equiosmolar dose (2ml/kg/6h) between mannitol 20% and hypertonic saline 3% in reducing nICP and PI.

Scalfani et al., studied the effects of mannitol and HTS on cerebral blood flow in 8 patients with severe TBI. They used positron emission tomography (PET) to measure regional CBF before and 1h after the administration of equiosmolar quantities of 20% mannitol at 1g/kg or 23.4% HTS at 0.686ml/kg in the regions with focal injury and baseline hypoperfusion (CBF <25mL per 100g/min). They found that both agents are effective in lowering ICP (22.4±5.1 to 15.7±7.2mm Hg, p=.007) and increasing CPP (75.7±5.9 to 81.9±10.3mm Hg, p=.03). Also they did not find significant differences between the two agents in neurological outcome, but the sample size is very small to allow a definitive conclusion [12].

Cottenceau et al., conducted a prospective, randomized controlled trial (RCT) which include 47 patients with severe TBI and increased ICP. The patients were recruited in two university hospitals and randomly treated with equiosmolar infusions of either MTL 20% (4mL/kg; n=25 patients) or HTS 7.5% (2mL/kg; n=22 patients). Serum sodium, hematocrit, ICP, arterial blood pressure, cerebral perfusion pressure (CPP), global indices of cerebral blood flow (CBF) and metabolism were measured before, and 30 and 120min following each infusion during the course of illness. Outcome was assessed at 6 months. Both HTS and MTL effectively and equally reduced ICP levels with subsequent elevation of CPP and CBF. Accordingly, there was no significant difference in neurological outcome between the two groups. In conclusion, MTL was as effective as HTS in decreasing ICP in TBI patients although both solutions failed to improved cerebral metabolism [13].

Systematic review in by Burgess et al., found that there was no significant difference between mannitol and hypertonic saline in reducing mortality, ICP and the neurological output in the patients with severe TBI. This review involved seven well publicized trials until November 2015. The failure

rate of ICP lowering therapy was less found in the hypertonic saline group. This systematic review wrote that the data which were currently used were still limited due to the high heterogeneity of each study **[14]**. A review by Boone et al., also found that because of the heterogeneity among studies, the superiority between hypertonic saline and mannitol in reducing ICP in patients TBI could not be concluded. Seven articles included in this review: 5 were prospective, randomized trials; one was a prospective, nonrandomized trial; and one was a retrospective, cohort study **[15]**.

Furthermore, Francony et al., studied 20 patients with intracranial hypertension secondary to TBI in a parallel, RCT and found that a single equimolar infusion of 20% mannitol was as effective as 7.45% hypertonic saline in reducing ICP using cerebral perfusion pressure, blood flow velocities of middle cerebral artery using continuous transcranial Doppler and brain tissue oxygen tension **[16]**.

Likewise, Sakellaridis et al., also found that hypertonic saline and mannitol were equally effective in reducing ICP. In this study, the authors used an alternating treatment protocol to compare the effect of hypertonic saline with that of mannitol given for episodes of increased intracranial pressure in patients treated for severe head injury in their hospital during 2006-2008. Doses of similar osmotic burden (mannitol 20%, 2ml/kg, infused over 20 minutes, or saline 15%, 0.42ml/kg, administered as a bolus via a central venous catheter) were given alternately to the individual patient with severe brain injury during episodes of increased pressure **[17]**.

Battison et al., conducted a prospective cross over randomized controlled study that compared the efficacy of hypertonic saline and dextran mixture with 20% mannitol to reduce the increase of ICP. This study included nine patients, consisting of six patients with TBI and three patients with SAH. The fluids that being used are 200mL of 20% mannitol (249mOsm) and mixture of 100mL of Saline 7.5% and 6% dextran-70 (250mOsm), which infused over 5 minutes. The study found that both mannitol and hypertonic saline significantly reduced ICP, but hypertonic saline decreased ICP more significantly and had longer duration effect than mannitol. But the sample size is very small to allow a definitive conclusion **[18]**.

Oddo et al., conducted a prospective, nonrandomized, and cross over study in 12 patients with severe TBI who experienced episodes of intracranial hypertension by comparing the effects of oxygen pressure in the brain tissue (PbtO2) on the administration of mannitol (25%, 0.75g/kg) and hypertonic saline (7.5%, 250ml). The study found that the administration of hypertonic saline produced lower ICP and cerebral perfusion pressure (CPP) and also improved brain tissue oxygenation compared to mannitol **[19]**.

In a Systematic Review and meta-analysis by Li et al., randomized controlled trials and 2-arm prospective studies in which elevated ICP was present after TBI treated with mannitol or hypertonic saline were included. The primary outcome was the change of ICP from baseline to termination of the infusion, while the secondary outcomes were change from baseline to 30, 60, and 120 minutes after terminating the infusion and change of osmolarity from baseline to termination. A total 7 studies with 169 patients were included. It is concluded that Hypertonic saline is more effective than mannitol for reducing ICP in cases of TBI. But There are limitations of this study that should be considered (e.g., the overall number of patients was relatively small and the concentrations, dosages, and infusion rates of mannitol and hypertonic saline varied between the studies) **[20]**.

Two other meta-analyses have compared hypertonic saline and mannitol for reducing ICP. A study by Kamel et al., included 5 trials with 112 patients and 184 episodes of elevated ICP found that the relative risk of ICP control was 1.16 (95% CI: 1.00-1.33), and the mean difference in ICP reduction was 2.0mm Hg (95% CI: 1.6 to 5.7), both in favor of hypertonic saline over mannitol. (21) A systematic review and meta-analysis by Mortazavi et al., included 36 studies (10 prospective RCTs, 1 prospective and nonrandomized trial, 15 prospective observational trials, and 10 retrospective studies), and concluded that hypertonic saline was more effective than mannitol in reducing ICP. The authors also pointed out that the analysis was limited by low patient numbers, limited RCTs, and inconsistent methods between studies **[22]**.

In the current study, we did not find significant differences in GCS at the end of treatment and GOS at one month from admission and decrease nICP between the two agents, besides there was highly-ve significant correlation between change in Pi and GOS ($p<0.001$). These results are correlated with Li et al., and Cottenceau et al., they reported that successful control of ICP does not guarantee a good neurologic outcome **[13,20]**. Furthermore, Systematic review by Berger-Pelleite et al., found that no mortality benefit or effect on the control of intracranial pressure with the use of

hypertonic saline when compared to other solutions (e.g mannitol or sodium bicarbonate) **[23]**.

However, not correlated with the study done by Bouzat et al., it reported that TCD measurements upon admission may provide additional information about neurologic outcome after mild to moderate traumatic brain injury, **[24]** but most of the patients in our study are severe (n=60) and moderate (n=30).

As regard side effects during the therapy in the three studied groups, no side effects are recorded but the duration of therapy is small (48h) to detect a definitive conclusion. Liorente and De Mejia, concluded that HTS therapy does not increase the incidence of infection or DVT rates. However, hypernatremia is closely linked to HTS infusions and renal dysfunction when sodium levels rise above 155 and 160mEq/l **[25]**. In our study, the serum sodium increases during infusion of HTS 3% but usually decreases before the next dose, however, There are eight patients in group B and four patients in group C excluded from receiving hypertonic saline 3% because the serum sodium exceeds 150meq/l and not return to level below before the next dose These patients are replaced by others in each group.

Conclusion:

This study recommends that in absence of contraindications, no superiority of hypertonic saline 3% over mannitol 20% as hyperosmolar therapy in TBI patients as the both are equally effective in reducing ICP and neurological outcome. Besides, encourage using TCD which is a non-invasive simple bedside procedure that does not measure cerebral blood flow directly but provides calculated data based on the velocity of blood.

Conflict of interest: None.

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المقارنة بين المحلول الملحى المركز والمانيتول فى مرضى إصابات المخ بإستخدام المؤشر النبضى لإشعة دوبلر عبر الدماغ بمستشفى جامعة الزقازيق

العلاج بعقاقير الفرط الاسموزيه هو من الاستراتيجيات الأولية فى علاج الوذمه الدماغية ورفع الضغط داخل الجمجمة. وهذا العلاج سواء بالمانيتول أو المحلول المركز يستند إلى مبدأ أن هذه العوامل تساعد على إدالة المياه من أنسجة المخ وكن. هناك نقاض حول أيهما أكثر فاعلية فى مرضى إصابات المح عندما يتم إعطاؤهما بنفس الجرعه.

وقد أجريت هذه الرسالة فى وحدات الرعاية الخاصة بالحوادث والعمليات الجراحية الحرجة ذات مستوى الوعى المضطرب (أقل من ١٣) فى مستشفى جامعة الزقازيق خلال الفترة من مارس ٢٠١٦ إلى مارس ٢٠١٧، وقد شملت الدراسة ٩٠ حالة (٦٥ ذكور و٢٥ إناث تم تصنيفها إلى ثلاث مجموعات (ثلاثين مريضاً لكل مجموعة)، المجموعة أ: شملت أولئك الذين يعالجون بالمانيتول ٢٠٪، مجموعة ب: شملت الذين يعالجون بالمحلول الملحى المركز ٣٪ ومجموعة ج: شملت الذين يعالجون بالمحلول الملحى المركز ٣٪ بالتناوب مع المانيتول ٢٠٪.

وفى دراستنا لم يكن هناك فرق ملحوظ فى نتيجة التقييم العالمى بين المانيتول ٢٠٪ والمحلول الملحى المركز ٣٪ فى إنخفاض الضغط داخل الجمجمة والمؤشر النبضى لأشعة دوبلر عبر الدماغ. أيضاً، لم: يكن هناك فرق ملحوظ فى منيجة التقييم العالمى فى النتائج العصبية بين المجموعات فى شهر واحد بإستخدام مقياس غلاسكو للغيبوبة.