Tropical Journal of Pharmaceutical Research February 2022; 21 (2): 349-358
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v21i2.18

Original Research Article

Effects of different hypertonic resuscitations on traumatic brain injuries and cranioencephalic trauma: A single centre, retrospective analysis

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Sent for review: 6 September 2021 *Revised accepted: 5 February 2022*

Abstract

Purpose: *To compare the efficacies of 3 % (w/v) hypertonic saline, 20 % (w/v) mannitol, and 10 % (w/v) mannitol plus 10 % (v/v) glycerol in the management of intracranial hypertension.*
Methods: *Patients with intracranial pressure > 20 mmHg received 3 % (w/v) hypertonic saline (HT cohort, n = 78) or 20 % w/v mannitol (MT cohort, n = 82) or 10 % (w/v) mannitol plus 10 % (v/v) glycerol (MG cohort, n = 73) until intracranial pressure was reduced below 15 mmHg. Neurologic outcomes, hemodynamic parameters, and clinical biochemistry were evaluated as indices of intracranial pressure and pathological parameters.*
Results: *Serum sodium levels and serum osmolarity were significantly increased by 3 % (w/ v) hypertonic saline, relative to the other hypertonic resuscitations. At the end of 1 h observation period, 60 (77 %), 36 (44 %), and 41 (56 %) of patients from HT, MT, and MG cohorts, respectively, had their cerebral perfusion pressure successfully maintained at > 70 mmHg. At the end of 1 h observation period, intracranial pressure ≤ 20 mmHg was successfully maintained in 78 (100 %), 81 (99 %), and 73 (100 %) patients from HT, MT, and MG cohorts, respectively. The mean values of arterial pressure of patients in HT, MT, and MG cohorts were increased after 1 h, 15 min, and 30 min of interventions, respectively.*
Conclusion: *These results indicate that 3 % (w/v) hypertonic saline was the most rapid and most effective resuscitation for the management of intracranial hypertension in traumatic brain injuries or cranioencephalic trauma.*

Keywords: *Cerebral haemorrhage, Cerebral perfusion pressure, Hypertonic resuscitation, Intracranial pressure, Traumatic brain injury*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, International Pharmaceutical Abstract, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Intracranial hypertension is a medical emergency which requires proper resuscitation in acute traumatic brain injuries [1]. Prolonged intracranial hypertension could lead to acute cerebral hemorrhage and undesirable neurological outcomes [2]. Osmotherapy has been used since the twentieth century for the management of intracranial hypertension [1]. Barbiturates [3] and

hyperventilation [4] are generally recommended, but they reduce cerebral perfusion pressure and negatively affect systemic blood pressure. However, hypertonic fluids effectively decrease intracranial hypertension without negatively affecting cerebral perfusion pressure [1]. Studies have shown that glycerol and mannitol decrease brain edema in acute traumatic brain injuries [5]. Hypertonic saline is recommended in cases of acute cerebral hemorrhage [2].

Hypertonic agents used for the management of brain edema in acute traumatic brain injuries and acute cerebral hemorrhage reduce intracranial hypertension, but they maintain cerebral perfusion pressure [1]. Current guidelines recommend the use of mannitol for management of intracranial hypertension in acute traumatic brain injuries [6] and acute cerebral hemorrhage [7]. Moreover, mannitol is considered the gold standard for the management of intracranial hypertension in acute traumatic brain injuries [8] and acute cerebral hemorrhage [9]. However, mannitol may cause acute renal failure [1]. A single dose of mannitol reduces intracranial hypertension [10]. However, repeated administration of mannitol aggravates brain edema and causes dehydration over time [1].

Thus, mannitol administration may produce rebound effect on brain edema [11]. Glycerol (glycerine) [5] and hypertonic saline [12] are effective in the management of intracranial hypertension and brain edema in acute traumatic brain injuries and acute cerebral hemorrhage [9]. Although mannitol and glycerol are effective when used singly for the management of intracranial hypertension, the combination of mannitol and glycerol produces better osmotic diuretic properties because of the presence of two sugar groups [1]. Moreover, the combined treatment increases the diffusion of water from cerebrospinal fluid back into plasma, thereby increasing plasma osmolality [13].

Hypertonic saline maintains normovolemia and cerebral perfusion [1]. Prophylactic use of a hypertonic agent is not recommended for mannitol, but this is possible with hypertonic saline [14]. In a study, the osmolarity values of 3 % (w/v) hypertonic saline, 20 % (w/v) mannitol, and 10 % (w/v) mannitol plus 10 % (v/v) glycerol were 1027, 1100 and 1049 mOsm/L, respectively [1]. The short- and long-term efficacies of 3 % (w/v) hypertonic saline, relative to those of 20 % (w/v) mannitol and 10 % (w/v) mannitol plus 10 % (v/v) glycerol in the management of acute traumatic brain injury, is still under investigation [11]. There is only one available randomized trial that compared 3 % (w/v) hypertonic saline + 20 % (w/v) mannitol, with 10 % (w/v) mannitol plus 10 % (v/v) glycerol, with respective to their efficacies in acute traumatic brain injury, but the sample size used was small (n = 40). There is also the ACETatE trial for acute cerebral hemorrhage, but it is only protocol-based [9].

The objective of the study was to compare the effectiveness and safety of different hypertonic resuscitations {3 % (w/v) hypertonic saline, 20 % (w/v) mannitol, and 10 % (w/v) mannitol plus 10 % (v/v) glycerol} in the management of brain edema (to reduce intracranial pressure below 15 mmHg and maintain cerebral perfusion pressure > 70 mmHg) in patients with acute traumatic brain injuries or acute cerebral hemorrhage who had intracranial pressure > 20 mmHg for a minimum of 5 min. The key indexes used were neurologic outcomes, hemodynamic parameters, and clinical biochemistry.

METHODS

Study population

From December 15, 2009 to May 1, 2021, a total of 256 patients aged 18 years or above, who had acute traumatic brain injuries or acute cerebral hemorrhage, with Glasgow Coma Scale score of 8 or less, and who required management of intracranial pressure, were admitted to the Department of Emergency of The First Affiliated Hospital of Soochow University, Suzhou, China, and the referring hospitals. Among them, 15 patients required at least one cranial surgery, two patients had leakage of cerebrospinal fluid, 1 patient had polytrauma, and 1 patient had renal failure. In addition, 1 patient had oliguria, two patients had hemoglobin count less than 8 mg/dL, while 1 patient had serum osmolality more than 320 mOsm/L. Therefore, the data of these patients (n = 23) were excluded from the analyses. Data regarding demography and clinical conditions, Glasgow coma scale (GCS), intracranial pressure, hemodynamic parameters, and clinical biochemistry of 233 patients who received hypertonic resuscitations were retrospectively collected from the hospital records of the patients.

Ethical approval and consent of subjects

The protocol of the study was approved by The First Affiliated Hospital of Soochow University Review Board and the Chinese Society of Traumatology (approval no. FHSU dated October 12, 2020). The study reporting adhered to the law of China and the V2008 Declarations of Helsinki. Informed consent forms were signed by the relatives of patients regarding treatment and

publication of anonymized information on patients in the form of a paper during hospitalization.

Inclusion criteria

Patients aged 18 years or above, who had acute traumatic brain injuries or acute cerebral hemorrhage, with Glasgow Coma Scale 8 or less, and requirements for management of intracranial pressure (intracranial pressure more than 20 mmHg for minimum 5 min), were included in the study.

Exclusion criteria

Patients who required at least one cranial surgery (extra- or intracranial surgery), and those who had drainage or leakage of cerebrospinal fluid, polytrauma, renal failure, oliguria, hemoglobin count of 8 mg/dL or less, and serum osmolality more than 320 mOsm/L, were excluded from the study.

Determination of sample size

The sample size was calculated based on the assumption that about 60 % of patients would have intracranial pressure < 15 mmHg after 15 min of hypertonic resuscitations, barring 10 % type-II error. The sample size (minimum number of patients required in each cohort) was 70.

Cohorts

A total of 78 patients received 3 % (w/v) hypertonic saline until intracranial pressure was below 15 mmHg (HT cohort), while 82 patients received 20 % (w/v) mannitol until intracranial was less than 15 mmHg (MT cohort). A total of 73 patients received 10 % (w/v) mannitol plus 10 % (v/v) glycerol until intracranial pressure was less than 15 mmHg (MG cohort). Analgesia was provided to all patients. Dexmedetomidine (Precedex™, Hospira, Inc., Lake Forest, IL, USA) was used as sedative for patients in irritable conditions. Norepinephrine (Levophed®, Hospira, Inc., Lake Forest, IL, USA) was administered to hypotensive patients, while insulin (Novolog, Novo Nordisk A/S, Bagsværd, Denmark) was used to maintain blood glucose level at 140 mg/dL. Hypertonic resuscitations (Roche Diagnostics, Risch-Rotkreuz, Switzerland) were administered through the central venous line at the rate of 6 mL/min or 120 drops/min when intracranial pressure was more than 20 mmHg for a minimum of 5 min. When intracranial pressure was below 15 mmHg, hypertonic resuscitations were stopped [1]. Patients received 3 % (w/v) hypertonic saline if there were requirements for immediate benefits of hypertonic agents [11] and requirement for maintenance of vasodilation [1], in addition to intracranial pressure management. Moreover, hypertonic resuscitations were given to patients with elevated serum creatinine levels in the absence of any known cardiac diseases [1]. Patients were given 10 % (v/v) glycerol with 10 % w/v mannitol if there was a risk of rebound edema and acute kidney injury, especially for subjects with history of cardiac diseases [5]. Other than these conditions, patients received 20 % w/v mannitol infusion [6].

Evaluation of outcome indices

Data on demography and clinical conditions, Glasgow Coma Scale score, intracranial pressure, hemodynamic parameters, and clinical biochemistry of patients who received hypertonic resuscitations, were collected from the hospital records of the patients.

Measurement of intracranial pressure

Intracranial pressure was continuously measured with a Codman Microsensor® ICP transducer (Codman & Shurtleff Inc, Raynham, MA, USA) [15] and Spiegelberg ICP transducer and Monitor (Spiegelberg GmbH & Co. KG, Tempowerkring, Hamburg, Germany) [16].

Statistical analysis

InStat 3.0.1, (GraphPad Software, San Diego, CA, USA) was used for statistical analysis. One-way analysis of variance (ANOVA; between cohorts), or two-sided unpaired *t*-test (within cohorts), following Tukey *post hoc* test [considering as significant, critical value (q) > 3.344 for between cohorts, and > 3.659 for within cohorts] was used for continuous variables [1]. The Chi-square (χ^2) test of independence was performed for categorical variables [10]. Differences were considered significant at $p < 0.05$.

RESULTS

Demographic, clinical, and pathological parameters

At the time of hospital admission, there were no significant differences in gender, age, cause of brain injuries, intracranial pressure, heart rate, mean arterial pressure, cerebral perfusion pressure, and clinical biochemistry among patients of the three cohorts ($p > 0.05$). These data are shown in Table 1.

Table 1: Demographic, clinical, and pathological data for patients at the time of hospital admission

Parameter		Cohorts			*P*-value
		HT	MT	MG	
Hypertonic resuscitation		***3 % (w/v) NaCl***	***20 % (w/v) Mannitol***	***10 % (w/v) Mannitol + 10 % (v/v) glycerol***	
Number of patients		***78***	***82***	***73***	
Gender	Male	46 (59)	57 (70)	41 (56)	0.191
	Female	32 (41)	25 (30)	32 1(44)	
Age (years)	Minimum	19	19	20	0.833
	Maximum	67	67	66	
	Mean ± SD	39.21±16.48	40.21±17.11	40.89±18.11	
Cause of brain injuries	Motor vehicle accident	48(62)	48(59)	38(52)	0.922
	Acute cerebral hemorrhage	25(32)	27(33)	28(38)	
	Fall	3(4)	5(6)	4(6)	
	Assault	2(2)	2(2)	3(4)	
The Glasgow Coma Scale	Minimum	3	3	3	0.816
	Maximum	7	7	7	
	Mean ± SD	4.96±1.42	4.98±1.56	4.83±1.46	
Intracranial pressure (mmHg)	Minimum	21	21	21	0.113
	Maximum	31	31	30	
	Mean ± SD	25.41±2.96	24.99±2.53	25.93±2.89	
Heart rate (beats per minute)	Minimum	51	57	52	0.618
	Maximum	92	91	94	
	Mean ± SD	74.54±10.22	75.85±8.49	76.01±11.94	
Mean arterial pressure (mmHg)	Minimum	59	62	58	0.674
	Maximum	90	84	86	
	Mean ± SD	76.14±8.00	77.13±5.52	76.67±7.53	
% Hematocrit	Minimum	24	23	23	0.759
	Maximum	46	47	47	
	Mean ± SD	34.12±3.15	34.23±4.18	34.56±3.89	
Serum Sodium (mEq/L)	Minimum	120	120	120	0.247
	Maximum	145	145	145	
	Mean ± SD	135±7	136±7	137±8	
Serum osmolarity (mOsm/kg)	Minimum	260	264	265	0.198
	Maximum	300	300	302	
	Mean ± SD	290±8	289±11	292±12	
Cerebral perfusion pressure (mmHg)	Minimum	29	32	30	0.051
	Maximum	69	70	71	
	Mean ± SD	54.63±10.75	50.45±11.15	52.86±10.50	

Intracranial pressure

Fifteen minutes after administration of hypertonic resuscitations, intracranial pressure of patients of HT cohort was markedly lower than those of MT cohort (12.96 ± 1.54 mmHg *vs*. 15.23 ± 2.28 mmHg, $p < 0.0001$; $q = 10.814$) and MG cohort (12.96 ± 1.54 mmHg *vs*. 15.04 ± 1.69 mmHg, $p < 0.0001$, $q = 9.621$). However, there were no significant differences in intracranial pressure between patients of MG cohort and patients of MT cohort at 15 min after administration of hypertonic resuscitation(s) ($p < 0.0001$, $q = 0.893$). At 30 min after administration of hypertonic resuscitations, intracranial pressure of patients of HT cohort was markedly lower than those of MT cohort (13.13 ± 1.62 mmHg *vs*. 14.71 ± 1.78 mmHg, $p < 0.0001$; $q = 9.601$) and MG cohort (13.13 ± 1.62 mmHg *vs*. 13.95 ± 0.72 mmHg, $p < 0.0001$; $q = 4.824$).

Moreover, 30 min post-administration of hypertonic resuscitations, intracranial pressure of patients of MG cohort was significantly lower than those of MT cohort ($p < 0.0001$, $q = 4.554$). At 1 h after administration of hypertonic resuscitations, intracranial pressure of patients of HT cohort was markedly lower than those of MT cohort (13.69 ± 1.83 mmHg *vs*. 15.04 ± 1.69 mmHg, $p < 0.0001$; $q = 7.792$) and MG cohort (13.69 ± 1.83 mmHg *vs*. 14.42 ± 0.91 mmHg, $p < 0.0001$; $q = 4.123$). Moreover, at 1 h after administration of hypertonic resuscitations, intracranial pressure of patients of MG cohort was lower than that of MT cohort ($p < 0.0001$, $q = 3.486$). These results are shown in Figure 1.

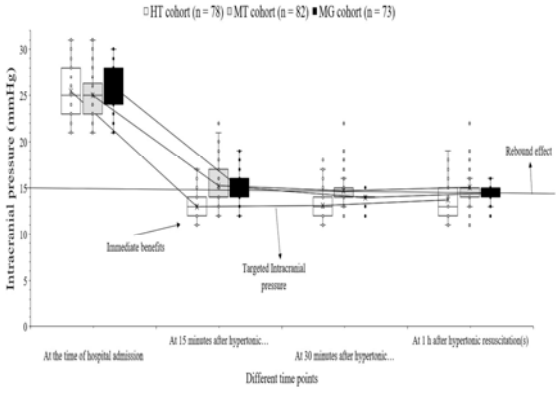

Figure 1: Intracranial pressure of patients after administration of hypertonic resuscitations at different time points

Time required to reach intracranial pressure < 15 mmHg

The times required for intracranial pressure to decrease to values less than 15 mmHg as a result of hypertonic resuscitation were 13.00 ± 2.29, 16.60 ± 3.16 and 16.08 ± 1.96 min for patients of HT, MT, and MG cohorts, respectively. The time lag before intracranial pressure decreased to less than 15 mmHg due to 3 % (w/v) hypertonic saline administration was lower than those of 20 % (w/v) mannitol ($p < 0.0001$, $q = 12.659$) and 10 % (w/v) mannitol plus 10 (v/v) glycerol ($p < 0.0001$, $q = 10.533$). The times required to decrease intracranial pressure below 15 mmHg in patients who received 20 % (w/v) mannitol and those who received 10 % (w/v) mannitol plus 10 (v/v) glycerol were statistically similar. These data are presented in Figure 2.

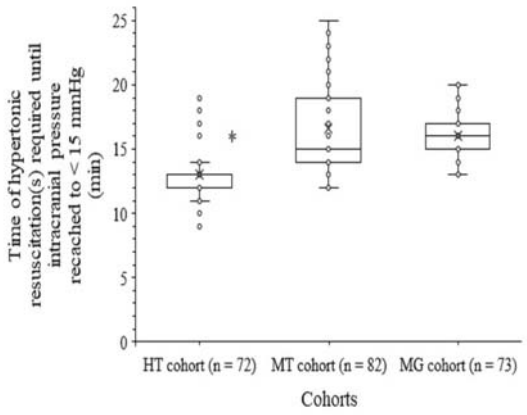

Figure 2: Duration of times required to decrease intracranial pressure below 15 mmHg in patients taking different hypertonic resuscitations. *Lower than those of MT and MG cohorts

Rebound effect

A total of 25 (32 %), 58 (71 %), and 40 (55 %) patients from HT, MT, and MG cohorts, respectively, had intracranial pressure more than 15 mmHg after 1 h of observation. A lower number of patients in the HT cohort had intracranial pressure higher than 15 mmHg after 1 h of observation, than in the MT and MG cohorts ($p < 0.0001$). At the end of 1 h of the observation period, 78 (100 %), 81 (99 %), and 73 (100 %) patients from HT, MT, and MG cohorts, respectively, had their intracranial pressure successfully maintained at 20 mmHg or below. All hypertonic resuscitations effectively maintained intracranial pressure at 20 mmHg or below at the end of 1 h of the observation period ($p = 0.397$).

Heart rate

After 1 h of observation, there were no significant differences in heart rate among the cohorts ($p = 0.567$).

Mean arterial pressure

There was significant increase in mean arterial pressure among patients of HT cohort after 1 h of observation, when compared to the condition at the time of hospital admission (76.14 ± 8.00 mmHg *vs*. 79.83 ± 6.99 mmHg, p = 0.014, q = 4.523). Mean arterial pressure was increased in patients of MT cohort 15 min after administration of 20 % (w/v) mannitol (77.13 ± 5.52 mmHg *vs*. 79.28 ± 4.68 mmHg, p = 0.003, q = 4.063). Mean arterial pressure was increased in patients of MG cohort 30 min after administration of 10 % (w/v) mannitol plus 10 % (v/v) glycerol (76.67 ± 7.53 mmHg *vs*. 79.52 ± 6.07 mmHg, p = 0.021; q = 3.709). The mean arterial pressure values of patients after administration of hypertonic resuscitations at different time intervals are shown in Figure 3.

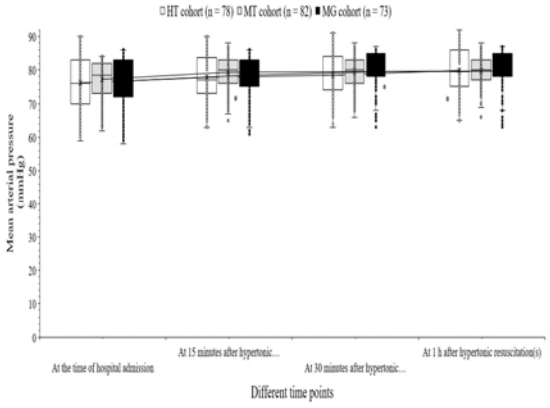

Figure 3: Mean arterial pressure of patients after administration of hypertonic resuscitations at different time intervals. *Significantly higher mean arterial pressure than condition at the time of hospital admission

Dose of hypertonic resuscitation

Lower volume of 3 % (w/v) hypertonic saline was required for patients of HT cohort than for 20 % (w/v) mannitol for MT cohort (1.34 ± 0.14 mL/kg *vs*. 2.10 ± 0.33 mL/kg, p < 0.0001, q = 29.064) and 10 % (w/v) mannitol plus 10 % (v/v) glycerol for MG cohort (1.34 ± 0.14 mL/kg *vs*. 1.49 ± 0.19 mL/kg, p < 0.0001, q = 5.774) in the reduction of intracranial pressure below 15 mmHg. Moreover, the volume of 10 % (w/v) mannitol plus 10 % (w/v) glycerol needed to achieve intracranial pressure less than 15 mmHg in MG cohort was lower than that of 20 % (w/v) mannitol for MT cohort (p < 0.0001, q = 22.721). These results are shown in Figure 4.

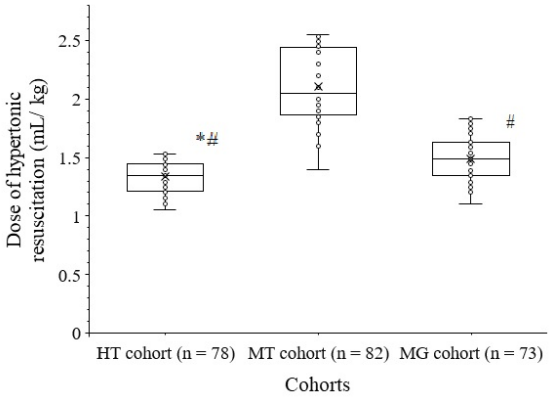

Figure 4: Doses of hypertonic resuscitation needed to reduce intracranial pressure below 15 mmHg. *: Significantly lower than that of MG cohort. #: Significant lower than that of MT cohort

Clinical biochemistry

There were no significant differences between hematocrit values before resuscitation and hematocrit values after hypertonic resuscitation in patients in all cohorts (p > 0.05). Serum sodium levels and serum osmolarity were increased after hypertonic resuscitation in all cohorts (p < 0.05). However, serum sodium levels were significantly increased after administration of 3 % (w/v) hypertonic saline in patients of HT cohort, when compared to those of the MT cohort (p < 0.0001, q = 9.625) and the MG cohort (p < 0.0001, q = 7.011) after administration of hypertonic resuscitation. Serum osmolarity was markedly increased after administration of hypertonic resuscitation in all cohorts (p < 0.0001). Serum osmolarities were significantly increased after administration of 3 % (w/v) hypertonic saline in patients of the HT cohort, when compared to those of the MT cohort after administration of hypertonic resuscitation (p = 0.009, q = 4.396). These data are shown in Table 2.

Glasgow coma scale

At the end of 1 h of observation period, there were improvements in Glasgow coma scale in patients of HT cohort (4.96 ± 1.42 *vs*. 7.09 ± 1.68, p < 0.0001), MT cohort (4.98 ± 1.56 *vs*. 6.70 ± 1.40, p < 0.0001), and MG cohort (4.84 ± 1.46 *vs*. 7.10 ± 1.66, p < 0.0001). There were no significant differences in Glasgow coma scale scores among patients of all cohorts at the end of 1 h of the observation period (p = 0.188). These results are presented in Figure 5.

Table 2: Pathological parameters of patients

Parameter		Cohorts								
		HT			***MT***			***MG***		
Hypertonic resuscitation		***3 % (w/v) NaCl***			***20 % (w/v) mannitol***			***10 % (w/v) mannitol + 10 % (v/v) glycerol***		
Level		BL	AL	*P*-value	BL	AL	*P*-value	BL	AL	*P*-value
Numbers of patients		78	78		82	82		73	73	
% Hemat-ocrit	Min	24	23		23	23		23	24	
	Max	46	47	0.216	47	48	0.542	47	48	0.566
	Mean ± SD	34.12±3.15	34.82±3.85		34.23±4.18	34.65±4.61		34.56±3.89	34.92±3.66	
Serum Na (mEq/L)	Min	120	125		120	122		120	123	
	Max	145	155	<0.0001	145	147	0.026	145	148	0.047
	Mean ± SD	135±7	142±4		136±7	138±4		137±8	139±3	
Serum osmol-arity (mOsm/kg)	Min	260	270		264	266		265	267	
	Max	300	310	<0.0001	300	304	<0.0001	302	308	<0.0001
	Mean ± SD	290±8	305±10		289±11	301±6		292±12	303±8	

BL: Before administration, AL: After administration

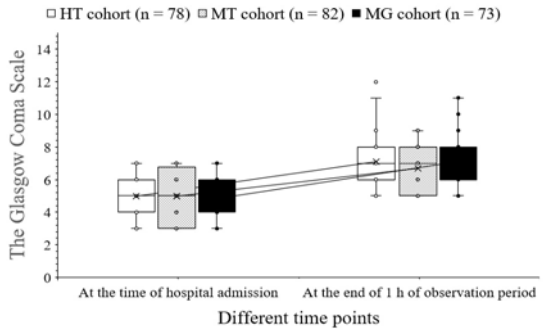

Figure 5: Glasgow coma scale of patients

Cerebral perfusion pressure

During the observation period, cerebral perfusion pressure was increased in patients after administration of hypertonic resuscitations. However, 3 % (w/v) hypertonic saline increased cerebral perfusion pressure of patients more significantly than 20 % (w/v) mannitol and 10 % (w/v) mannitol plus 10 (v/v) glycerol. At the end of 1 h observation period, cerebral perfusion pressure was successfully maintained above 60 mmHg in 70 (90 %), 62 (76 %), and 60 (82 %) patients from HT, MT, and MG cohorts, respectively. There was a higher number of patients in the HT cohort with cerebral perfusion pressure above 60 mmHg at the end of 1 h of the observation period than in MT and MG cohorts, although this was not statistically significant (p = 0.064). At the end of 1 h of the observation period, cerebral perfusion pressure was successfully maintained above 70 mmHg in 60 (77 %), 36 (44 %), and 41 (56 %) patients from HT, MT, and MG cohorts, respectively. Thus, cerebral perfusion pressure above 70 mmHg was successfully maintained in a higher number of patients in the HT cohort at the end of 1 h of the observation period, than in MT and MG cohorts (p = 0.006). These results are shown in Figure 6.

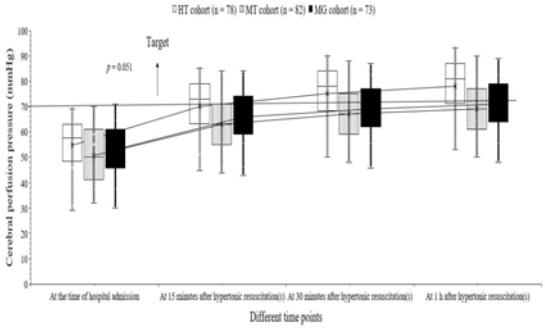

Figure 6: Cerebral perfusion pressure in patients of the 3 cohorts

DISCUSSION

This study has shown that the administration of 3 % (w/v) hypertonic saline, 20 % (w/v) mannitol, and 10 % (w/v) mannitol plus 10 % (v/v) glycerol resulted in reduced intracranial pressure below 15 mmHg within 30 min after administration. All hypertonic resuscitations were effective in maintaining intracranial pressure at 20 mmHg or below in all patients at the end of 1 h of the observation period. The results of the intracranial pressure management in the current study are consistent with those of a randomized trial [1] and a Cochrane database systematic review [11]. Intracranial pressure above 20 mmHg is responsible for adverse neurologic outcomes and mortality [17]. Moreover, 3 % (w/v) hypertonic saline, 20 % (w/v) mannitol, and 10 % (w/v) mannitol plus 10 % (v/v) glycerol produced the same level of neuroprotection during management of acute traumatic brain injury or acute cerebral hemorrhage.

However, 3 % (w/v) hypertonic saline produced superior and early effect on intracranial pressure, relative to 20 % (w/v) mannitol and 10 % (w/v) mannitol plus 10 % (v/v) glycerol. These results are consistent with those of a randomized trial reported earlier [1]. The effect of 3 % (w/v) hypertonic saline on intracranial pressure was rapid.

Hypertonic saline (3 %, w/v) produced significantly lower effects on mean arterial pressure than 20 % (w/v) mannitol and 10 % (w/v) mannitol plus 10 % (v/v) glycerol. These results are consistent with those obtained in an earlier randomized trial [1]. The effect of 3 % (w/v) hypertonic saline on hemodynamic parameters was negligible.

Serum sodium levels and serum osmolarity were significantly increased by 3 % (w/v) hypertonic saline, relative to 20 % (w/v) mannitol and 10 % (w/v) mannitol plus 10 % (v/v) glycerol. These clinical biochemistry results are in agreement with those of a randomized trial reported earlier [1]. Elevated serum sodium levels and increased serum osmolarity lead to lung edema, heart failure, and coagulation disorders [18]. Thus, administration of 3 % (w/v) hypertonic saline in patients with compromised cardiac functions requires close monitoring.

The use of 3 % (w/v) hypertonic saline resulted in fewer doses and shorter intervention time in management of intracranial pressure, when compared with the other hypertonic resuscitations. In this study, the time required to reach intracranial pressure < 15 mmHg and the

doses of hypertonic resuscitations are consistent with those of a randomized trial reported earlier [1]. There is no consensus on the optimum concentration of 3 % (w/v) hypertonic saline [19]. A randomized trial [1] has recommended 1.4 mg/kg bolus 3 % (w/v) hypertonic saline. Indeed, 3 % (w/v) hypertonic saline was superior for management of acute traumatic brain injury or acute cerebral hemorrhage than any of the other hypertonic resuscitations.

All hypertonic resuscitation improved Glasgow coma scale scores, but there were no significant differences in Glasgow coma scale score among patients of all cohorts at the end of 1 h of observation period. The results on Glasgow coma scale scores in this study are in agreement with those of a randomized trial [1]. The small sample size of a randomized trial [1] was responsible for type-I error. All hypertonic resuscitations produced comparable improvements in Glasgow coma scale score.

A higher number of patients in the HT cohort had cerebral perfusion pressure above 70 mmHg at the end of 1 h of the observation period than in the MT and MG cohorts. The results on changes in cerebral perfusion pressure in the current study agree with those of a randomized trial [1]. The general treatment goal for management of acute traumatic brain injury or acute cerebral hemorrhage, is to keep cerebral perfusion pressure above 70 mmHg [20]. In this respect, 3 % (w/v) hypertonic saline was superior to other resuscitations in achievement of this treatment goal for acute traumatic brain injury or acute cerebral hemorrhage.

Limitations of the study

There are several limitations in this study. For example, it was a retrospective analysis, and there was no randomized trial. Moreover, only immediate effects of hypertonic resuscitations were studied, while long-term effects (repeated infusion, adverse effects related to intracranial pressure measurement method, and maintenance dose) were not evaluated. In the time range for selecting cases, two intracranial pressure-monitoring probes were used. The possible justification for this is that the intracranial pressure monitoring probe used in the past few years in the institutes was a Codman Microsensor® ICP transducer. However, in recent years, there has been a switch to Spiegelberg ICP transducer and monitor, such that Codman's products are rarely used. The reference value of the two transducers are similar. The time range for selecting cases was more than 10 years. The possible justification for this is that in the parent hospital and referring hospitals, pressure gauges are generally used for lumbar puncture, and very few intracranial pressure probes are placed. Lumbar puncture is contraindicated for intracranial hypertension, which means that lumbar puncture is generally not preferred when measuring intracranial hypertension. An intracranial pressure probe is generally implanted during craniotomy operation, and patients with craniotomy in the current study were excluded from the study.

CONCLUSION

Severe increase in intracranial pressure is a major cause of death in intensive care units, especially after acute traumatic brain injury or haemorrhagic stroke. Thus, lack of a proper management protocol may prove deleterious to patient survivability. The current study has found that 3 % hypertonic saline, 20 % mannitol, and 10 % mannitol plus 10 % glycerol produce the same neuroprotection during the management of acute traumatic brain injury or acute cerebral hemorrhage, as well as improves Glasgow coma scale score. In addition, 3 % hypertonic saline is the most rapid and most effective resuscitation fluid, followed by 10 % mannitol plus 10 % glycerol, and then 20 % mannitol, for the management of acute traumatic brain injury or acute cerebral hemorrhage. However, administration of 3 % (w/v) hypertonic saline in patients with compromised cardiac functions requires close monitoring. The results of this retrospective analysis will be helpful to critical care physicians in the choice of hypertonic resuscitation when osmotherapy is required.

DECLARATIONS

Acknowledgement

The authors are thankful for the medical, non-medical, and nursing staff of the First Affiliated Hospital of Soochow University, Suzhou, China.

Conflict of interest

No conflict of interest is associated with this work

Contribution of authors

The authors declare that this work was done by them and all liabilities pertaining to claims relating to the content of this article will be borne by them. All authors have read and approved the manuscript for publication. Fei Han and Yingzhu Wang contributed equally to supervision, the literature review, supervision, validation,

methodology, and visualization of the study. Zhengjie Sun was project administrator, contributed to data curation, resources, formal analysis, and literature review of the study. Junyi Gu contributed to conceptualization, investigation, and literature review of the study, draft and edited the manuscript for intellectual content.

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