The Effect of Mannitol and Hypertonic Sodium Administration on Hemodynamic Parameters Under LiDCO Monitoring in Patients Undergoing Elective Craniotomy

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Received: 20 Apr. 2023; Accepted: 21 Aug. 2023

Abstract- In craniotomy surgery, it is important to maintain hemodynamics and prevent the increase of intracranial pressure. Using semi-invasive methods such as LiDCO monitoring is a good option in this situation. This study aimed to evaluate the effectiveness of mannitol and hypertonic sodium on hemodynamic parameters in patients undergoing elective craniotomy. This randomized clinical trial was done on 40 patients of both genders. Patients whose ages were between 18-65 years, who had American Society of Anesthesiologists (ASA) score I and II, and who underwent craniotomy surgery were eligible for this study. Participants were divided into two groups receiving hypertonic sodium and mannitol. Hemodynamic parameters were evaluated before surgery, 20 minutes, and 60 minutes after surgery in both groups, under Lithium dilution cardiac output (LiDCO) monitoring. The results showed that there was no difference between groups in terms of the average fluid intake, the duration of the operation, the amount of urinary output, and the primary hemodynamic characteristics. Significant differences were recorded in the evaluation of hemodynamic parameters. The results demonstrated a reduction in systolic, diastolic, and mean arterial blood pressure during 20 to 60 minutes after mannitol injection compared to hypertonic sodium injection. Additionally, the effectiveness of both therapies on maintaining cardiac function was similar, but the use of mannitol led to a greater decrease in arterial and peripheral vascular resistance. It can be concluded that mannitol may be more effective than hypertonic sodium during craniotomy procedures in terms of reducing blood pressure monitored with LiDCO.

Acta Med Iran 2023;61(9):508-512.

Keywords: Hemodinamic monitoring; Lithium dilution cardiac output (LiDCO); Craniotomy; Mannitol; Hypertonic sodium

Introduction

A Craniotomy is a neurosurgical procedure commonly performed both electively and in an emergency setting (1). It is applies to a range of conditions, including brain tumors, aneurysms, arteriovenous malformations, subdural empyemas, subdural hematomas, and intracerebral hematomas (2,3), which is indicative of its importance and frequency. Despite their life-saving impact, it is imperative to recognize that, like all surgeries, these procedures may lead to neurological, regional, or systemic complications. There is also an estimated mortality rate of 1.2% and morbidity rate of 8-12% following craniotomies (4). A variety of complications can occur following craniotomy, including electrolyte imbalances (hyponatremia and hypernatremia are two of the most prevalent) (1). Furthermore, the management of brain

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relaxation and intracranial pressure (ICP) is vital to the success of neurosurgical procedures such as craniotomies (5). In patients with elevated ICP, brain perfusion can be impaired, neurological outcomes can be poor, and mortality can occur. Studies have shown that death rates rose to 55.6% in patients with ICP>40 mmHg as compared to 18.4% for those with ICPs20 mmHg (6). When an elevated ICP needs urgent treatment, hyperosmotic therapy is often the first choice (7). Mannitol and hypertonic sodium are common hyperosmolar solutions used in neurosurgery and critical care units to reduce intracranial pressure and brain volume (8-11). According to the Monro-Kellie Doctrine and the fluid shift theory, both agents reduce ICP primarily by mobilizing brain fluid into intravascular compartments through an osmolar gradient (12,13). Additionally, maintaining hemodynamics can be achieved through the administration of appropriate drugs and fluid management. Controlling hemodynamic parameters in patients undergoing craniotomy is of paramount clinical importance (14). Patient management can be improved by using hyperosmolar solution that are minimally disruptive to hemodynamic parameters. Although there have been studies examining the effects of hyperosmolar solutions on intracranial pressure, their hemodynamic effects remain undetermined. Thus, mannitol and hypertonic sodium were investigated in this study for their effect on ICP reduction under LiDCO monitoring in patients undergoing elective craniotomy.

Materials and Methods

This single center, randomized, double-blind clinical trial was conducted at Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran, between February 2022 and March 2023. This study has been approved by the ethics committee of Tehran University of Medical Sciences (Ethics no.: IR.TUMS.SINAHOSPITAL.REC.1400.016) and registered at Iranian Registry of Clinical Trials (IRCT no.: IRCT20170805035510N7).

Eligibility criteria included adult patients aged 18 to 65 with ASA levels I and II who had undergone elective craniotomy at Sina Hospital. Patients were excluded if they met any of the following criteria: ASA level of 3 or higher, previous history of cranial surgeries, pregnancy, BMI> 40 kg/m^2, abnormal sodium levels before surgery and patients treated with hyperosmotic fluids within 24 hours before surgery. All participants gave their informed written consent before entering the study.

The patients included in the study were randomly divided into two groups mannitol (receiving 5 ml/kg mannitol 20%) or hypertonic sodium (receiving 3 mg/kg hypertonic sodium 5%). Patients were evaluated during surgery using the LiDCO monitoring system. Hemodynamic parameters and oxygenation were recorded before the administration of mannitol and hypertonic sodium (T0) and then continued 20 minutes after the administration (T1), one hour later or the end of the surgery (T2). The amount of bleeding, normal saline intake, furosemide and thiopental injection, fluid challenge, urinary output, and vasopressors were recorded. Hemodynamic parameters including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), pulse pressure variation (PPV), cardiac output (CO), systemic vascular resistance (SVR), was recorded from the LiDCO system.

The data were analyzed using SPSS software version 22.

Results

This study assessed hemodynamic changes in 40 eligible patients undergoing craniectomy. Patients were randomized into two groups receiving either mannitol or hypertonic sodium infusion.

Regarding gender distribution (P=0.235), and the mean age (P=0.542), there were no significant differences between the two groups. Additionally, past medical histories including hypertension, diabetes mellitus, ischemic heart disease, and chronic kidney disease did not differ significantly between groups (Table 1).

Furthermore, there were no statistically significant differences between the mannitol and hypertonic sodium groups in characteristics such as mean fluid intake (P=0.880), mean urine output (P=0.286), mean operative time (P=0.093), and mean bleeding (P=0.882) (Table 2).

Other factors evaluated in this study were parameters related to LiDCO monitoring before injection, 20 and 60 minutes after injection (Table 3). Based on this, there was no significant difference in systolic blood pressure before injection (P=0.089) and 20 minutes after injection (P=0.115). However, 60 minutes after the injection, a difference between the two groups of mannitol and hypertonic sodium groups was determined, which showed lower systolic blood pressure in the mannitol group (P=0.001). Unlike systolic blood pressure, in diastolic blood pressure, not only a difference between the two groups observed within 60 minutes after injection (P=0.001), but this difference

was also evident in 20 minutes after injection (*P*=0.001). Therefore, it seems that mannitol has a stronger blood pressure-lowering effect than hypertonic sodium. Heart rate and cardiac output did not differ between groups at any time points (*P*>0.05).

There was no difference in SVR between the two groups before injection (*P*>0.05), but significant differences were reported at 20 (*P*=0.008) and 60 minutes (*P*=0.001) later, which was lower in the mannitol group than in the other one.

Although there was no significant difference was shown between groups before injection in SVV and PPV parameters (*P*>0.05); 20 and 60 minutes after injection, they were significantly lower in the mannitol group (*P*<0.05).

Table 1. Baseline characteristics of participants

Characteristics		Mannitol Group N=20 N (%); mean±SD	Hypertonic Sodium Group N=20 N (%); mean±SD	*P*
Gender	**Male**	14 (70)	18 (90)	0.235
	Female	6 (30)	2 (10)	
Age; y/o		48.5±10.96	50.75±12.14	0.542
Cause of Craniotomy	**Brain tumor**	16 (80)	20 (100)	0.106
	Brain aneurism	4 (20)	0 (0)	
Past Medical History	**HTN**	8 (40)	5 (25)	0.311
	DM	4 (20)	5 (25)	0.751
	IHD	2 (10)	0 (0)	0.147
	CKD	3 (15)	0 (0)	0.456

Abbreviation: y/o: Years old; HTN: Hypertension; DM: Diabetes Mellitus; IHD: Ischemic Heart Disease; CKD: Chronic Kidney Disease

Table 2. Clinical charactersitic differences between groups

Characteristics	Mannitol Group N=20 Mean±SD	Hypertonic Sodium Group N=20 Mean±SD	*P*
Fluid intake (input); L	2.10±0.59	2.12±0.42	0.880
Urine output; mL	740.25±139.17	925±99.17	0.286
Operation duration; h	4.38±1.10	3.75±1.77	0.093
Bleeding; mL	365±247.14	375±168.19	0.882
Primary SBP; mmHg	125.9±20.07	134.75±21.24	0.184
Primary DBP; mmHg	76.30±15.55	82.5±8.78	0.129
Primary HR, beats/min	85.10±19.53	87.5±30.12	0.767
MAP; mmHg	84±19.12	79±6.76	0.277

Abbreviation: L: Liter; mL: milliliter; h: Hour; mmHg: milliliter of mercury; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; MAP: Mean Arterial Pressure

Table 3. Hemodynimc parameters changes between groups via LIDCO monitoring system

Parameters		Mannitol Group N=20 Mean±SD	Hypertonic Sodium Group N=20 Mean±SD	*P*
SBP	**Before injection**	109.6±12.77	106±39.23	0.089
	20 mins after injection	104.4±26.16	118.25±28.15	0.115
	60 mins after injection	97.7±12.98	128.25±30.99	0.001
DBP	**Before injection**	66.2±11.11	70±12.5	0.316
	20 mins after injection	58.2±10.1	71±12.75	0.001
	60 mins after injection	55±9.29	78±18.68	0.001
MAP	**Before injection**	80.8±12.67	85.75±21.89	0.316
	20 mins after injection	74.3±14.86	88.5±17.35	0.001
	60 mins after injection	69.2±12.17	96.5±26.95	0.001
HR	**Before injection**	74.4±8.04	68.75±13.14	0.726
	20 mins after injection	69.9±8.18	72.75±13.5	0.425
	60 mins after injection	67.4±7.48	69.75±10.29	0.414
CO	**Before injection**	5.18±2.11	4.42±2.15	0.270

Cont. table 3

	20 mins after injection	5.47±1.68	4.7±1.24	0.108
	60 mins after injection	5.27±1.31	4.66±1.44	0.169
	Before injection	12.5±8.02	11.25±5.59	0.571
PPV	**20 mins after injection**	8.7±2.51	10±1.62	0.003
	60 mins after injection	11.4±4.47	15.75±4.12	0.001
	Before injection	1547.8±804.38	1829.25±517.79	0.196
SVR	**20 mins after injection**	1110.6±499.35	1473±287.09	0.008
	60 mins after injection	1005.8±286.5	1619±548.66	0.001
	Before injection	9.6±4.96	10.5±6.18	0.615
SVV	**20 mins after injection**	7±3.14	10.5±2.35	0.002
	60 mins after injection	9.2±3.45	11.25±3.72	0.001

Abbreviation: SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MAP: Mean Arterial Pressure; HR: Heart Rate; CO: Cardiac Output; CI: Cardiac Index; SPV: Systolic Pressure Variation; PPV: Pulse Pressure Variation; SVR: Systemic Vascular Resistance; SVV: SVV: Stroke Volume Variation

Discussion

In this study, we investigated the effect of mannitol and hypertonic sodium administration to reduce ICP on hemodynamic parameters in patients undergoing craniotomy procedures. According to our results, the two treatment methods gave similar results in terms of average fluid intake and urinary output (indicators of kidney function) as well as primary hemodynamic characteristics. Nevertheless, hemodynamic parameters evaluated with LiDCO monitoring differed significantly between the two groups.

In patients undergoing craniotomies, increased ICP is a common clinical condition, which may make surgical exposure and operative procedures more challenging and may lead to poor outcomes if it is associated with localized cerebral ischemia (15,16). Globally, more studies are being conducted on the optimal treatment for getting satisfactory brain relaxation and ICP during neurosurgical procedures (17).

There is a substantial body of evidence to suggest that hypertonic sodium is a valuable alternative to hyperosmotic treatments. Aside from its positive effects on brain relaxation, it is also as effective in treating increased intracranial pressure as mannitol (5). Nevertheless, some reports have indicated that many patients with elevated ICP do not respond to mannitol (18), and vigorous and repeated administration may result in excessive diuresis, electrolyte abnormalities, and secondary hypovolemia. However, the latter may result in hypovolemic conditions intraoperatively in patients undergoing neurosurgical procedures (19,20).

Here, compared to the hypertonic sodium group, the mannitol group experienced a decrease in systolic and diastolic blood pressure and MAP at 20 and 60 minutes following the reduction of systemic vascular resistance, stroke volume variation, and pulse pressure variation.

Patients undergoing craniotomies have consistently shown that hypertonic sodium significantly increases intraoperative serum sodium. However, data on the maximal serum osmolality indicated there was no significant difference in serum osmolality (5). The hemodynamic parameters such as MAP and CVP during surgery were similar in both groups treated with HS or mannitol (17). Patients treated with HS had significantly higher serum sodium than mannitol-treated patients without differences in serum osmolality between the groups (5).

Furthermore, both drugs maintained cardiac function quite similarly, but mannitol further reduced arterial and peripheral vascular resistance when used. Hence, mannitol can be preferred over hypertonic sodium for maintaining hemodynamic indicators and stabilizing cerebral and systemic blood flow. As a result of increasing the osmotic gradient across the blood-brain barrier, mannitol reduces ICP (21). In addition to reducing peripheral resistance of blood vessels, it also improves cardiac output by temporarily increasing preload and inotropic effects (22). However, systemic blood pressure tends to decrease as the intravascular volume decreases. Therefore, the administration of mannitol should be accompanied by evaluation and monitoring of intravascular volume.

It has been demonstrated that mannitol may be more effective than hypertonic sodium during craniotomy procedures in terms of reducing blood pressure monitored with LiDCO.

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