Original Article

Comparison of the effects of two different formulas of fluids in craniotomy patients

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Abstract

Background: Intraoperative fluid management of the patients who had undergone neurosurgery presents special challenges for the anesthesiologist. In this study, we aimed to compare the effects of two fluid combinations (half-normal + bicarbonate with saline + Ringer's lactate) on brain relaxation, and acid, base, and hemodynamic balance in patients undergoing elective craniotomy surgery.

Materials and Methods: This randomized double-blind controlled clinical trial study was done on 50 patients, of age 20–60 years, undergoing craniotomy in Alzahra Hospital in 2012. They were divided in two groups of 25 patients each. In the control group, after the patients received hypertonic saline, normal saline serum and Ringer's lactate was administered, and in the half-normal study group, 80 ml of sodium bicarbonate for every liter of it was added. Arterial blood gas (ABG) was taken before the last suture. Brain relaxation before dura opening was registered.

Results: There was no significant difference in heart rate changes ($P = 0.054$). No significant difference was observed in the mean arterial pressure between the two groups ($P = 0.99$). Changes in pH, HCO3, and BE were not significantly different ($P = 0.99$) between the two groups. Urine output in half-normal saline group was significantly higher than in normal saline group. The mean bleeding volume was higher in normal saline group, but was not significantly different ($P = 0.54$). The mean volume of injected blood was higher in half-normal group with a significant difference ($P = 0.54$). The injected blood volume mean in half-normal group was higher with no significant difference ($P = 0.55$). The mean of brain relaxation was not different ($P = 0.5$).

Conclusion: These two fluids did not show any significant differences in the studied variables in this research.

Key words: Acid–base hemodynamic parameters, brain relaxation, craniotomy, half-normal and bicarbonate with saline, Ringer's lactate

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INTRODUCTION

Fluid management and its method of usage in patients during surgery are particularly important for anesthesiologists. Patients undergoing neurosurgery should be managed by choosing the correct type and volume of intravascular fluid because of the risk of bleeding, use of diuretics, and the incidence of insipidus diabetes in them.[1]

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Considering fluid therapy in neurosurgery, emphasis is on two main points: Keeping the patients in normovolemia and prevention of plasma osmolality reduction.[2] Using solutions with lower osmolarity have relation with blood compensates, the amount of liquid needed of the fluid retention and the lost fluid decreased serum osmolarity. Chloride is the dominant negative ion in extracellular space and hyperchloremic metabolic acidosis results from excessive or improper disposal or release of it because of improper functioning of the kidney.[3] On the other hand, normal saline 9.0% is isotonic and isosmotic, but has more chloride compared to the soluble extracellular space; and when it is used in excess, it causes hyperchloremic metabolic acidosis.

Hyperchloremic metabolic acidosis is an important condition to be considered by anesthesiologists during operation with saline fluids used during surgery because hyperchloremic metabolic acidosis in these patients will cause hypoperfusion and tissue hypoxia. In this regard, it usually is tried to reach the highest tissue perfusion with acceptable amounts of fluids to keep the ideal cardiac output.[4]

The equation of Frank Starling explained the cause of fluid motion between the intravascular and extracellular spaces (in the lungs, intestines, and muscles), but the brain and spinal cord differ from body tissues because of the specific structure of the blood–brain barrier in relation to the intravascular space. Endothelial cells have particular structures (tight junctions) that protect the brain and spinal cord. This special barrier prevents the movement of not only protein but also sodium ions, chloride, and potassium between the intravascular space and extracellular space in the brain.[5]

Normal saline and Ringer's lactate are the most common fluids used during surgery. Normal saline has more osmolarity (308 mOsm/l) compared to plasma (295 mOsm/l), and its usage alone in an operation may cause hyperchloremic metabolic acidosis.[6] For this reason, some experts use Ringer's lactate (273 mOsm/l). This fluid has less osmolarity compared to plasma and if we use it in excess, it causes decrease of serum osmolarity and then cerebral edema.[2] Therefore it is advised to use it in high volume in neurological surgery and also to use Ringer's lactate and normal saline in the same concentrations.

The sodium concentration in hypertonic solutions ranges from 250 to 1200 mEq/l. High concentration of sodium in the solution to restore intravascular volume is known as a good solution. The difference in sodium concentration causes severe osmotic force for the movement of water from the intracellular space to the extracellular space. Reducing the amount of water may reduce edema when using this solution. This is very important and useful, especially for patients with prolonged intestinal surgery, burn patients, and patients with brain damage.[7]

In recent researches, it is shown that hypertonic saline, in comparison with mannitol, is a better option to reduce the intracranial pressure in patients whose hemodynamic condition may be at risk.[8] It is clear that hypersmolar solution causes cellular and intracellular fluid movement between the intravascular spaces into the central nervous system. Another effect of the mentioned solutions is to reduce the production of cerebrospinal fluid.[9]

Use of hypertonic saline solution increases the mean arterial pressure, reduces vascular resistance, decreases pulmonary vascular resistance, and decreases the need for blood transfusions.[10-12] It is shown that use of this fluid for revival reduces morbidity and mortality. During surgery, after induction and before starting the surgery, 5 ml/kg hypertonic saline is used for reducing the intracranial pressure, and this causes hyperchloremic metabolic acidosis. Sodium bicarbonate is one of the solutions that are used for treatment of metabolic acidosis. In this study, sodium bicarbonate solution along with half-normal saline (0.45%) was used for fluid retention and prevention of hyperchloremic metabolic acidosis caused by saline, as well as for compensating and maintaining the fluid osmolarity for fluid treatment.

MATERIALS AND METHODS

This study is a randomized double-blind controlled clinical trial that was done in 2012 in Alzahra (Al) educational treatment center. This project has been approved by the Ethical Committee of Isfahan University of Medical Sciences with the code 391234. The study population included 20–60-year-old patients who had undergone craniotomy.

Inclusion criteria included the following: Age 20–60 years, having undergone craniotomy surgery, II-ASA (American Society of Anesthesiologists) I grading patients, and the absence of any metabolic diseases, gastrointestinal, respiratory, and urinary tract diseases in the patients. Moreover, patients who developed severe complications during surgery and unusual events during anesthesia like heavy bleeding that needed massive blood transfusion were excluded.

Simple non-random sampling was used, and the samples were divided into two groups by random allocation. In this study, by using the sample volume assessment formula in order to study the correlation, considering a confidence level of 95% and a test power of 80%, it was estimated that a minimum of 25 patients per group was needed to compare two means [Figure 1].

The working method was as follows. On arrival at the operating room after assigning the patients to the respective exposure group (isotonic saline and Ringer's lactate) and (half-normal saline and bicarbonate), vital signs of the patients were recorded. Before starting the study, the situation of the research performance was described to the patients and their consent forms were obtained. Routine monitoring including pulse oximetry, electrocardiogram (ECG), noninvasive blood pressure (NIBP), core temperature, urinary output, contact capnography, and vital signs were recorded before induction. In this experiment, neither the participants nor the researchers knew which participants belonged to the control group, as opposed to the test group.

After injection of premedication with 100 μg fentanyl and 2 mg midazolam via intravenous anesthetic, 2 mg/kg propofol and 3 mg midazolam, as well as muscle relaxants, 0.2 mg/kg as neuromuscular relaxant, and 1.5 mg/kg lidocaine were administered about 2 min before intubation. After induction, arterial lines for anesthesia were placed immediately and then basic arterial blood gas (ABG) samples were taken. For all patients, before removal of the bone flap and opening the dura, and 10–15 min before extubation, 0.1 mg/kg morphine was injected for reducing the irritation and completing the analgesia intravenously. Then 5 ml/kg hypertonic saline was injected and ABG-dimensional sample was measured. Maintenance of anesthesia was achieved with propofol 50–150 μg/kg/min and remifentanil infusion 0.1 μg/kg/min and then cisatracurium 1–2 μg/kg/min. During surgery, $EtCO_2$ was maintained between 25 and 30 mmHg.

In the control group, after administering hypertonic saline, normal saline serum (0.9%) and Ringer's lactate were added, and in the half-normal saline studied group, 80 ml of sodium bicarbonate per liter was added and injected to compensate the fluid retention and loss. Two hours after starting the surgery, ABG was measured and the final ABG was taken before the last

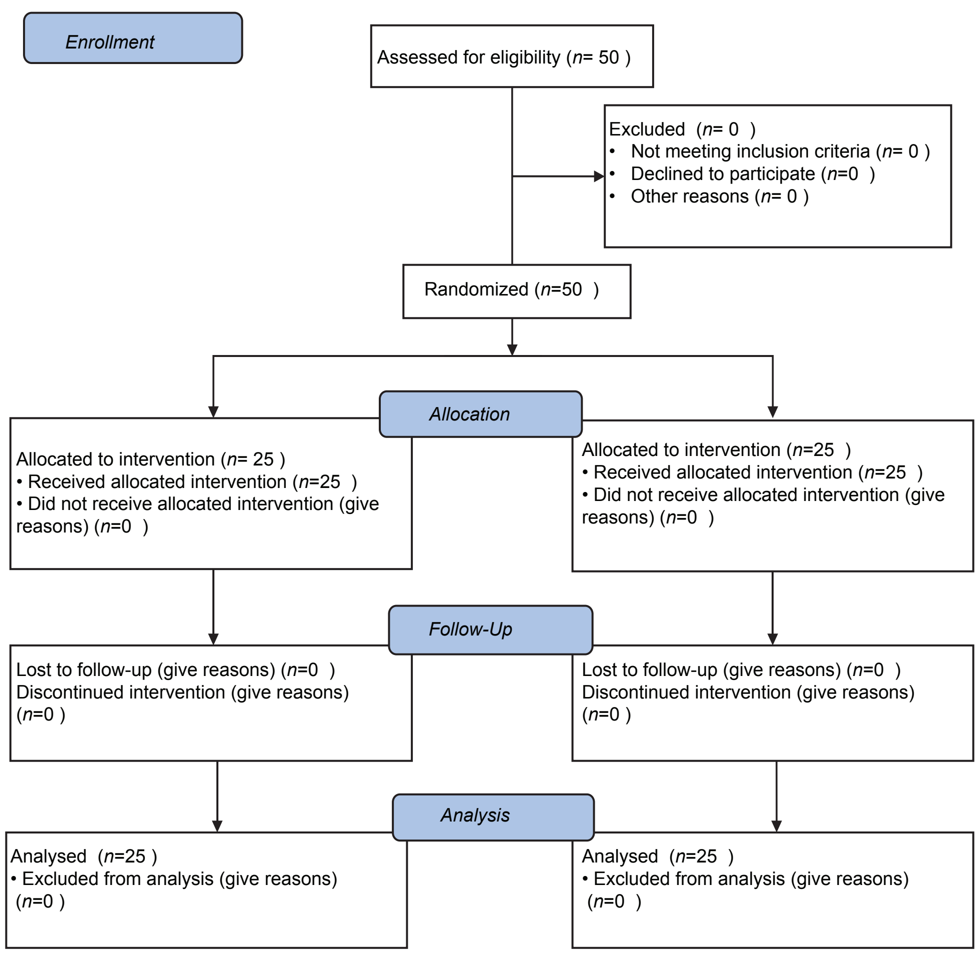

Figure 1: Study CONSORT flow chart

suture. Finally, the patient was extubated if he/she was in good condition. The amount of brain relaxation before dura opening was noted from the surgeon and recorded. Moreover, the surgeon was unaware of the type of fluid therapy.

During surgery, the mean arterial pressure was maintained between 80 and 90 mmHg. When there was a decrease in the mean arterial pressure from this value, 50 μg phenylephrine was injected. To reduce the high blood pressure, antihypertensive drugs were used.

Data of the study were entered into the computer and analyzed by SPSS software, version 2, and independent statistical *t*-tests as well as analysis of variance (ANOVA) with repeated observations were used for analysis.

RESULTS

In this study, 50 patients undergoing elective craniotomy were studied and 25 of them were treated with half-normal + sodium bicarbonate and the other 25 with normal saline + Ringer's lactate. In Table 1, the mean heart rate is shown from the start of the surgery till 220 min. According to this table, the heart rate changes in the normal saline group were lower, but according to ANOVA with repeated observations, there was no significant difference in changes in the heart rate ($P = 0.054$). Moreover, the mean arterial pressure decreased in both groups at 15 min. But subsequently, it increased in both groups in a balanced way; according to the test, no significant difference was observed between the two groups ($P = 0.99$). Mean changes in pH, HCO3, and Base Excess (BE) at the start of surgery, after drug injection, 2 h after the operation and at the end of the operation were measured in the two groups. The results obtained are shown in Table 2. According to this table, there was no significant difference in the two groups and the changes observed in these three markers were balanced between the two groups. ANOVA with repeated testing also showed no significant differences between the two groups ($P = 0.99$). Changes in these three markers were balanced between two groups. The mean level of each of these markers in the measured time periods was consistent in the two groups.

Table 1: Mean changes in heart rate and mean arterial pressure between the two groups

Time variable, min	Mean arterial blood pressure (mmHg)		Heart rate (bpm)	
	Case	Control	Case	Control
Zero	85±9.3	86±2.4	4.81±7.5	6.81±8.5
15	6.78±3	6.78±4.4	2.81±6.5	2.79±4.6
30	3.79±1.3	5.79±8.3	2.81±6.4	4.78±3.6
45	4.82±3.3	5.80±2.3	1.81±4	9.78±5.5
60	8.83±8.3	7.81±3	3.81±4	8.78±6
75	8.83±8.3	2.82±4	1.81±5	5.78±6.5
90	83±5.3	2.84±4	4.81±9.4	2.78±2.5
105	1.83±4.2	2.83±5.3	6.81±8.4	3.78±5.4
120	83±7.1	4.83±4	6.81±9.4	2.78±9.4
135	83±7.1	4.83±3.4	3.81±7.4	9.77±6.4
150	83±5.1	84±8.6	2.81±8.4	1.78±9.4
165	8.82±9.1	6.83±3.3	81±6.4	3.78±2.5
190	83±5.2	6.83±7.3	7.80±7.4	1.78±5.4
205	8.82±4.1	8.82±9.3	5.80±2.5	6.78±7.4
220	3.82±6.1	1.83±6.3	6.81±5.6	1.79±5
P		0.99		0.054

In Table 3, the volume of urine output, bleeding volume, the volume of liquid injected, and the amount of blood injected, and brain relaxation of the patients in the two groups are shown. According to this table, the average urine output in half-normal saline group was significantly higher than in half-normal group. Also, according to *t*-test, there was a significant difference between the two groups ($P = 0.024$). Moreover, the mean bleeding volume was higher in normal saline group; but according to the mentioned test, there was no significant difference between the two groups ($P = 0.54$). The mean of injected liquid volume in half-normal group was higher, but there was no significant difference between the two groups ($P = 0.54$). The mean of injected blood volume in half-normal group was higher, but no significant difference was found between the two groups ($P = 0.55$). As a result, the mean of brain relaxation does not differ between the two groups ($P = 0.5$).

DISCUSSION

The aim of this study was to compare the effects of two fluids (half-normal + bicarbonate with saline + Ringer's lactate) with regard to brain relaxation, and acid, base, and hemodynamic balance in patients undergoing elective craniotomy surgery. According to the obtained results, hemodynamic changes of patients, such as blood pressure, did not differ in the two groups during the procedure and after that. Use of intravenous fluids causes adverse changes in plasma volume and electrolytes of the patient and the anesthesiologist has the responsibility to prevent changes in plasma osmolarity and keep the patient in normovolemia. Therefore, use of half-normal liquid lowers the risk of creating the above complications and has no effect on hemodynamic and ABG indices. In our study, except urine output volume, no studied parameters in the group receiving half-normal and bicarbonate (case group) had detrimental changes; therefore, we can conclude that in craniotomy surgery, using fluids in the case group improved hemodynamic stability and caused better relaxation in the patient's brain and appropriate blood gas exchange in patients. Up

Table 2: The mean changes of pH, HCO3, and BE between the two groups

Time variable	BE		HCO3		pH	
	Case	Control	Case	Control	Case	Control
Zero	−25.2±31.1	−25.2±31.1	16.22±25.1	16.22±25.1	39.7±02.0	4.7±02.0
After injection	−24.4±9.1	−24.4±9.1	6.20±36.1	6.20±36.1	37.7±02.0	37.7±02.0
2 h after operation	−46.2±07.1	−46.2±07.1	22±94.0	22±94.0	4.7±02.0	4.7±02.0
At the end of operation	−27.3±5.1	−27.3±5.1	55.21±46.1	56.21±46.1	39.7±03.0	39.7±03.0
60 minutes in recovery		*P*=0.99		*P*=0.99		*P*=0.99

Table 3: The mean±SD of volume of urine output, bleeding volume, the volume of liquid injected, the amount of transfused blood, and relaxation of patients in both groups

Parameters	Control	Case	*P*
Urine output unit	804±2.128	728±1.100	0.024
Bleeding volume	760±5.146	736±3.130	0.54
Injected liquid volume	3988±614	4104±5.438	0.45
Transfused blood unit	44.0±65.0	56.0±77.0	0.55
Brain relaxation	2±65.0	12.2±6.0	0.5

SD: Standard deviation

to now, several studies have been carried out on this and most of them confirm that injection of half-normal liquid and bicarbonate in patients undergoing various surgical procedures is more useful. Morgani *et al.*, in a study on cardiopulmonary bypass surgery, used sodium bicarbonate–based crystalloid solution to prevent metabolic acidosis caused by fluids, and there is no remarkable study between hemodynamic parameters and blood gases.[13] Adolph *et al*. used sodium bicarbonate in comparison with normal saline 0.9% for preventing nephropathy caused by contrast during coronary angiography. In this study, 71 persons were injected with sodium bicarbonate and 74 persons were injected with 9.0% normal saline. No significant difference was observed between the two groups in terms of hemodynamic changes. The incidence of diabetic nephropathy in the sodium bicarbonate group was lower.[14] Vasheghani-Farahani *et al*. used sodium bicarbonate solution and isotonic saline in one group and isotonic saline in another group for preventing the risk of contrast-induced nephropathy induced by contrast agents in coronary artery angiography. Bicarbonate solution was prepared as 75 ml sodium bicarbonate 4.8% isotonic in 1 l of isotonic saline and similar results were obtained in this study.[15]

Navaneethan *et al*. did a case study about the use of sodium bicarbonate for the prevention of radiocontrast drug-induced nephropathy. This study was done according to search the Medline information in the years of 1966 till 2008 regarding EMBASE 2008. The content of this information is comparison of sodium bicarbonates with normal saline for preventing radiocontrast drug-induced nephropathy. The result is that use of sodium bicarbonate reduces the amount of contrast nephropathy.[16]

Normal saline and Ringer's lactate are the most common fluids used during surgery. Normal saline has more osmolarity (308 mOsm/l) compared to plasma (295 mOsm/l) and using it alone in surgery causes hyperchloremic metabolic acidosis.[6] Therefore, some experts use Ringer's lactate (273 mOsm/l). This liquid has less osmolarity compared to plasma and its use may cause decrease in serum osmolarity and thus result in brain edema.[2] The limitation of our study was the low sample size because of the lack of patients undergoing craniotomy. It is suggested that to do the same study with a larger sample size and by measuring the Cl^-.

CONCLUSION

Therefore, use of half-normal fluid and bicarbonate did not show any significant differences in osmolarity and brain edema, as well as improved brain relaxation in patients undergoing surgery, while it had no adverse effect on the patient's hemodynamic status. So, we suggest to do further studies with a larger sample size and by measuring the Cl – in the patients' serum to evaluate hyperchloremic metabolic acidosis.

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