Original Article

Effect of hypertonic saline on hypotension following induction of general anesthesia: A randomized controlled trial

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Abstract

Background: The aim of this study was to examine the effects of preoperatively administered i.v. hypertonic saline on hypotension following induction of general anesthesia.

Materials and Methods: Fifty-four patients who scheduled for elective surgery were randomly allocated to two groups of 27 patients who received hypertonic saline 5% (2.3 ml/kg) or received normal saline (13 ml/kg). Infusion of hypertonic saline was done half an hour before induction of anesthesia during 30 minutes. Anesthesia was conducted in a standard protocol for all patients. Age, sex, body mass index (BMI), systolic and diastolic blood pressure (SBP, DBP), heart rate (HR) and mean arterial pressure (MAP) were assessed in all patients.

Results: The mean age of patients was 36.68 ± 10.8 years. Forty percent of patients were male. The mean SBP at min 2 and min 5, mean of DBP at min 2, 5, and 15, mean of HR at all time points and mean of MAP at min 2 and 15 between groups were no significantly different ($P > 0.05$), but mean of SBP at min 10 and 15, mean of DBP at min 10, and mean of MAP at min 5 and 10 in hypertonic saline group was significantly more than the normal group ($P < 0.05$). Trend of SBP, DBP, HR and MAP between groups were not significantly different ($P > 0.05$).

Conclusions: Infusion of hypertonic saline 5% (2.3 mg/kg) before the general anesthesia led to a useful reduction in MAP and reduced heart rate, with no episodes of severe hypotension.

Key Words: Blood pressure, general anesthesia, hypertonic saline, hypotension, mean arterial pressure

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Received: 27.04.2014, **Accepted:** 18.06.2014

INTRODUCTION

General anesthesia is often preferred because of the discomfort and incomplete block that may accompany topical anesthesia as well as providing hypotensive anesthesia.[1] Hypotension is commonly encountered during anesthesia.[2,3] Drugs are the main causes of hypotension during anesthesia, such as intravenous induction agents or inhalational agents, regional anesthesia, hypovolemia due to bleeding and dehydration, and so on.[3,4] Hypotension and bradycardia following induction of general anesthesia may lead to insufficient organ perfusion such a degree as to result in irreversible ischemic damage.[4,5]

Fluid preloading which is usually well tolerated by healthy patients is commonly used for the prevention

Access this article online	
Quick Response Code:	Website: www.advbiores.net
	DOI: 10.4103/2277-9175.140088

How to cite this article: Kashefi P, Montazeri K, Hashemi ST. Effect of hypertonic saline on hypotension following induction of general anesthesia: A randomized controlled trial. Adv Biomed Res 2014;3:183.

of hypotension.[6,7] Hypertonic saline (HS) which refers to any saline solution with a concentration of sodium chloride greater than physiologic saline (0.9%) has been extensively investigated in animal models with regard to its efficacy in treating hemorrhagic hypotension. Also, it can be used as a continuous infusion or in bolus form to prevent and/or treat intracranial hypertension.[8] The infusion of a small volume of a hypertonic solution is an option to increase blood volume and to improve hemodynamics as well as organ blood flow under conditions of hemorrhagic shock and brain trauma.[9-11] Infusion of HS causes intravascular and interstitial fluid volume expansion due to its high osmolality, thus improving the hemodynamics; the suggested mechanisms were a direct myocardial stimulation with high cardiac output maintenance, increase of intravascular volume, and subsequent peripheral arterial vasodilatation, increased renal blood flow, reduced sympathetic tone.[5,12-14]

HS affected rapid and short lasting and before anesthesia could be a suitable fluid for preloading. Therefore, it could be a suitable fluid for preloading before spinal anesthesia.[15,16] Clinical use of HS solutions, despite further trials, remains inconsistent and few clinical guidelines exist, and only a few studies have been performed on the use of HS solution before anesthesia. So, this randomized, placebo-controlled, study was designed to assess the effect of preoperatively administered i.v. HS technique on hypotension following induction of general anesthesia.

MATERIALS AND METHODS

In this randomized trial 54 patients who scheduled for elective surgery were randomly allocated according to a list of random digits to two groups of 27 patients after obtaining an institutional study approval from the ethics committee of Isfahan University of Medical Sciences and written informed consent from all patients. Patients of any gender aged between 18 and 50 years old who scheduled to undergo elective surgery with American Society of Anesthesiologists classification I and II were eligible, if they had no history of chronic disease, no use of NSAIDs drugs up to 2 weeks before surgery, no uncontrolled systemic hypertension, no preoperative treatment for hypertension, no ischemic heart disease with clinical symptoms, no history use of opioids. Also, patients with hemodynamic instability (active bleeding, hypovolemia or loss of body fluid) were excluded from the study.

At the night before surgery all patients remain NPO for a minimum of 8 hours before scheduled elective surgery, and all patients were premedicated with 0.1 mg/kg diazepam. In the operating room, a 16-gauge cannula was inserted in a peripheral vein in the cubital fossa. Patients in group HS received 2.3 mg/kg of HS 5%. Also, patients in group normal saline (NS) received 13 mg/kg of NS. Infusion of HS was done half an hour before induction of anesthesia during 30 minutes.

Anesthesia was conducted using a total i.v. technique consisting of infusion of fentanyl (2 mcg/kg), sodium thiopental (5 mg/kg) and atracurium (0.5 mg/kg). Endotracheal intubation was performed with a single-lumen tube. Balanced anesthesia was maintained using with inhalation of isoflurane (1-2%) and morphine (0.1 mg/kg). Patients' lungs were mechanically ventilated with the same setting during ventilation (VT, 10 mL/kg and RR, 10 min). Ventilation was controlled to maintain end-tidal CO2 35 to 40 mmHg. The patients were monitored and observed using an electrocardiogram, non-invasive arterial blood pressure device, and pulse oximeter.

Age, sex, body mass index (BMI) as demographic and clinical parameters including systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate and mean arterial pressure (MAP) were assessed in all patients. SBP, DBP, heart rate (HR) and MAP were measured non-invasively before injection of study drugs and 2, 5, 10 and 15 minutes after injection of study drugs in all patients. Also, in each time points SBP, DBP, heart rate and MAP were measured three times, and the mean values used as final value.

The sample size was calculated using the comparison of means formula with two-sided log-rank test, $\alpha = 0.05$, and 80% power. All collected data were analyzed using SPSS-20 software. Variables were presented as mean ± SD, and number (percent). Age, BMI, duration of anesthesia, SBP, DBP, heart rate and MAP compared between study groups by the independent sample *t*-test. The Chi-square test was used to assess sex combination between groups, and also trend of SBP, DBP, heart rate and MAP at time points were compared between study groups by repeated amusements of ANOVA. Statistical significance was accepted at a $P < 0.05$.

RESULTS

Figure 1 shows the flowchart of study. As shown of 60 patients who assessed for eligibility, 6 patients did not enter to the study; 4 patients did not meet the inclusion criteria and 2 patients refused informed consent. Finally, 54 patients entered the study, randomly divided to the study group, completed the study and analyzed.

Total mean age of the studied patients was 36.68 ± 10.8 years old, the mean BMI of 26.12 ± 4.11. Of 54 studied patient 22 (40.1%) were males and 32 (59.9%) were females. In Table 1, baseline characteristics and clinical parameters in studies patients are compared to one another among the studied groups, based on the results of which there was no statistically significant difference in regard to these variables between the studied groups ($P > 0.05$).

Table 2 shows the comparison of clinical parameters between studied groups. As shown, SBP at time points (min 2,5,10 and 15) in the HS group was higher than the NS group. The mean of SBP at min 2 and 5 between groups was similar and no significant differences was observed ($P > 0.05$), but at min 10 and 15, the mean of SBP in the HS group was significantly more than the other group ($P < 0.05$). The differences in the mean of DBP at min 2, 5, and 15 were not statistically significant between groups ($P > 0.05$). But at min 10 mean of DBP in the HS group was significantly higher than the NS group ($P = 0.022$). The mean of HR at time points between groups were similar and no significant differences was observed ($P > 0.05$). The mean of MAP at min 2 and 15 between groups were not significantly different ($P > 0.05$), but at min 5 and 10, the mean of MAP in the HS group was significantly higher than the other group ($P < 0.05$). Trend of SBP, DBP, HR and MAP between groups were assessed by repeated amusements of ANOVA and results are reported in Figure 2. As shown trends of SBP, DBP, HR and MAP in both groups were similar and no significant differences were noted between groups ($P > 0.05$).

DISCUSSION

During induction of general anesthesia, patients with hypertension may exhibit significant increases in heart rate and blood pressure, though the agents used for this often cause hypotension.[17] A frequent complication of anesthesia is arterial hypotension after anesthetic induction.[18-20] In this randomized study we assessed the effect of preoperatively administered i.v. HS on hypotension following induction of general anesthesia in 54 scheduled elective surgeries. Based on our results, the HS group as case group received 2.3 mg/kg of HS 5% before the induction of anesthesia, show a steady and smooth reduction in MAP and reduced heart rate, with no episodes of severe hypotension. When the HS infusion was stopped, which can occur with hypotensive anesthesia techniques using arterial vasodilators, rebound hypertension was not observed in any patients in the HS group.

HS was chosen as it is a vasodilator with minimal myocardial depression and important advantages, such as, reduction in post resuscitation complications (renal

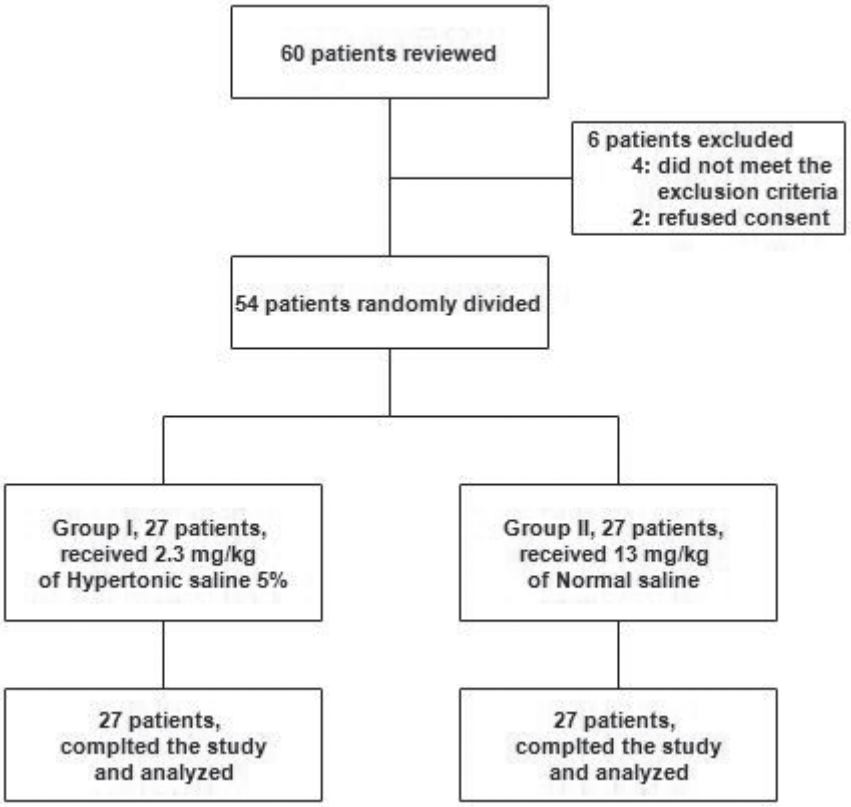

Figure 1: Study flowchart

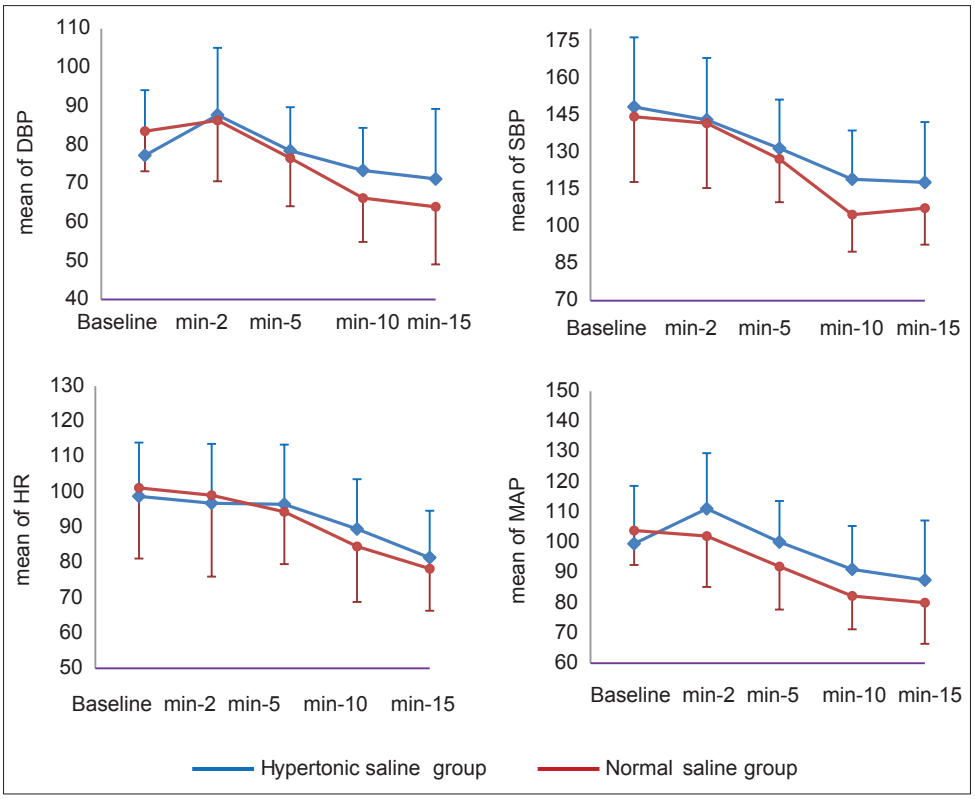

Figure 2: Compare of trend of studied variables in time points between the hypertonic saline group and normal saline group. SBP = Systolic blood pressure, DBP = Diastolic blood pressure, HR = Heart rate, MAP = Mean arterial pressure Statistical analyses were done using repeated amusements of ANOVA and no significant differences were noted between groups for trend of SBP, DBP, HR, and MAP at time points ($P > 0.05$)

Table 1: Baseline characteristics and clinical parameters in 54 studies patients by groups

Variables	Hypertonic saline group	Normal saline group	*P* value
Age (year)	36.59±11.37	36.77±10.02	0.95*
Body mass index	26.31±3.92	25.83±4.44	0.67*
Male/Female	10 (37)/170 (63)	12 (56)/15 (44)	0.78†
Duration of anesthesia (min)	59.49±5.61	62.10±4.38	0.062*
Systolic blood pressure (mmHg)	148.36±28.13	144.43±26.41	0.59*
Diastolic blood pressure (mmHg)	77.25±16.85	83.51±10.35	0.11*
Heart rate	98.76±15.23	101.16±20.03	0.62*
Mean arterial pressure	99.55±19.14	103.92±11.42	0.31*

Data expressed as mean±SD or number (percent), *P* values calculated by *independent sample *t*-test and †Chi-square test

Table 2: Comparison of clinical parameters in 54 patients at time points in regard to study groups

	Hypertonic saline group	Normal saline group	*P* value
SBP-min-2, (mmHg)	143.14±25.02	141.77±26.23	0.83
SBP-min-5, (mmHg)	131.62±19.73	127.31±17.45	0.34
SBP-min-10, (mmHg)	119.14±19.68	107.44±14.99	0.017
SBP-min-15, (mmHg)	117.85±24.40	104.81±14.78	0.021
DBP-min-2, (mmHg)	87.70±17.36	86.29±15.72	0.75
DBP-min-5, (mmHg)	78.48±11.22	76.55±12.43	0.55
DBP-min-10, (mmHg)	73.37±11	66.22±11.33	0.022
DBP-min-15, (mmHg)	71.18±18.06	63.96±14.87	0.11
HR-min-2, (b.p.m.)	96.81±16.81	99.07±23.06	0.68
HR-min-5, (b.p.m.)	96.51±16.91	94.37±14.82	0.62
HR-min-10, (b.p.m.)	89.51±14.11	84.55±15.74	0.81
HR-min-15, (b.p.m.)	81.37±13.29	78.25±11.94	0.37
MAP-min-2, (mmHg)	111.11±18.40	102.07±16.84	0.065
MAP-min-5, (mmHg)	100.11±13.58	92±14.23	0.037
MAP-min-10, (mmHg)	91.07±14.34	82.25±11.03	0.014
MAP-min-15, (mmHg)	87.51±19.73	80.03±13.59	0.11

Data expressed as mean±SD, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, MAP: Mean arterial pressure, *P* values calculated by the independent sample *t*-test

failure, coagulopathies), and acute respiratory distress syndrome, possibly by modulation of the systemic inflammatory response.[21-26] The effect of HS on cardiac function is offset by lowering of the peripheral vascular resistance, thus maintaining cardiac pump function.[27] Evidence showing that HSS may be an effective treatment for brain edema and elevated increased intracranial pressure after head trauma, and also the beneficial effects during hemorrhagic shock in the presence of IH associated with systemic hypotension have been noted.[28-31] The impact of HS on hypotension following induction of general anesthesia has not been well studied; however, in a randomized double-blind study by Jarvela *et al.*[8] the effect of

75 mg/ml (7.5%) HS on extracellular water volume and hematocrit in patients under spinal anesthesia was evaluated and results show that HS is an alternative for preloading before spinal anesthesia in situations where excess free water administration is not desired.

The development of neurologic complications due to osmotic demyelination syndrome is the most serious theoretical complication of HS therapy and also because of induces a rapid change in serum sodium concentration after infusion of HS some risks may include. Central pontine myelinolysis is a hazardous complication that is more likely to occur after rapid correction of chronic hyponatremia.[32] In a large cohort of emergency patients severe hypernatremia as a result of HS has been reported,[21] also in some clinical trials, after the rapid infusion of HS arterial hypotension was seen initially.[33-35] There is no clear evidence for any adverse effects with the use of bolus doses of intravenous HS even though the question of safety is a genuine clinical concern. In the present study after the use of bolus single doses of intravenous HS no adverse effects were noted in the two groups, so, there seems to be no contraindication for HS use.

The major limitations of the study were the small number of patients and performed as a single center trial and the single blind design, So more large-scale, multicenter prospective and randomized clinical studies are needed to elucidate the effect of HS on hypotension following induction of general anesthesia.

In conclusion, the results of this study showed that infusion of 2.3 mg/kg of HS 5% half an hour before the induction of anesthesia during 30 minutes led to a useful and smooth reduction in MAP and reduced heart rate, with no episodes of severe hypotension. However, further studies of this technique are warranted.

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Source of Support: Nil, **Conflict of Interest:** None declared.