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Clinical Study

Cardiovascular effects of hypertonic solution NaCl 7.5% infusion depended on administration duration

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ABSTRACT

Cardiovascular effects of hypertonic solution NaCl 7,5% infusion depended on administration duration.

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Hypertonic solutions have been widely used for several years for the treatment of hypovolemia, in the context of small volume resuscitation. The aim of the present study was to investigate the possible impact of total infusion time of NaCl 7.5% on its efficacy in normovolemic patients. One Hundred Twenty-Five patients were included in this study, in all of whom fluid and electrolyte homeostasis was restored (adequate substitution of preoperative fasting). After anaesthesia induction and initiation of mechanical ventilation 4ml/kg hypertonic solution NaCl 7.5% were administered to all patients. Patients were randomized into five groups of 25 patients each, depending on administration duration. Group A: total infusion time 6min, Group B: total infusion

time 8min, Group C: total infusion time 10min, Group D: total infusion time 20min and Group E: total infusion time 30min. Besides standard monitoring, Oesophageal Doppler Monitoring-ODM (ODM II Abbot Laboratories) was used. Recorded parameters included: Heart Rate-HR, Systolic Arterial Blood Pressure-SAP, Diastolic Arterial Blood Pressure-DAP, Mean Arterial Blood Pressure-MAP, Cardiac Output-CO, Stroke Volume-SV, Peak Velocity-PV, Mean Acceleration-MA, Flow Time corrected-FTc. Measurements were taken before administration (Phase 1), after completion of administration (Phase 2) and every 10min for 1hr (Phases 3-8). After completion of 4ml/kg NaCl 7.5% administration, the following recorded parameters CO, SV, PV, MA and FTc changed statistically significant compared to baseline values in Groups A, B and C. In Groups D and E there were no statistically significant changes in comparison with baseline values. Systemic arterial blood pressure and heart rate showed statistically significant alterations only in Groups A and B. According to our study results, it seems that hypertonic NaCl 7.5% efficacy decreases to zero when total infusion time exceeds 10min.
Keywords: Hypertonic Saline (7.5%), Hypertonic Solutions, Volume Expander, Fluid therapy

INTRODUCTION

According to *basic knowledge of physiology* up to 60% of a human adult body is composed by water, which is approximately 42L in a normal adult with body weight (BW) of 70kg. As far as distribution of total water in the body is concerned, 2/3 is intracellular fluid (ICF) and 1/3 extracellular fluid (ECF). ICF comprises around 40% of total BW. ECF subcategorizes as interstitial fluid volume (ISFV) in 75% and as plasma volume (PV) in 25%. Intracellular and extracellular compartments are separated by cell membranes, which are freely permeable to water but only relatively permeable to electrolytes. Osmotic pressure difference defines balance between those two compartments. Any osmotic pressure change will cause water to move from one compartment to the other. Intravascular and extravascular space is separated by endothelium, which is freely permeable to water, electrolytes and small molecules, while being less permeable under normal circumstances to big molecules (>35kD). Ion and molecule permeability differs between organs and is low in the brain whereas it is higher in other organs such as the liver[1-3].

Preoperative fasting along with specific factors such as bowel preparation for surgery could result in a hypovolemic or dehydrated state. Adequate perioperative fluid administration is necessary for achievement of hemodynamic stability, adequate oxygen transportation and preservation of cardiac and renal function. Intraoperative fluid management is a complex procedure which should start with assessment of intravascular volume status and also take into consideration and evaluate cardiac function, underlying pathology, fasting period, co-medications, anesthesia drugs, mechanical ventilation, patient positioning, type and duration of surgery, fluid and blood losses and finally should take into account all possible complications and the systemic inflammatory response. Defining an optimum intraoperative fluid therapy protocol (type and volume of fluids) remains an issue of scientific debate in the literature[1,4,5]. Depending on their osmolarity compared to plasma osmolarity (280-300mOsm/L), fluids are categorized in hypotonic (<280mOsm/L), isotonic (280-300mOsm/L) and hypertonic (>300mOsm/L)[6].

Hypertonic NaCl solutions (HS) have been widely used for several years have a higher osmolarity compared to plasma and their administration creates an osmotic gradient, which drives fluid from the intracellular to the extracellular compartment. HS have the ability to greatly expand the intravascular fluid volume multiple times more than the actual infused fluid volume[7,8]. Other HS effects besides intravascular fluid increase include: Visceral, renal and coronary vasodilation, muscle and skin vasoconstriction, myocardial contractility increase, intracranial pressure decrease and lung function improvement. Despite the fact that HS can cause a greater intravascular volume expansion than isotonic solutions, due to fluid movement form the extracellular to the intravascular compartment, this effect has a short duration.

There are different types of HS available, among which, NaCl 7.5% is the most commonly used one. NaCl 7.5% has an osmolarity of 2568mOsm/L (it contains 1284meq Na^+ and 1284meq Cl^-) and its administration is followed by intravascular volume expansion multiple times more than the actual infused fluid volume[9]. Recommended dosage of NaCl 7.5% is 4ml/kg and administration should be bolus, given over 4 to 5 min in order to achieve a positive impact. HS are usually not associated with side effects. Hypotension and relative tachycardia could occur sometimes but they both have short duration. Moreover, HS could cause sodium concentrations to rise up, but sodium levels usually return shortly to normal without need for specific treatment.

Most data on HS effects come from trauma literature and usage of HS in the trauma setting[10]. Rapid NaCl 7.5% administration for initial management of hemorrhagic shock has been widely used since several years now[11-15]. There are some clinical trials in the literature recording HS administration in cardiothoracic surgery, in abdominal aortic aneurysm open repair, in neurosurgical procedures and before performance of spinal anesthesia[16]. Despite the fact that there are trials in the literature concerning data about defining the optimum infused volume and osmolarity of HS, there isn't any study investigating the possible impact of the total infusion time on HS efficacy[17-19].

The aim of the present study was to investigate the possible impact of total infusion time of NaCl 7.5% on its efficacy in normovolemic patients.

MATERIALS AND METHODS

One Hundred Twenty-Five patients were included in this study, in all of whom fluid and electrolyte homeostasis was restored (adequate substitution of preoperative fasting). After anaesthesia induction and initiation of mechanical ventilation 4ml/kg hypertonic solution NaCl 7.5% were administered to all patients. Demographic data of study patients are depicted on Table 1 and did not differ between study groups in a statistically significant manner. Patients were randomized into five groups of 25 patients each, depending on administration duration. **Group A:** total infusion time 6min, **Group B:** total infusion time 8min, **Group C:** total infusion time 10min, **Group D:** total infusion time 20min and **Group E:** total infusion time 30min.

	Group A	Group B	Group C	Group D	Group E
Age (yrs)	65,7± 8,1	68,2 ±8,8	64,8± 10	66,7 ± 9,6	65,9 ±9
Body Weight (kg)	76,4 ± 7,8	74,5±12,2	77,3±9	71,1±8,2	75,2±9
ASA - PS	2,5 ± 0,58	2,9 ± 0,51	2,8 ± 0,45	2,8 ± 0,6	2,8 ± 0,62
Gender	♂= 16, ♀ = 9	♂=18, ♀= 7	♂=15, ♀ =10	♂=17 , ♀ = 8	♂=16, ♀ = 9

Table 1. Demographic data.

Hypertonic solution (HS) infusion was initiated and completed before surgical incision to exclude possible effect of any blood loss. After HS infusion completion, maintenance fluids therapy was provided by administration of Lactated Ringer (LR) infusion according to recommended rates.

Standard monitoring included 5 leads ECG, invasive arterial blood pressure and end tidal CO_2 monitoring and pulse oximerty. After anesthesia induction, Oesophageal Doppler Monitoring-ODM (ODM II Abbot Laboratories) was used for measurement of cardiac output,stroke volume and all other parameters according to ODM device properties. Recorded parameters included:

HR: Heart rate (b/min), SAP: Systolic arterial blood pressure (mmHg), DAP: Diastolic arterial blood pressure (mmHg), MAP: Mean arterial blood pressure (mmHg), CO: Cardiac output (L/min), SV: Stroke volume (ml), PV: Peak velocity (cm/sec), MA: Mean acceleration (m/sec^2), FTc: Flow time corrected (sec).

Measurements were taken:

before administration (Phase 1), after completion of administration (Phase 2) and every 10min for 1hr (Phases 3-8). The independent samples t Test and the repeated measures

ANOVA procedure were used for the statistical analysis

RESULTS

After completion of 4ml/kg NaCl 7.5% administration, the following recorded parameters CO, SV, PV, MA and FTc changed statistically significant compared to baseline values in Groups A, B and C. In Groups D and E there were no statistically significant changes in comparison with baseline values.

Comparison between groups revealed statistically significant differences.

Heart rate and systemic arterial blood pressure showed statistically significant alterations only in Groups A and B. In more detail, HR increased in Groups A and B after NaCl 7.5% administration.

This increase was statistically significant compared to baseline values only in Phase 2. There were no statistically significant HR alterations compared to baseline values in Groups C, D and E (Figure 1).

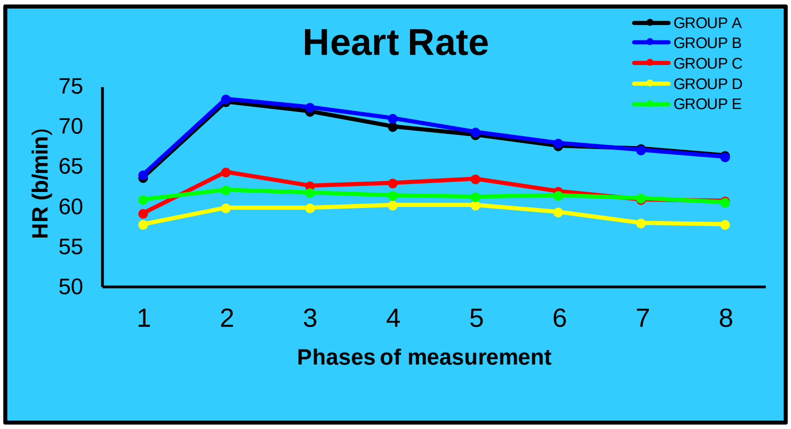

Figure 1. Heart Rate (HR) alterations.

Systolic arterial blood pressure (SAP), diastolic arterial blood pressure (DAP), and mean arterial blood pressure (MAP) decreased in Groups A and B after HS administration in Phase 2 (Figures 2, 3, 4)).

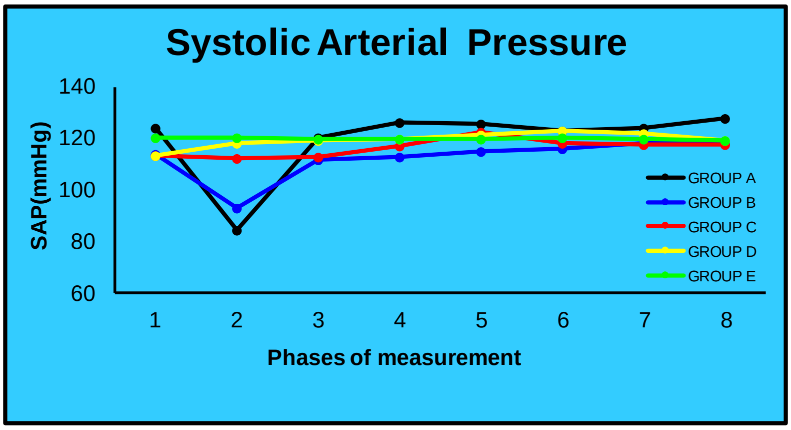

Figure 2. Systolic arterial blood pressure (SAP) alterations.

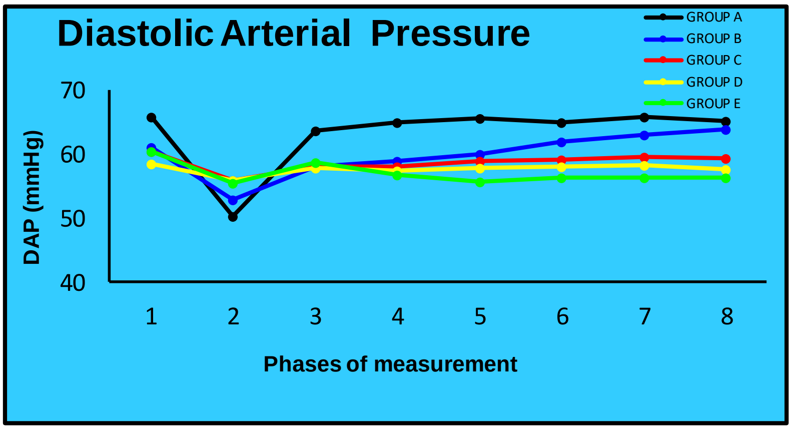

Figure 3. Diastolic arterial blood pressure (DAP) alterations.

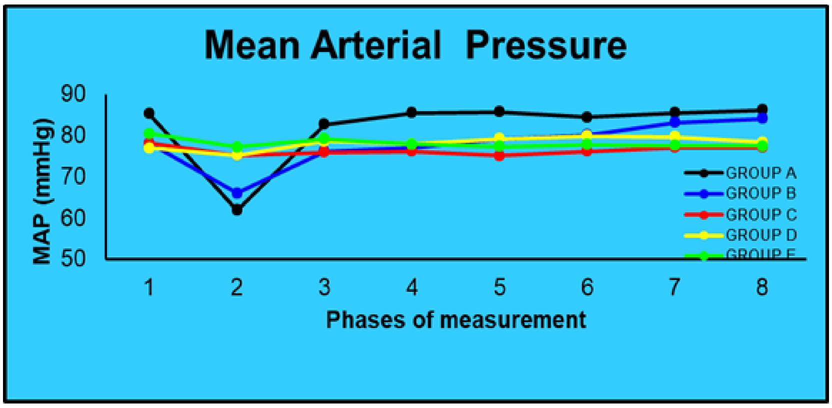

Figure 4. Mean arterial blood pressure (MAP) alterations.

Cardiac Output (CO) increased after HS administration in Groups A, B and C and didn't show any alterations in Groups D and E (Figure 5).

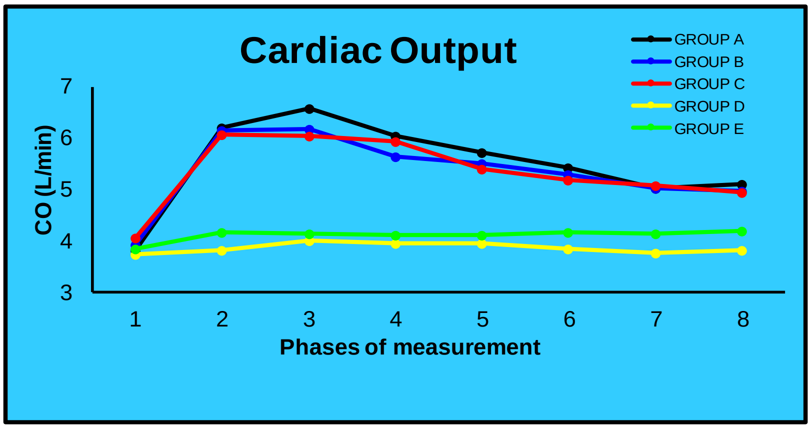

Figure 5. Cardiac Output (CO) alterations.

Stroke Volume (SV) showed similar to CO alterations in the study groups (Figure 6).

Peak Velocity (PV) of the descending aorta increased statistically significant after HS administration in Groups A, B and C. Those groups differed in a statistically significant manner compared to Groups D and E (Figure 7).

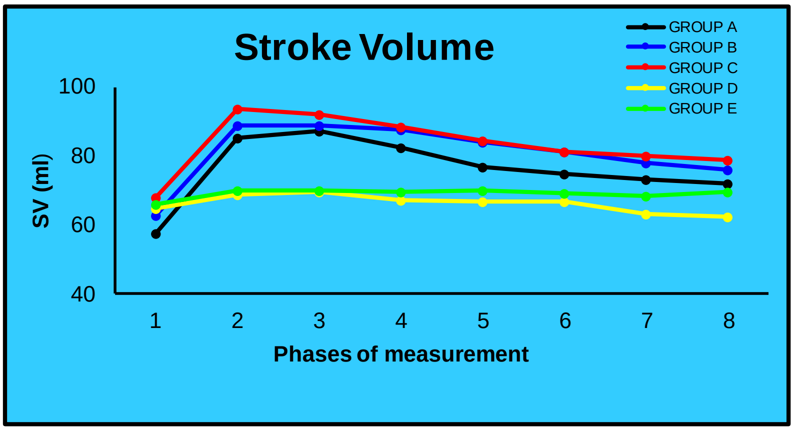

Figure 6. Stroke Volume (SV) alterations.

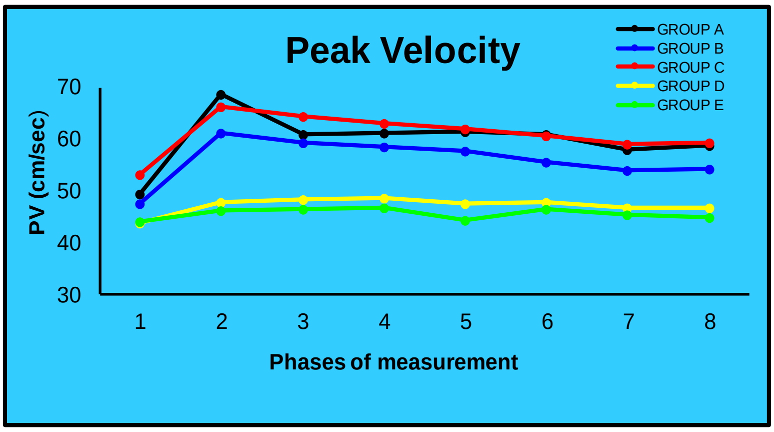

Figure 7. Peak Velocity (PV) alterations.

Mean acceleration (MA) increased after HS administration in Group A and remained elevated for the whole study. MA increased after HS administration in Groups B and C and remained elevated until Phase 6 and 8 respectively. In Groups D and E there were no statistically significant alterations compared to baseline values (Figure 8).

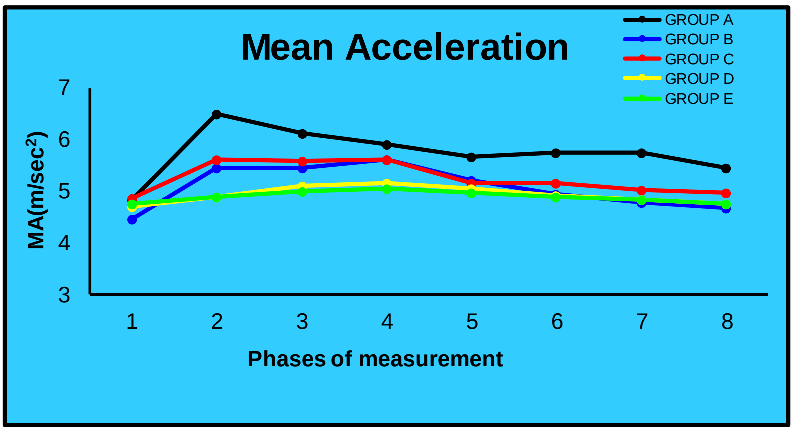

Figure 8. Mean acceleration (MA) alterations.

Flow time corrected (FTc) increased in Groups A, B and C. However, FTc remained elevated for the whole study period only in Group A (Figure 9).

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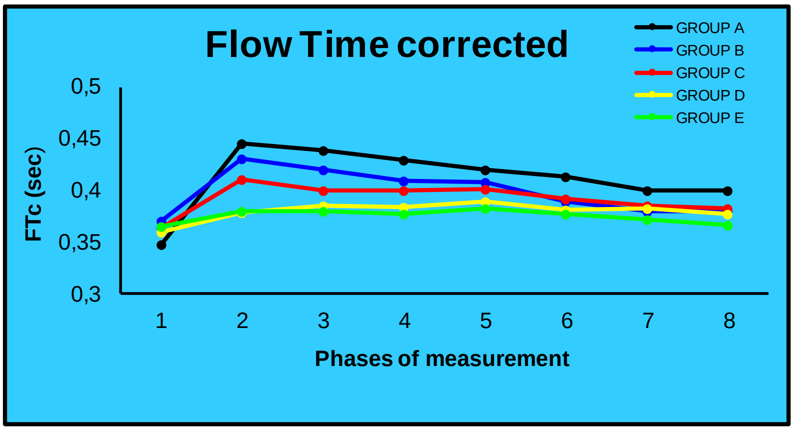

Figure 9. Flow time corrected (FTc) alterations.

DISCUSSION

Hypertonic solution (HS) NaCl 7.5% has an osmolarity of 2568mOsm/L and its infusion results in a temporary expansion of the intravascular volume, which is multiple times more than the actual infused fluid volume[12]. According to available literature data, it seems that HS administration causes an immediate CO increase[15] and its efficacy regarding intravascular volume expansion is greater in hypovolemic patients[20]. HS administration increases CO, HR and myocardial contractility, decreases peripheral vascular resistance and moreover results in improvement of microcirculation by decreasing endothelium edema[21]. Recommended dosage is 4ml/kg and the infusion should be given over 4 to 6min[21-24]. Those specific characteristics define HS as resuscitation fluids.

In this study, NaCl 7.5% was administered in normovolemic patients under general anaesthesia and mechanical ventilation. Duration of administration differed between study groups and total infusion time varied from 6 min (Group A) to 30 min (Group E).

Our results showed that CO and SV increased only in Groups A,B and C. It seems that longer total infusion times have a negative impact on HS efficacy since 20min and 30min (Groups D and E respectively) resulted in non-statistically significant alterations compared to baseline. CO is a very significant parameter, which reflects the efficacy of our treatment interventions such as fluids or vasoactive drugs administration[25]. Measurement of CO is an integral part of any study protocol investigating the clinical impact of fluids administration.

PV and MA changed statistically significant only in Groups A, B and C and FTc showed similar alterations. PV and MA are indicators of left ventricle contractility, whereas FTc could be used as an indicator of hypovolemia[26-29]. Improvement of contractility is mainly attributed to preload increase and afterload decrease and less to the positive inotropic effects of HS[30-32]. FTc alterations are attributed to the rapid increase of the intravascular volume after

HS NaCl 7.5% administration.

Rapid HS administration could cause hypotension, which is attributed to systemic vascular resistance decrease[33-35]. In general, HS associated hypotension has a short duration and is well tolerated. However, it could cause problems in patients already suffering from impaired organ function[36].

According to our results, it seems that administration of 4ml/kg NaCl 7.5% in normovolemic patients increases intravascular volume and improves CO, provided that infusion is fast. Those effects are immediate and remain similar for the whole study period namely for 60min, although they gradually fade over time. Moreover, one could say that total infusion time of 10min might be the safest choice since it is associated with the occurrence of less hypotension compared to 6min and 8min. However, HS efficacy seems to be greater with shorter infusion times. Therefore, total infusion time of HS should be a clinical choice depending on the individual needs of the patient, its medical background and the specific features and characteristics of each clinical setting. However, total infusion time of HS should not exceed 10min to ensure efficacy.

Our results are in accordance with other literature studies documenting the short term efficacy of HS. Based on results of experimental studies it is known that HS administration causes CO increase and circulation improvement[10.] In our study, total infusion time had an impact on HS effects in all recorded parameters. Despite the fact that there is lack of corresponding documentation in the literature, recommended dosage is 4ml/kg and infusion should be fast[22,23]. Our study concluded that both the positive (CO, SV, PV, MA, FTc increase) and the negative (SAP, DAP, MAP decrease) effects of HS correlate with total infusion time.

Despite occurrence of transient hypotension, NaCl 7,5% is considered safe and efficient[37,38] and can be used in clinical settings, where there is an absolute indication for rapid intravascular volume increase[16,22,37].

Limitations of the present study include the fact that NaCl 7.5% was administered in patients in whom all preoperative fasting deficits were already adequately restored and were therefore theoretically considered to be normovolemic. Moreover, patients were under general anesthesia and mechanical ventilation. It is rational to assume that HS hemodynamic effects recorded in our study will be greater in hypovolemic, spontaneously breathing patients. If there were more groups included in the study protocol, we might have been able to record and document HS effects not only after total infusion time of 10min but possibly also after total infusion time of 15min.

Based on the monitoring used according to our protocol, it was not possible to study in depth right ventricular function and pulmonary circulation and its performance after acute volume overload. Patients with impaired heart function could show a different response to rapid intravascular volume increase, while mechanical ventilation attenuates any negative effects on the left ventricle.

CONCLUSION

Hypertonic solution (HS) NaCl 7.5% administration effects (whether positive or negative) decrease to zero, when total infusion time exceeds 10min. HS NaCl 7.5% total infusion time should not be more than 10min, when NaCl 7.5% is infused for intravascular volume expansion.

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