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Case reports

Hypertonic Saline Resuscitation in acute intraoperative hemorrhage:Case Series presentation

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ABSTRACT

Hypertonic saline resuscitation in acute intraoperative hemorrhage:Case Series presentation.

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Four patients (♂/♀: 1/3), aged 51, 52, 50 and 58 years old, who underwent general surgery procedures, suffered acute major blood loss intraoperatively. For the management of acute hemorrhage, 4ml/kg NaCl 7.5% were administered in each patient at the fastest possible rate through the existing intravenous line. Both standard monitoring and Oesophageal Doppler Monitoring (ODM) were applied and heart rate (HR), mean arterial pressure (BPmean), stroke volume (SV), peak velocity (PV), mean acceleration (MA) and corrected flow time (FTc) were

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recorded at six different phases, before blood loss (Phase 1), before and after completion of NaCl 7.5% administration (Phases 2 & 3), 10min and 20min after NaCl 7.5% administration (Phases 4 and 5) and at the end of the surgical procedure (Phase 6). After completion of NaCl 7.5% infusion, all patients received Lactated Ringers, vasoactive drugs and packed red blood cells (pRBCs). All recorded parameters showed significant deterioration after blood loss, they improved after NaCl 7.5% infusion and remained stable until the end of the surgery. Infusion of NaCl 7.5% was completed in 5min, 4.2min, 6min and 5.3min respectively. Lowest Hb values were 7.6g/dL, 4g/dL, 5g/dL and 6.6g/dL and the corresponding patients received 3, 5, 4 and 3 units pRBCs respectively. Bleeding was surgically controlled, noradrenaline was discontinued before the end of the surgery and all patients were transferred intubated to the Intensive Care Unit (ICU) after the end of the surgery. Three of them were extubated on the same day and the fourth patient on the next. During their ICU stay patients were hemodynamically stable and were discharged from the ICU on the 1st postoperative day. Outcome was overall positive and all patients were discharged home at a good physical status. Based on our results, it seems that hemodynamic instability can be treated with safety by NaCl 7.5% infusion, provided that bleeding can be managed surgically.

Keywords: Hypertonic saline solutions, acute blood loss, Oesophageal Doppler Monitoring

INTRODUCTION

Perioperative fluid administration is the cornerstone for the establishment of hemodynamic stability and homeostasis during the perioperative period and is correlated with the outcome[1].
Since several years the type and volume of the administered fluid remains a matter of scientific debate[2,3]. Isotonic crystalloids, normal saline and lactated Ringer (RL) are the most common used solutions for the restoration of the intravascular fluid volume during the perioperative period[4].
Hypertonic saline solutions (HSS) are crystalloids which contain high NaCl[5].
The main mechanism of action of hypertonic salt solutions is that they create an excessive osmotic gradient which drives fluid from the interstitial (mainly the intracellular) space into the intravascular space. This action has an immediate clinical impact after fluid administration[6,7].
The efficiency of HSS in the acute treatment of major blood loss has been documented in several experimental and clinical studies. In an experimental study in 1919, Penfiled et al restored low blood pressure, which was induced by acute blood loss, by administration of hypertonic NaCl 1.8%. In an another experimental study in 1980, Velasco et al restored immediately both cardiac output and blood pressure after administration of 4ml/kg BW NaCl 7.5%[8,9]. This study of Velasco et al has been the catalytic agent into promoting further scientific re-

search in this field, investigating the clinical impact and usefulness of HSS in the management of hemorrhagic shock[10-12]. All those studies, both clinical and experimental, proved that administration of a small amount of HSS can restore hemodynamics after major blood loss.

Nakayama suggested in 1984 to use the term small volume resuscitation because the administered amount of fluid is lower to the blood volume loss and this term has been used ever since[13,14].

Hypertonic NaCl 7,5% contains 1284meq Na^+ and 1284meqCl^- and its osmolarity is 2568 mOsm /l[15]. Rapid intravenous administration creates an osmotic gradient due to the excessive increase of plasma sodium concentration. This osmotic shift drives fluid into the intravascular space and results in a transient but significant increase of the intravascular volume[15,16]. On average, 1ml of HSS raises the intravascular volume by 2-4ml, whereas isotonic crystalloids result to an intravascular volume increase, which is no more than 1/3 of the infused fluid volume[17-21].

It has been calculated that approximately a fourfold volume of fluids (depending on the administration rate) should be infused for the restoration of intravascular volume after acute blood loss. On the contrary, intravascular volume can be restored quickly and efficiently by small volume infusion of hypertonic solutions. This is the concept of small volume resuscitation[22,23].

Hypertonic resuscitation restores blood pressure and improves cardiac output. Those effects are not only attributed to the expansion of the intravascular volume, but also to circulation enhancement due to vasodilation and to direct positive inotropic effects[6,24]. Moreover, it improves microcirculation by causing endothelial edema decrease[25] and has anti-inflammatory properties[26].

The effect of HSS on the circulatory system is of limited duration due to osmotic equilibrium between the intravascular and interstitial fluid compartment. Several researchers have recommended the use of colloids in an effort to postpone its effect [22,27,28]. The advantages and disadvantages of HSS solutions are presented in table 1[5,21,29].

Table 1. Advantages and disadvantages of HSS solutions.

Advantages	Disadvantages
• Rapid increase of the intravascular volume • Intracranial pressure decrease • Endothelial edema decrease • Low risk of fluid volume overload • Low incidence of adverse effects	• Positive effects last for a short time period • Positive clinical impact has not yet been proven

Several methods have been used for intravascular volume assessment and prediction of fluid responsiveness, some of which are difficult to be applied in the operation theatre[30,31].

Static parameters, such as Central Venous Pressure (CVP), Pulmonary Artery Occlusion Pressure (PAOP) Right Ventricular End Diastolic Volume (RVEDV), have not been proven to be reliable for intravascular volume assessment[32]. However, dynamic parameters, such as stroke volume, pulse pressure, diameter of inferior vena cava, which correlate with intrathoracic pressure during spontaneous breathing and under mechanical ventilation have been used for this cause[32-34].

Since 1870, when Adolf Fick first described a method for the measurement of cardiac output (CO), several other methods have been discovered[35,36].

Development of non-invasive methods for CO determination allowed continuous intraoperative CO monitoring[37].

CO is the main determinant of oxygen transport to the tissues. However, standard normal values do not exist. Nevertheless, low values are associated with poor outcome. In clinical practice, there is still no agreement in which CO alterations should be considered as clinically important[38].

One patient might have a “normal” CO value and still be suffering from circulatory shock because CO at that specific time phase can meet metabolic needs of the body. In most operations, CO monitoring is not considered as standard monitoring.CO increase following fluid administration is a reliable indicator of fluid responsiveness[39].

Oesophageal Doppler Monitor (ODM) is a noninvasive monitoring device, which is designed to measure blood flow by using Doppler technology in the descending thoracic aorta and to calculate stroke volume and CO by a specific algorithm[40-42].

Altogether, ODM can measure or calculate following parameters, Stroke Volume (SV), Cardiac Output (CO), Peak Velocity in the descending thoracic aorta (PV), Flow Time Corrected (FTc) and Mean Acceleration (MA)[40,41].

Therefore, ODM provides a good estimate of preload, afterload and left ventricular contractility[41]. Namely, FTc is inversely related to afterload and directly to preload. Low FTc values could be an indicator of hypovolemia and/or increase of resistance/afterload increase. PV is an indicator of contractility and is inversely related to afterload. Low PV values may be caused by decreased contractility or increased resistance/afterload. MA is directly correlated to contractility[40,43,44].

Nevertheless, none of those parameters alone is specific to draw any conclusions regarding preload, afterload or contractility. In clinical practice, alterations of one parameter might cause compensatory alterations of another parameter. Combination of different parameters and their assessment in relation to the result of treatment interventions might provide a complete picture of patient's hemodynamic status at a certain time point.

MATERIAL AND METHODS

Four patients (♂/♀: 1/3), aged 51, 52, 50 and 58 years old, ASA-PS: 2-3, who underwent general surgery procedures, suffered acute major blood loss intraoperatively. For the management of acute hemorrhage, 4ml/kg NaCl 7.5% were administered in each patient at the fastest possible rate through the existing intravenous line.

After completion of NaCl 7.5% infusion, all patients received Lactated Ringers (RL), vasoactive drugs and packed red blood cells (pRBCs).

Applied monitoring consisted of ECG, direct arterial pressure monitoring, capnography, pulse oxymetry and Oesophageal Doppler Monitoring (ODM) (ODM II, Abbot Laboratories) and following parameters were recorded:

- **HR:** Heart Rate (b/min),
- **SAPs:** Systemic Arterial Pressure, systolic (mmHg),
- **SAPd:** Systemic Arterial Pressure, diastolic (mmHg),
- **SAPm:** Systemic Arterial Pressure, mean (mmHg),
- **CO:** Cardiac output (L/mim),
- **SV:** Stroke Volume (ml),
- **PV:** Peak Velocity (cm/sec),
- **MA:** Mean Acceleration (m/sec^2),
- **FTc:** Flow time corrected(s).

Study parameters were recorded at six different phases:

- Before blood loss **(Phase 1)**,
- Before and After completion of NaCl 7.5% administration **(Phases 2 & 3)**,
- 10min and 20min after NaCl 7.5% administration **(Phases 4 and 5),**
- End of the surgical procedure **(Phase 6)**

All patients were transferred intubated to the Intensive Care Unit (ICU) after the end of the surgery.

RESULTS

All recorded parameters showed significant deterioration after blood loss. At the time of hemorrhage patients were euvolemic/normovolemic, since fluids had already been administered to them in order to compensate preoperative fasting and any negative hemodynamic effects of anesthesia induction and mechanical ventilation.

The cause of hemodynamic collapse was clinically obvious without any doubt and it was managed immediately.

All patients received 4ml/kg NaCl 7,5% and its infusion was completed in 5min, 4.2min, 6min and 5.3min respectively.

Alterations of recorded parameters are depicted on Table 2.

Table 2. Alterations of recorded parameters at the six study phases.

Study phases	1	2	3	4	5	6
HR (b/min)	70 62 72 75	112 95 92 120	86 88 85 83	75 80 83 78	80 82 78 80	75 80 76 75
BP(mean) (mmHg)	99 100 90 95	37 45 43 40	65 70 65 70	100 96 95 85	105 100 96 95	103 102 98 97
SV (ml)	68 70 65 75	18 31 23 20	47 54 77 70	99 78 88 90	75 70 82 85	80 68 81 80
CO (L/min)	4,8 4,3 4,7 5,3	2,1 2,8 2,1 2,4	4,1 4,7 6,5 5,9	7,4 4,7 6,5 5,9	6 5,7 6,4 6,8	6 5,4 6,2 6
PV (cm/sec)	60 65,7 56 70	31,3 38.9 35 35	65 65 64 65	74 66 71 75	73 62 76 76	62 60 73 73
FTc (msec)	0,391 0,382 0,365 0,410	0,268 0,265 0,23 0,220	0,368 0,303 0,406 0,305	0,361 0,320 0,401 0,402	0,349 0,315 0,387 0.370	0,360 0,310 0,376 0,386
MA (cm/sec^2)	6,5 6,2 5,7 5,4	3,8 4,24 4,5 3,5	7,8 6,2 7,5 7,4	7,34 6,1 7,2 6,9	7,4 5,8 6,5 6,5	7,5 5,5 6,2 6,8

Heart rate (HR), mean arterial pressure (SAPm), stroke volume (SV), cardiac output (CO), peak velocity (PV),flow time corrected (FTc), and mean acceleration (MA).

HR increased immediately after blood loss, it was restored after NaCl 7.5% infusion and remained stable until the end of the surgery (Fig. 1).

Systemic arterial pressure (systolic, diastolic and mean) decreased dramatically after blood loss, it improved immediately after NaCl 7.5% infusion and remained at acceptable levels until the end of the surgery (Fig 1).

Stroke Volume, Cardiac Output, Peak Velocity, Mean Acceleration and Flow Time corrected decreased after blood loss and increased after NaCl 7.5% infusion (Fig. 2, 3 & 4). All measured parameters remained increased until the end of the study.

Figure 1. HR and mean BP alterations at the six study phases.

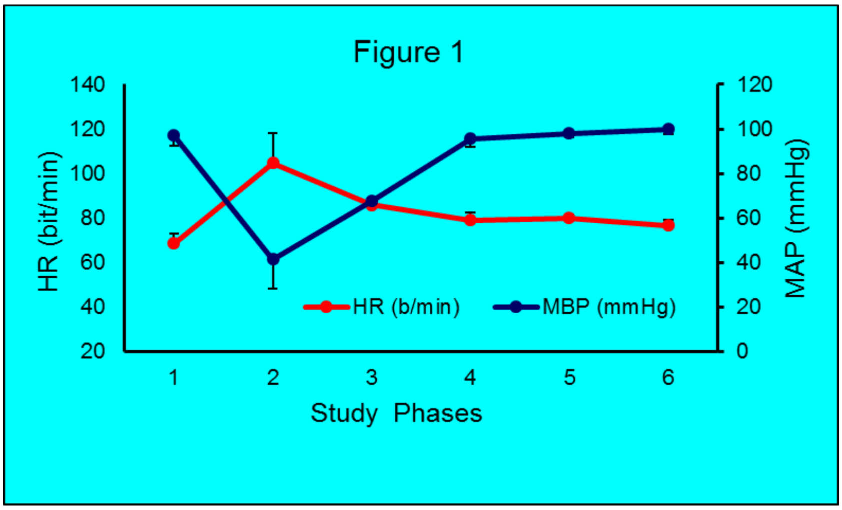


Figure 2. SV and CO alterations at the six study phases

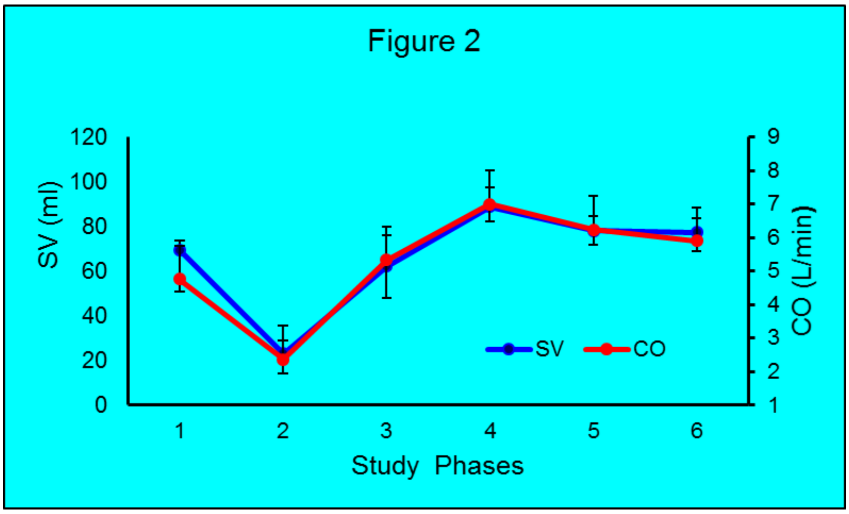


Figure 3. PV and MA alterations at the six study phases

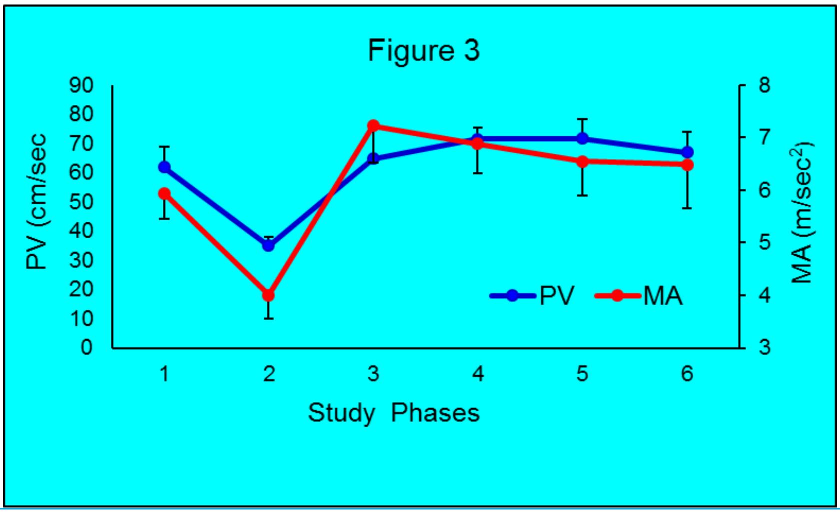
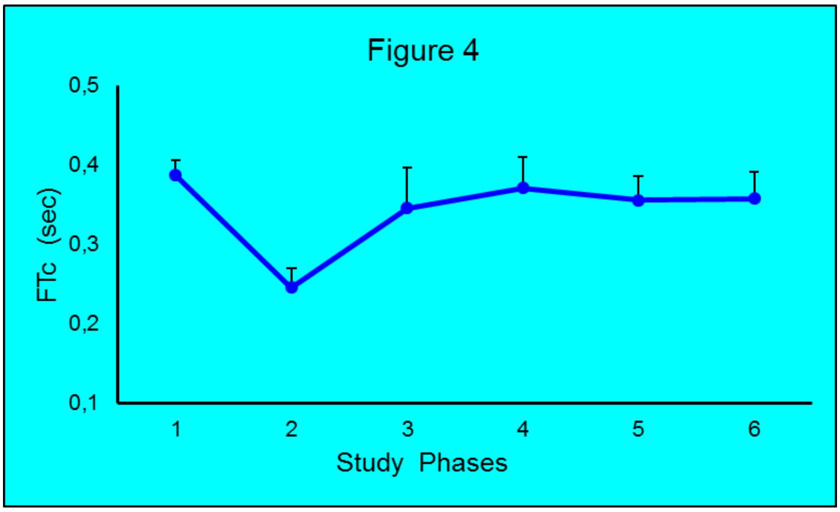


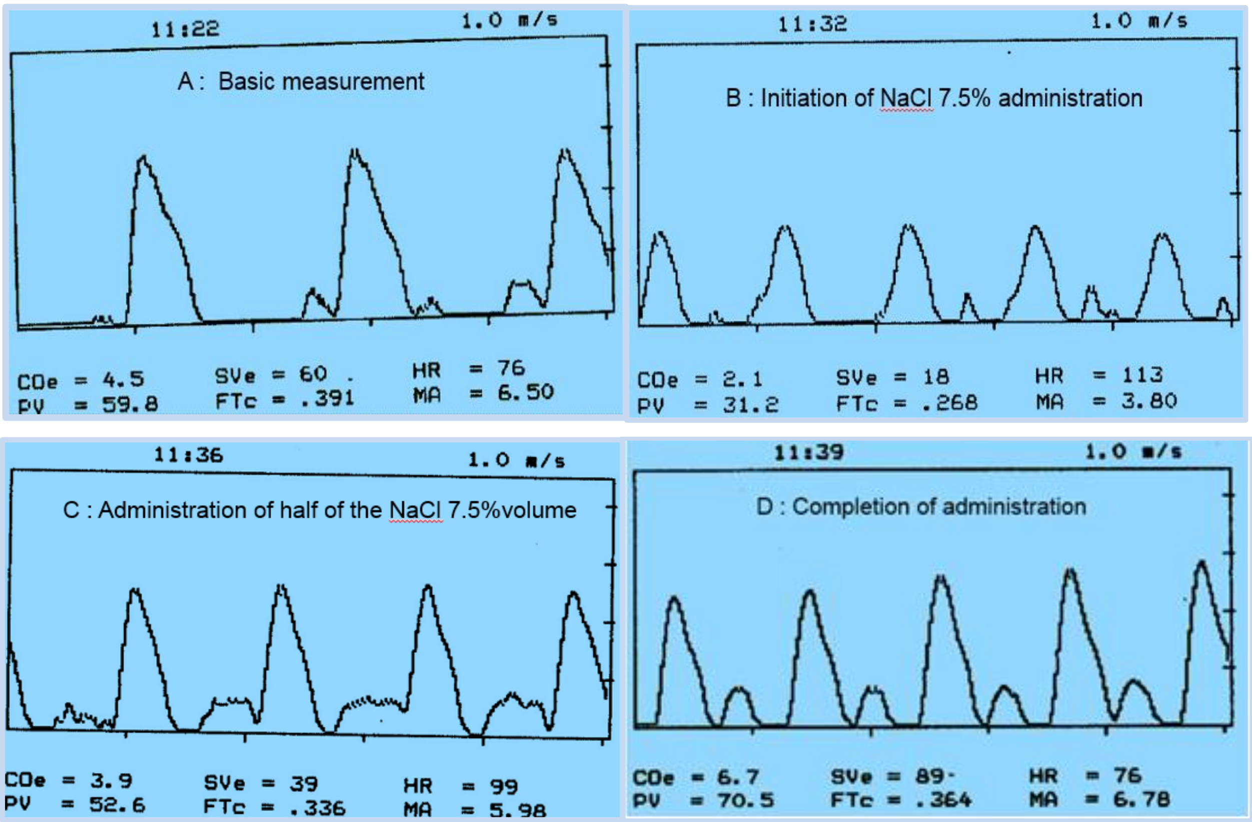
Figure 4. FTc alterations at the six study phases.

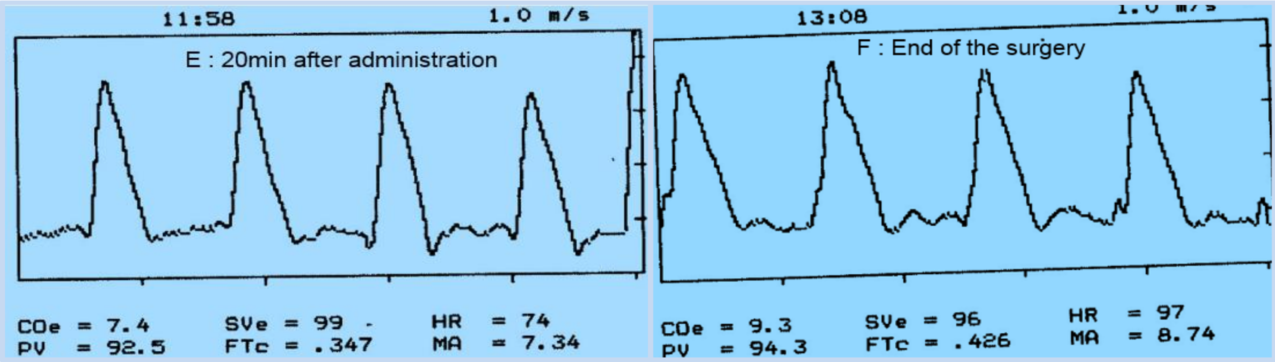


Measured parameters significantly improved before completion of NaCl 7.5% infusion (Image 1).

BIS changes in response to acute blood loss were characteristic. BIS decreased immediately after blood loss and remained decreased for a prolonged time period, whereas the hemodynamic status had improved (Image 2).

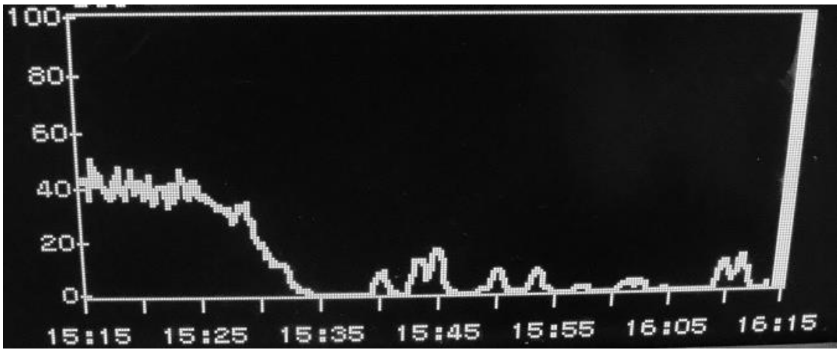
Image 1. The velocity-time Doppler waveform of one of the patients.





***A**: Basic measurement, **B:** Initiation of NaCl 7.5% administration, **C**: Administration of half of the NaCl 7.5%volume, **D:** Completion of administration, **E:** 20min after administration, **F**: End of the surgery.*

Image 2. BIS alterations in one patient at the six study phases.



Lowest intraoperative Hb values were 7.6g/dL, 4g/dL, 5g/dL and 6.6g/dL and the corresponding patients received 3, 5, 4 and 3 pRBCs units respectively.In addition to HSS, patients also received 3.5L, 3.3L, 4.5L and 5.1L RL. Diuresis remained at an acceptable level throughout the operation.

Bleeding was surgically controlled, operation was completed uneventfully (in one of the 4 cases there was a change of surgical plan) and vasoactive drugs were discontinued before the end of the surgery.

During ICU stay patients were hemodynamiccally stable without any need for vasoactive medication, three of them were extubated a few hours after the end of the surgery and one of them on the next day. All 4 patients were discharged to a ward on the 1st postoperative day, and overall outcome was positive. All of them were discharged home at a good physical status.

DISCUSSION

Maintenance of hemodynamic stability is one of the most important and challenging aspects of anesthesia since hypotension is associated with injury of organs such as kidneys and heart[45-47]. Intraoperative hypotension is common and its actual occurrence mainly depends on its definition since there is no universal definition. In a systematic review of the literature, Bijker et al identified 140 definitions for hypotension in 130 anesthesia articles[48].

Acute hemodynamic collapse is not as common as hypotension and can be attributed to several

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causes, which are not always obvious despite the applied monitoring. The most frequent cause is acute major bleeding. Its occurrence may lead to tissue hypoperfusion and increases the risk of sepsis and multimodal organ failure[49].

In the present study we present four patients, who suffered acute major blood loss intraoperatively, which led to hemodynamic collapse. For their management 4ml/kg NaCl 7.5% were administered in each patient and thereafter all patients received LR, pRBCs to correct low hemoglobin levels and vasoactive drugs for as long as necessary.

Fluid administration for intravascular volume restoration is the first line treatment after blood loss and crystalloids are widely used since they are already available[50]. Infusion of small volumes of HSS has been used for animal resuscitation in the setting of experimental hemorrhagic shock but also in clinical studies, which were mainly focusing on prehospital or intrahospital trauma management[16,51]. Small volume resuscitation has also been used in some surgical operations, such as aorta and cardiac surgery and before spinal anesthesia[52]. Furthermore, it has been used in the ICU, where it has been proved to have similar results as in hypovolemic patients[53]. All those studies have documented the efficacy of HSS for restoration of hemodynamics and microcirculation normalization.

Blood loss in our patients resulted in a dramatic decrease of SV, CO, BP and in HR increase. Those alterations are expected after acute volume loss because there is no time for compensatory mechanism to respond[54,55].

Hemodynamic response to bleeding is related both to the amount and speed of blood loss, but also to the volemic status at that specific time point. Body's response to hypovolemia is well described and documented in classic physiology handbooks. One of the commonest methods used for intraoperative blood loss estimation is visual estimation; however this is not very reliable[56].

Both SV and CO increased immediately after NaCl 7.5% administration. CO increase after hypertonic infusion is already known and has been described in previous studies[6,9,15,23]. The main mechanism of action of hypertonic salt solutions is that they create an excessive osmotic gradient that drives fluid into the intravascular space[7]. BP increased after NaCl 7.5% administration. In the existing literature it is mentioned that rapid NaCl 7.5% administration might cause hypotension in normovolemic patients.[57,58]. SV, CO, BP alterations are efficacy indicators of administered fluids and vasoactive drugs[59]. PV, MA and FTc also showed a remarkable increase. Those parameters are related to preload and contractility of the left ventricle[40-42]. NaCl 7.5% administration had a double positive effect by both increasing the intravascular volume and improving circulation. The transient positive effects of HSS can be prolonged by addition of colloids[22,27,28]. All crystal-

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loids have an impact on volume expansion for a restricted time period[60].

In the present study the beneficial effects of HSS remained until the end of the operation. This prolonged action is attributed to the administration of RL, pRBCs, to vasoactive support of the circulation and surgical control of the bleeding. Fluid administration is aiming to restoration of the intravascular volume and is only one of several suggested treatments according to the management algorithm of the hemodynamically unstable patient. Early catecholamine administration is vital for the support of circulation[61,62]. Record of hemodynamic parameters revealed that the administration of HSS immediately restored the intravascular volume and contributed to good outcome[63].However, NaCl 7.5% administration alone would not be capable of maintaining the beneficial effect. Rapid and efficient surgical control of the bleeding played a determinant role without which outcome would not be good despite any other management interventions.

According to existing literature, it seems that HSS administration with or without colloids results to immediate hemodynamic improvement of patients in shock. However, those studies have not proved whether HSS are superior to isotonic crystalloids as far as final outcome is concerned.

Wu et al conducted a meta-analysis of 12 randomized controlled clinical trials in trauma patients with hemorrhagic shock, in 6 of which hypertonic saline 7.5% was compared to 0.9% saline or RL and in 11 studies 7.5% hypertonic saline with dextran was compared to isotonic saline or RL. Authors did not find any differences as far as overall mortality, mortality in 28 days, survival to discharge, complication rate and acute respiratory distress syndrome free survival are concerned[11]. In another review by Dornelles et al, authors concluded that HSS could be beneficial in specific clinical settings despite the fact that they have no impact on mortality[64].

Blanchard et al compared prehospital administration of 250ml NaCl 7.5% to normal saline or RL in a meta-analysis of 5 studies which enrolled 1162 trauma hypotensive patients (systolic BP below 100mmHg). Authors concluded that there were no clinical significant differences related to outcome[65].

Pfortmueller and Schefold conducted another systematic review of 25 clinical trials in which all patients received HSS. Authors concluded that its administration might have positive effects in carefully selected patients[66].

Based on our results and on existing literature it seems that NaCl 7.5% administration can be beneficial in correcting hypovolemia and in restoring hemodynamic stability.

The limitations of this study concerned the facts that due to the limited number of patients included and the lack of control group, we could not generalize our results. Moreover, despite the fact that bleeding was significant, it lasted only for a short time period and it was rapidly controlled by the surgeon.

CONCLUSION

NaCl 7.5% administration was successful in restoring hemodynamics in our patients, who suffered hemodynamic shock due to acute major blood loss. NaCl 7.5% administration along with all other treatment interventions has been shown to be beneficial to achieving a good outcome.

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