Research Paper

Effect of Rapid Plasma Volume Expansion during Anesthesia Induction on Haemodynamics and Oxygen Balance in Patients Undergoing Gastrointestinal Surgery

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Abstract

Aims: To investigate the reasonable dose of Voluven for rapid plasma volume expansion during the anaesthesia induction patients receiving gastrointestinal surgery. **Methods:** Sixty patients were randomly divided into three groups (n=20): Group A (5 ml/kg), Group B (7 ml/kg) and Group C (9 ml/kg). HES 130/0.4 was intravenously transfused at a rate of 0.3 ml/kg/min) at 30 min before anaesthesia induction. Besides standard haemodynamic monitoring, cardiac index (CI), systemic vascular resistance index (SVRI) and stroke volume variation (SVV) was continuously detected with the FloTrac/Vigileo system. Haemodynamic variables were recorded immediately before fluid transfusion (T_0), immediately before induction (T_1), immediately before intubation (T_2), immediately after intubation (T_3) and 5 min, 10 min, 20 min and 60 min after intubation (T_4-T_7). Arterial and venous blood was collected for blood gas analysis, Hb and Hct before volume expansion (t_0), immediately after volume expansion (t_1) and at 1 h after volume expansion (t_2). Oxygen delivery (DO_2), oxygen extraction ratio (ERO_2) and volume expansion rate were calculated. **Results:** 1) MAP and CI decreased in Group A in T_2~T_7 and remained changed in Group B and C. 2) CVP increased in three groups after fluid infusion without significant difference. 3) The decrease in SVRI was more obvious in Group B and C than that in Group A after induction and more obvious in Group C than in Group B in T_2-T_4 and T_6~T_7. 4) SVV was lower in Group B and C than that in Group A after intubation, and lower in Group C than that in Group B in T_3-T_6. 5) Hb and Hct decreased after fluid infusion, and the decrease in Hb and Hct was in the order of C>B>A. 6) Volume expansion rate was in the order of C>B>A. 7) $ScvO_2$, PaO_2 and DO_2 increased in three groups after fluid infusion and the increase in DO_2 was in the order of C>B>A. **Conclusions**: Rapid plasma volume expansion with Voluven at 7-9 ml/kg can prevent haemodynamic fluctuation during anaesthesia induction, maintain the balance between oxygen supply and oxygen consumption during gastrointestinal surgery, and Voluven at 9 ml/kg can improve the oxygen delivery.

Key words: Hydroxyethyl starch; General anaethesia; Haemodynamics; Oxygen balance; Gastrointestinal surgery.

Introduction

In patients undergoing gastrointestinal surgery, some factors may cause blood volume depletion, such as long-time anepithymia, cleaning enema, gastrointestinal decompression and preoperative fasting. The

subsequent hypovolemia may be aggravated by the vasodilation and myocardial suppression of anesthetic agents. Volume depletion may cause haemodynamic fluctuation and deterioration in tissue perfusion and oxygen supply. Rapid plasma volume expansion with colloids before anaesthesia induction can effectively prevent the haemodynamic fluctuation, but the amount of colloids is appropriate for plasma volume expansion is unclear. Among the various colloids used for plasma volume replacement, 6% hydroxyethyl starch (HES) Voluven (HES 130/0.4; Fresenius Kabi, Beijing, China) is considered to offer a good compromise for both, a volume effect being sufficient by degree and duration to bridge the hypovolaemic conditions and to stabilize the circulatory function, and a low rate of adverse drug reactions.[1, 2] This study aimed to investigate the optimal dose of Voluven for rapid plasma volume expansion during the anaethesia induction in patients receiving gastrointestinal surgery.

Materials and Methods

Patient data

The whole protocol was approved by the institutional review board committee of the medical faculty of Tenth People`s Hospital of Tongji University, and written informed consent was obtained before study. A total of 60 ASA I-II patients aged 30~62 years who underwent elective gastrointestinal surgery were recruited into this study, and randomly divided into three groups: Group A (5 ml/kg), Group B (7 ml/kg) and Group C (9 ml/kg). Voluven was intravenously transfused at a rate of 0.3 ml/kg/min at 30 min before anaesthesia induction. Patients with a history of known hypersensitivity to HES, coagulation disorders, renal dysfunction (oliguria [urine output<500 ml/day] or anuria not related to hypovolemia), severe cardiac disease (New York Heart Association class III-IV), unstable angina and pregnancy were excluded from this study.

Haemodynamic monitoring

Routine haemodynamic monitoring was performed including heart rate (HR), pulse oximetry, electrocardiograph, and arterial blood pressure. Before anaesthesia induction, the left radial artery was cannulated with a 20-G cannula which was connected to a FloTrac sensor and a Vigileo monitor (software version 3.06 Edwards Lifesciences, Irvine, CA, USA) for continuous monitoring of cardiac output (CO), cardiac index (CI), stroke volume (SV), stroke volume index (SVI), SVV, systemic vascular resistance (SVR) and systemic vascular resistance index (SVRI). After anaesthesia induction, a 7.5-F central venous catheter was introduced via the right internal jugular vein for measurement of central venous pressure (CVP). All invasive cannulations were performed under local analgesia with 1% lidocaine.

Study protocol

Anesthesia was induced using atracurium (0.6-0.8 mg/kg iv.) and was maintained with atracurium (0.3 mg/kg iv.). Neuromuscular blockade was achieved with atracurium (0.3 mg/kg iv.). Following endotracheal intubation, all patients were mechanically ventilated with IPPV mode (tidal volume: 10 ml/kg, frequency: 12 breath/min, positive end expiratory pressure [PEEP]: 0, fractional inspired oxygen [FiO_2]: 0.8, oxygen flow: 2.0 L/min). Mechanical ventilation was maintained with an endexpiratory Pco_2 at 35-45 mmHg, peak airway pressure of <15 cmH_2O and pulse oximetry ranging from 98% to 100%. Bispectral index was monitored with the Aspect2000 Monitor (Aspect company, America) and ranged from 45 to 55.

Voluven was intravenously transfused at a rate of 0.3 ml/kg/min at 30 min before anaesthesia induction. Voluven was administered at 5 ml/kg; 7 ml/kg and 9 ml/kg in Group A, B and C, respectively. Ringer's lactate solution was infused at 3 ml/kg/h after anaesthesia induction until the end of surgery. Voluven was infused at a ratio of 1:1 to blood loss during surgery. Arterial and central venous blood was collected for blood gas analysis during the study period. Blood components were administered according to American Society of Anesthesiologists guidelines. [3]

Measurements and Statistical Analysis

Haemodynamic variables were recorded immediately before fluid infusion (T_0), immediately before induction (T_1), immediately before intubation (T_2), immediately after intubation (T_3) and at 5 min, 10 min, 20 min and 60 min after intubation (T_4-T_7). Left radial arterial and right internal jugular venous blood samples were collected for blood gas analysis and determination of lactic acid, blood glucose, Hb and Hct before fluid infusion (t_1), immediately after fluid infusion and at 1 h after fluid infusion. Oxygen delivery (DO_2), oxygen extraction ratio (ERO_2), volume expansion rate and arteriovenous difference in lactate content (ΔLac) were calculated.

Statistical analysis

Statistical analysis was performed using SPSS version 13.0 (SPSS; Chicago, IL). Data are presented as the mean ± standard deviation (SD). Differences in different variables among groups were evaluated by one-way analysis of variance. Chi square test and Fisher's exact test were used for comparisons of categorical data if necessary. A nonparametric test

(Wilcoxon rank sum test) was used for variables with abnormal distribution (Kolmogorov-Smirnov test). A value of $P<0.05$ was considered statistically significant.

Results

There were 20 patients in each group. None withdraw from the study. The biometric variables were comparable among three groups (Table 1). There were no differences in the HR, MAP, CVP, CI and SVRI at T_0 among three groups. 1) MAP and CI decreased in Group A in T_2-T_7 and remained unchanged in Group B and C. HR decreased in T_2 and T_4-T_7 and increased in T_3 in Group A, while remained changed in Group B and C. 2) CVP increased in three groups after fluid infusion without difference among three groups. 3) The decrease in SVRI was more obvious in Group B and C than in Group A after induction and more evident in Group C than in Group B in T_2-T_4 and T_6-T_7. 4) SVV was lower in Group B and C than in

Group A after intubation, and lower in Group C than in Group B in T_3-T_6 (Table 2). Hb and Hct decreased after fluid infusion, and the decrease was in the order of C>B>A. 6) Volume expansion rate was in the order of C>B>A (Table 3).

$ScvO_2$, PaO_2 and DO_2 increased in three groups after fluid infusion and the increase in DO_2 was in the order of C>B>A. ERO_2 decreased after fluid infusion in three groups. The amount of blood transfusion was lower in Group B and C than in Group A (Table 4).

Table 1. Biometric variables of patients in three groups.

Variables	Group A	Group B	Group C
Age (yr)	46±14	47±15	46±13
Male: female	10/10	11/9	11/9
Height (cm)	165±9	167±8	168±9
Weight (kg)	63±8	64±6	62±8

Table 2. Haemodynamic variables in three groups.

Variables	Group	T_0	T_1	T_2	T_3	T_4	T_5	T_6	T_7
HR (/min)	A	78.2±8.6	77.3±7.8	62.2±6.9**	84.1±6.7	69.2±7.0*	65.5±6.7**	66.3±8.1**	70.1±6.6*
	B	77.4±7.9	75.4±8.1	74.3±7.8△	75.3±7.4△	75.4±6.6△	75.3±7.0△	73.5±7.3△	74.2±7.5△
	C	76.5±8.2	76.1±8.5	75.8±7.6△	77.5±6.8△	75.3±7.2△	74.4±6.5△	74.1±7.7△	74.3±7.6△
MAP (mmHg)	A	86.2±11.1	86.5±10.8	65.7±12.1**	71.2±11.5**	76.3±10.6*	75.2±9.3*	75.3±11.1*	74.4±10.1*
	B	85.3±12.0	86.6±11.4	84.4±11.3△△	83.9±10.3△△	84.2±9.8△	83.5±8.9△	84.7±9.3△	82.9±9.7△
	C	85.6±10.9	87.1±10.3	85.6±12.0△△	84.1±9.9△△	85.3±8.9△	85.1±9.6△	83.4±9.5△	84.3±10.1△
CVP (mmHg)	A	2.9±0.8	5.3±1.0*	5.1±0.9*	5.2±0.8*	5.3±0.9*	5.2±1.0*	5.1±0.8*	5.1±1.1*
	B	3.1.±1.1	5.2±0.9*	5.2±1.0*	5.3±0.9*	5.4±1.1*	5.2±0.7*	5.4±0.9*	5.3±0.8*
	C	3.0±0.9	5.4±0.8*	5.8±0.9**	5.5±0.9*	5.4±1.0*	5.6±0.8*	5.5±1.1*	5.4±1.0*
CI (L/min/m)	A	3.0±0.3	3.0.±0.5	2.2±0.3**	2.4±0.5*	2.3±0.4*	2.4±0.3*	2.4±0.4*	2.5±0.4*
	B	2.9±0.4	3.1±0.4	2.8±0.3△△	2.8±0.3△	2.7±0.5△	2.8±0.3△	3.0±0.4△	2.8±0.5△
	C	2.9±0.3	3.1.±0.5	3.0±0.5△△	3.0±0.4△	3.0±0.4△△	3.1±0.4△	3.2±0.5△	3.1±0.3△
SVRI (dynes/s/m/cm⁻⁵)	A	2469±98	2401±79	2283±101*	2298±97*	2299±91*	2286±86*	2292±79*	2293±95*
	B	2472±95	2466±98	2213±99*△	2182±101*△	2190±96*△	2207±97*△	2198±87*△	2196±92*△
	C	2498±101	2451±89	2115±96*△☆	2079±99**△☆	2112±94**△☆	2162±79*△	2116±89*△☆	2108±93*△☆
SVV (%)	A				10.1±1.9	10.9±2.1	10.0±1.8	9.1±1.6	9.3±0.9
	B				6.2±1.2△	7.1±1.4△	6.5±1.0△	6.7±0.9△	6.4±1.1△
	C				3.1±0.6△☆☆	4.2±0.5△△☆	3.6±0.4△☆	3.8±0.7△△☆	5.2±0.8△

*$P<0.05$, **$P<0.01$ vs T_0; △$P<0.05$, △△$P<0.01$ vs Group A; ☆$P<0.05$, ☆☆$P<0.01$ vs Group B.

Table 3. Changes in Hb and Hct.

Variables	Group	t_0	t_1	t_2
Hb (g/L)	A	131±8	115±10**	116±7**
	B	130±9	109±7**△△	108±9**△△
	C	129±10	103±8**△△☆☆	101±7**△△☆☆
Hct (%)	A	38.0±3.2	34.2±2.8*	34.4±2.6*
	B	37.6±2.8	32.7±3.0**△	32.3±2.7**△△
	C	38.2±2.9	31.3±2.5**△△☆	30.9±2.5**△△☆☆
Volume expansion rate (%)	A		12±7	11±6
	B		15±6△	16±5△△
	C		20±5△△☆	21±6△△☆☆

*$P<0.05$, **$P<0.01$ vs t_0; ▲$P<0.05$, ▲▲$P<0.01$ vs t_1; △$P<0.05$, △△$P<0.01$ vs Group A; ☆$P<0.05$, ☆☆$P<0.01$ vs Group B.

Table 4. Changes in blood gas analysis and oxygen balance in three groups.

Variables	Group	t_0	t_1	t_2
ScvO$_2$ (%)	A	68.8±5	75.9±6*	76.2±6**
	B	69.1±6	77.3±7**	75.6±7*
	C	67.9±5	78.1±6**	75.3±5**
DO$_2$ (ml/min/m^2)	A	683±39	711±34*	713±40*
	B	695±36	731±37**△	732±36**△
	C	686±41	753±38**△△☆	752±41**△△☆
ΔLac (arterious-venous) (mmol/L)	A	-0.12±0.05	-0.13±0.03	-0.13±0.04
	B	-0.13±0.04	-0.15±0.03	-0.14±0.05
	C	-0.12±0.04	-0.14±0.05	-0.13±0.04
ERO$_2$ (%)	A	27.2±4.0	23.6±2.9**	23.2±3.0**
	B	26.6±3.1	22.7±3.2**	23.8±3.3**
	C	27.3±3.6	22.4±3.4**	23.9±2.8**
pH	A	7.396±0.053	7.405±0.040	7.403±0.044
	B	7.401±0.046	7.427±0.038	7.385±0.035
	C	7.393±0.039	7.381±0.041	7.395±0.043
BE (mmol/L)	A	-3.3±1.0	-3.2±0.9	-3.1±0.8
	B	-3.2±0.8	-3.4±1.0	-3.2±0.9
	C	-3.3±1.1	-3.3±1.1	-3.2±0.9
PaO$_2$ (mmHg)	A	85±13	291±42**	312±45**
	B	90±15	275±35**	290±43**
	C	87±13	311±38**	322±50**
PaCO$_2$ (mmHg)	A	40.6±3.2	40.8±2.9	37.6±2.7
	B	39.2±2.8	37.3±3.0	40.1±3.3
	C	38.5±3.0	39.6±3.1	41.3±3.2
HCO$_3^-$ (mmol/L)	A	20.5±2.1	21.4±1.9	19.8±1.8
	B	19.7±2.5	21.2±2.0	20.1±1.9
	C	20.7±2.2	20.5±2.3	21.1±1.7

*$P<0.05$, **$P<0.01$ vs t_0; △$P<0.05$, △△$P<0.01$ vs Group A; ☆$P<0.05$, ☆☆$P<0.01$ vs Group B.

Discussion

Voluven is a novel HES with a mean molecular weight of 130,000 dalton, a molar substitution of 0.4 (130/0.4), and a C2/C6 ratio of greater than 8. The molecular weight distribution of HES 130/0.4 is the narrowest among all available HES. It also has an improved *in vivo* molecular weight resulting in sustained volume effect despite higher elimination. [4]

Renal excretion of HES 130/0.4 is faster than that of pentastarch (HES 200/0.5) or hetastarch (HES 450/0.7), [5] and HES 130/0.4 does not accumulate in the plasma after multiple dosing over 10 days. [6] This pharmacologic property results in a 75% reduction of tissue storage of HES 130/0.4 when compared with HES 200/0.5.[7] In addition, the *in vitro* and *in vivo* measures of coagulation are less compromised by HES 130/0.4 as compared to other starch-based volume substitutes.[8-15, 16, 17]

In healthy volunteers, the volume expansion effect of Hextend (BioTime Inc., Berkeley, CA) is less well sustained than that of HES 130/0.4.[18] Other studies also report similar results regarding favorable volume expansion and lesser compromised coagulation in patients treated with HES 130/0.4 than with other HES.[10-12, 14-17, 19,20] Even at a dose of up to 70 ml/kg, HES 130/0.4 failed to cause complications such as coagulopathy or bleeding in patients with severe head injury.[21] Similar results were also observed in cardiac patients with infusion of HES 130/0.4 at as much as 50 ml/kg.[15] Less impairment of coagulation by HES 130/0.4 than other HES has also been demonstrated *in vitro*.[13, 16] The hemodynamic response, cardiac index, and right ventricular end diastolic pressure during and after acute normovolemic hemodilution are also comparable between patients treated with HES 130/0.4 and HES 200/0.5.[19] Since its approval in 1999/2000, HES 130/0.4 has been used widely in the volume substitution therapy in Europe, where the currently approved daily maximum dose for HES 130/0.4 is 50 ml/kg body weight.

Colloids infusion before induction can prevent the haemodynamic fluctuation during the induction of general anaesthesia.[22, 23] Whereas, there are some

risks, such as circulative overload and pulmonary edema, especially for old patients and those with cardiovascular diseases. In this study, the patients in three groups were intravenously transfused with Voluven at 5 ml/kg, 7 ml/kg and 9 ml/kg, respectively, before anaesthesia induction, and the results showed that CVP increased and SVRI decreased in three groups but remained at a normal level. In our study, the MAP and CI decreased significantly in Group A and maintain stable in Group B and Group C throughout the study. This suggests that rapid plasma volume expansion with Voluven at 7-9 ml/kg before general anaesthesia can prevent haemodynamic fluctuation during induction. The possible reasons are as follows: 1) Volume expansion before general anaesthesia can rectify the relative hypovolaemia due to pre-operative preparations and vasodilation induced by general anesthetic agents,[22] increase the cardiac preload to strengthen the cardiac constriction, prevent the hypotension and lower the CO effectively. 2) Haemodilution decreases the plasma viscosity. The decrease in SVR leads to the increase in microvascular blood flow and arterial O_2 content. Cardiac afterload decreases and CO increases as haemodilution progresses. [24] As haemodilution progressed in three groups, SVR decreased in the order of C>B>A. 3) General anesthetic agents themselves lead to the vasodilation and reduction in SVR.

FloTrac/Vigileo system acquire continuous CO by analyzing the arterial pulse wave with semi-invasive arterial catheterization in the absence of pulmonary artery catheterization or calibration with another method, which can monitor CO, CI, SV, SVI and SVV. With a CVP catheter placed, its signal can be interfaced with the Vigileo, allowing for the calculation of SVR and SVRI. [13] Several studies have shown that haemodynamic variables monitored by FloTrac/Vigileo system were highly correlated with those detected with other invasive haemodynamics monitors. [26, 27]

The frequently used standard preload indexes, such as central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), intrathoracic blood volume index (ITBI) and left ventricular end-diastolic area index (LVEDAI) often fail to provide reliable information and predict fluid responsiveness with conflicting results. [28-31] As an alternative to these static variables, assessment of SVV has been used as a strategy for haemodynamic monitoring to guide the fluid therapy in patients receiving mechanical ventilation [31-41]. SVV is the variation of beat-to-beat stroke volume from the mean value during the respiration cycle. Results showed that there was no significant difference in CVP among three groups. However, SVV was significantly different among three group and in the order of A<B<C. This means SVV can predict the responsiveness to volume therapy and more exactly evaluate the patients' volume state than CVP

As different volume infusion in three groups, volume expansion rate was different and in the order of C>B>A. The Hb and Hct decreased immediately after volume infusion and at 1 h after infusion. This may be explained that 100% volume expansion with Voluven *in vivo* can be maintained for 4-6 h. Woessner et al [42] found the similar results in a study on 40 wounded patients. They found that the volume expansion with Voluven remained stable within about 4 h, the longest time of stable volume expansion was 6 h and the half-life of Voluven *in vivo* was about 3 h. DO_2, lactate content in blood, saturation of mixed venous blood oxygen (S_VO_2) and ERO_2 reflect the oxygen supply and oxygen consumption in tissues. However, detection of S_VO_2 is costly and time consuming and has risk for complications. Schou et al [43] and Ladakis et al [44] proved that there was highly correlation between S_VO_2 and saturation of central venous blood oxygen ($S_{CV}O_2$). After volume infusion in three groups, the $S_{CV}O_2$ and arterial partial pressure of oxygen (PaO_2) increased and the DO_2 increased in the order of C>B>A, while the ERO_2 decreased. Besides PaO_2 increased for mechanical ventilation the reason were following: firstly, DO_2=CO×arterial oxygen content. Volume expansion increases circulating blood volume and cardiac preload. The stroke volume increases in a self-regulative mechanism (Frank-Starling Principal). The increasing CO compensates the decreasing arterial oxygen content due to haemodilution. Secondly, blood viscosity decreases following haemodilution. Red blood cells are hard to aggregate, which improves the microcirculation and increases the tissue oxygen supply. [45] Thirdly, SVR decreases as blood viscosity decreases. Under the same perfusion pressure, the blood flow rate accelerates and the distribution of blood flow is more even, which was beneficial for oxygen intake and consumption in tissue.

In conclusion, rapid plasma volume expansion with Voluven at 7-9 ml/kg before induction of general anaesthesia can effectively prevent the haemodynamic fluctuation, maintain the balance between oxygen supply and oxygen consumption during the gastrointestinal surgery. In addition, Voluven at 9 ml/kg can improve the oxygen delivery.

Competing Interests

The authors have declared that no competing interest exists.

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