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The effects of hypervolemic infusion on microcirculation perfusion of patients during laparoscopic colorectal surgery

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Abstract

The aim of this study is to assess the effects of hypervolemic infusion with different solutions on microcirculation perfusion during laparoscopic colorectal surgery.

Thirty-six patients were randomly divided into Ringer lactate solution [RL] group, succinylated gelatin injection [Gel] group, and hypertonic saline hydroxyethyl starch 40 injection [HS] group. Hypervolemic infusion was performed during the induction period of general anesthesia. Arterial blood–gas parameters, noninvasive hemodynamics, gastric tonometry values, and central venous pressure (CVP) were compared at baseline (T1); the end of hypervolemic infusion (T2); 5 min (T3), 15 min (T4), 30 min (T5), and 60 min (T6) during pneumoperitoneum; 5 min (T7), 15 min (T8), and 25 min (T9) after pneumoperitoneum. Patients were also grouped by age for further comparisons.

The hematocrit levels of all groups after T2 decreased. The gastric mucosal-arterial carbon dioxide partial pressure ($P_{g-a}CO_2$) started to decrease after T2 and rebounded after T5. There was no difference in the gastric mucosal perfusion when compared between 3 groups. The blood Na^+ of HS group increased significantly after T2, then gradually restored and returned to baseline by T8. The plasma bicarbonate (HCO_3^-) levels of RL and Gel groups elevated from T2 to T7, after which they started to decrease, but this phenomenon was not significant in HS group. In both RL and Gel groups, blood pressure has a significant fluctuation in elder patients.

Hypervolemic infusion of these solutions during the induction of anesthesia can improve gastric mucosal perfusion. HS can maintain a more stable hemodynamic effect when used with caution in patients with preoperative hypernatremia.

Abbreviations: AHFI = acute hypervolemic fluid infusion, BE = base excess, CVP = central venous pressure, DBP = diastolic blood pressure, Gel = succinylated gelatin injection, HS = hypertonic saline hydroxyethyl starch 40 injection, $P_{g-a}CO_2$ = gastric mucosal-arterial carbon dioxide partial pressure, RL = Ringer lactate solution, SBP = systolic blood pressure, SVRI = systemic vascular resistance index.

Keywords: gastric tonometry, hypertonic saline hydroxyethyl starch 40 hypervolemic fluid infusion, visceral perfusion

1. Introduction

At present, safety and humanization issues are widely valued in medical care, and perioperative volume management under general anesthesia is a powerful backing to ensure patients' stable intraoperative vital signs. In addition, with the development of laparoscopic surgery, the performance of long-duration surgeries, such as colorectal surgery, for elderly patients has been increasing. Because laparoscopic surgery under pneumoperitoneum has a great impact on normal physiological conditions, which can cause significant changes in circulation, respiration, and the internal neuroendocrine environment, the intraoperative visceral perfusion level deserves our special attention.

Researches[1,2] have shown that laparoscopic surgery can affect the perfusion of the abdominal viscera. As an intraoperative volume management method, acute hypervolemic fluid infusion (AHFI) during the induction of anesthesia can improve the perfusion and oxygen supply of internal organs.[3,4] This study used gastric tonometry to assess the effects of AHFI with different solutions on gastric mucosal perfusion during the anesthesia of laparoscopic colorectal surgery.

2. Materials and methods

This study was approved by the Ethics Committee of the Ruijin Hospital, Shanghai Jiao Tong University School of Medicine. All patients or their designated representatives were fully informed of the objectives of the study and the possible risks, and all signed the informed consent form. All patients maintained the right to terminate the study at any stage of the experiment.

Thirty-six patients who underwent elective laparoscopic colorectal surgery were randomly divided into 3 groups in our

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observational trial: Ringer lactate solution [RL] group, succinylated gelatin injection [Gel] group, and hypertonic saline hydroxyethyl starch 40 injection [HS] group. The anesthesiologists who performed anesthesia were blinded to the assignment of patients. The age was between 40 and 80 years, body mass index was $<30\,kg/m^2$, and American Society of Anesthesiologists grade was I to II among the including patients, of which 20 were males and 16 were females. Patients with severe cardiopulmonary disease, or liver/kidney dysfunctions were excluded. None of patients has any major abdominal surgery history, special drug allergy history, or addiction to alcohol and drugs. The 3 groups were also divided into 2 subgroups by age: subgroup A <65 years; subgroup B ≥65 years. (Supplemental Content 1, http://links.lww.com/MD/B952).

During preparation of anesthesia in the operation room, a gastric tonometry apparatus (Tonometrics Catheter, TONO-16F, Datex-Ohmeda Inc, Finland) was inserted into the stomach through the nose after the patient was sedated; the catheter's location was determined by auscultation or by the stomach contents aspirated via the catheter. The catheter was then connected to the tonometry module. Electrode plates were placed on patients' skin after locally degreased, and were then connected to a noninvasive hemodynamic monitor (BioZ.com). The right arm was connected to a regular monitoring of noninvasive blood pressure, and the left arm was used to monitor the noninvasive blood pressure (BioZ.com). Intravenous infusion pathway and radial artery cannulation were opened on the left forearm for blood withdrawal. After local anesthesia, a double-lumen central venous catheter was catheterized into right internal jugular vein for infusion and monitoring the central venous pressure (CVP). Before the induction of anesthesia, RL was infused gradually to supplement the physiological need. After the completion of infusion, arterial blood gas analysis was conducted and the results were input into the tonometry module to calculate relevant data.

During induction of anesthesia, drugs were administered through peripheral veins. Propofol was given by target-controlled infusion at 4 μg/mL; atracurium 0.6 mg/kg and fentanyl 2 μg/kg were injected intravenously. The patient inhaled pure oxygen for 3 min by manual control. After tracheal intubation, mechanical ventilation was conducted with a mixed gas flow of 1.5 L/min. The tidal volume was set 8 to 10 mL/kg, and respiratory rate was set 10 to 12 times/min. Subsequently, the respiratory parameters were adjusted after changes in body position, pneumoperitoneum pressure (intraoperative pressure was limited to 15 mm Hg, 1 mm Hg = 0.133 kPa), and partial pressure of $EtCO_2$ so as to maintain $EtCO_2$ between 35 and 40 mm Hg. At the same time, the pressure limit was modulated so that the airway peak pressure (P_{peak}) would not exceed 25 cm H_2O (1 cm H_2O = 0.098 kPa).

AHFI also started during anesthesia induction. RL and Gel groups were given 12 mL/kg of RL/Gel solution, HS group was given 3.5 mL/kg of HS. Although the infusion was completed before the pneumoperitoneum was established, all 3 groups continued to receive infusion with RL solution at 7 mL/kg per h. During operation, if the estimated blood loss volume was >200 mL, the same amount of gelatin infusion was given to compensate for the lost volume. A combination of inhalational anesthesia (0.6 MAC desflurane) and intravenous anesthesia (2.0 μg/mL propofol) were performed to maintain the anesthetic depth; single dosage atracurium and fentanyl were given intermittently as needed. If systolic blood pressure (SBP) >140 mm Hg or (and) diastolic blood pressure (DBP) >90 mm Hg occurred, then Nicardipine was given to lower the blood pressure. All data including urine and blood loss volumes were recorded. For patients with urine volumes <40 mL/h, 10 to 20 mg of furosemide was intravenously injected before end of operation.

Data were collected at the following time points: baseline value (after supplementing the amount of physiological need) (T1); after AHFI (T2); 5 min (T3), 15 min (T4), 30 min (T5), and 60 min (T6) into pneumoperitoneum; and 5 min (T7), 15 min (T8), and 25 min (T9) after the pneumoperitoneum. The collected data included the following 4 items: iSTAT arterial blood gas analysis: arterial blood pH (pH_a) value, partial pressure of carbon dioxide (P_aCO_2), HCO_3^-, plasma base excess (BE), Na^+, K^+, iCa^{2+}, and hematocrit (Hct); BioZ noninvasive cardiac output data: heart rate, SBP, DBP, cardiac index, stroke index, systemic vascular resistance index (SVRI), and thoracic fluid content; gastric tonometry indicators: gastric mucosal partial pressure of carbon dioxide (P_gCO_2), gastric mucosal pH (pHi) value, gastric mucosal-arterial carbon dioxide partial pressure ($P_{g-a}CO_2$), and gastric mucosa-partial pressure of carbon dioxide at the end of an exhaled breath ($P_{g-et}CO_2$); and CVP.

The experimental data were analyzed using the SPSS 13.0 software package. Measurement data with normal distributions are represented by means ± standard deviations. Measurement data between groups were compared with 1-way analysis of variance, and the S-N-K method was used for pair-wise comparisons. When $P < .05$, the differences were considered to be statistically significant; when $P < .01$, the differences were considered to be extremely statistically significant.

3. Results

There were no significant statistical difference in demographics, blood loss, urine output, and the Hct dilution ratio after AHFI between patients in the 3 groups ($P > .05$).

The differences in various indicators (including arterial blood gas analysis, BioZ noninvasive cardiac output data, and gastric tonometry indicators) between the 3 groups before the induction (T1) were not statistically significant ($P > .05$). After T2, the Hct levels of all 3 groups had decreased and gradually rebounded in the subsequent time points. The decrease of Gel group was the most significant and lasted longer. The Gel group had a certain extent of blood iCa^{2+} decline (Fig. 1); this phenomenon continued until the end of data collection. The blood iCa^{2+} of HS group did not decrease significantly.

Starting from T3 time point, all 3 groups showed increases in CVP, which then gradually decreased; by T7 time point, the CVP abruptly decreased to a level before that of T3 ($P < .01$). There

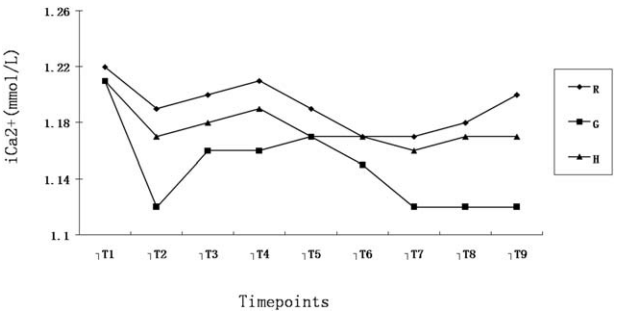

Figure 1. Trends of iCa^{2+} at different time points in various solution groups. The Gel (G) group showed significant statistical differences at T2, T8, and T9 compared with the other 2 groups ($^*P < .01$). The G and RL (R) groups were significantly different at T4 and T7 ($^{\&}P < .05$). RL = Ringer lactate solution.

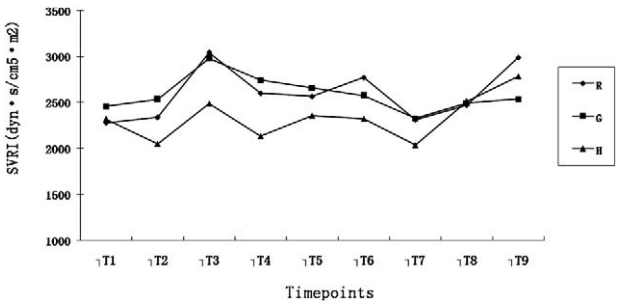

Figure 2. Trends of systemic vascular resistance index at different time points in various solution groups. The HS (H) and Gel (G) groups were significantly different at T4 ($P < .01$); the H and RL (R) groups were significantly different at T4 ($P < .01$). HS = hypertonic saline hydroxyethyl starch 40 injection, RL = Ringer lactate solution.

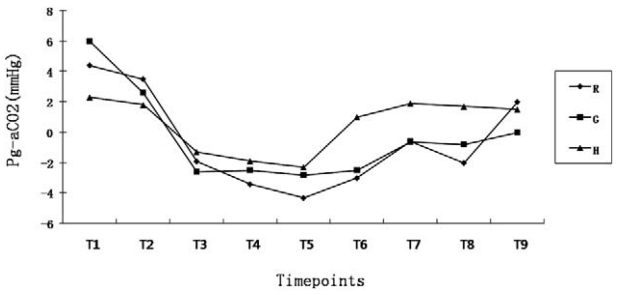

Figure 4. Trends of $P_{g-a}CO_2$ at different time points in various solution groups. The RL (R) group was significantly different between the T5 and T1 time points ($P < .05$); there were no significant differences at various time points between the 3 groups. $P_{g-a}CO_2$ = gastric mucosal-arterial carbon dioxide partial pressure, RL = Ringer lactate solution.

were no significant differences between the 3 groups (all $P > .05$). From T2 to T7 time points, the SVRIs value of HS group was lower than those of the other groups (Fig. 2), and there were no significant differences in noninvasive hemodynamics between various time points of HS group (all $P > .05$), while the noninvasive BP levels of the other 2 groups had large fluctuation ranges (Supplemental Content 2, http://links.lww.com/MD/B952).

Compared with T1 time point, the P_aCO_2 levels after T3 time point in all 3 groups increased significantly (all $P < .01$), which was accompanied with significant decreases in pH_a (all $P < .01$), though the differences between the 3 groups at various time points were not statistically significant (all $P > .05$). After T2 time point, the HCO_3^- concentrations in both RL and Gel groups increased significantly, while the HCO_3^- concentration and BE value of HS group were lower than those of RL and Gel groups starting from T2 (Supplemental Content 2, http://links.lww.com/MD/B952). Compared with T1 time point, the blood Na^+ concentration at T2 time point in HS group increased suddenly and was significantly different compared with that of the other 2 groups (all $P < .01$); this tendency continued until the end of the data collection (Fig. 3). There were significant differences in the blood K^+ concentrations between the 3 groups at various time points (all $P > .05$).

The $P_{g-a}CO_2$ levels after T2 time point in all 3 groups started to decrease but rebounded after T5 time point; however, they never exceeded the baseline value, and only the difference between T5 time point and T1 time point in RL group was statistically significant ($P < .05$, Fig. 4). There were no statistically significant differences in P_gCO_2, pHi, and $P_{g-et}CO_2$ between the 3 groups and between various time points (all $P > .05$, Supplemental Content 3, http://links.lww.com/MD/B952).

There were statistically significant differences in various indicators in subgroup A and B of HS group (all $P > .05$). In RL and Gel groups, the fluctuations in blood pressure in subgroup B were more significant than those of subgroup A. In RL group, the CVP at T4 time point in subgroup A was lower than that of subgroup B ($P < .05$). In Gel group, the SVRI at T2 time point in subgroup A was significantly higher than that of subgroup B ($P < .05$). In Gel group, the $P_{g-a}CO_2$ levels at T2, T3, T4, and T6 time points in subgroup B were significantly lower than those of subgroup A (P = .05 and .01, respectively, Supplemental Content 3, http://links.lww.com/MD/B952).

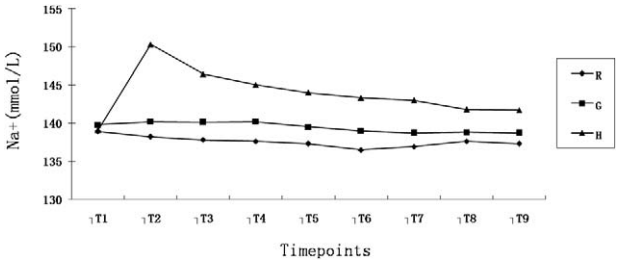

Figure 3. Trends of Na^+ at different time points in various solution groups. The HS (H) group was significantly different from the other 2 groups during the T2–T9 time points ($^*P < .01$). HS = hypertonic saline hydroxyethyl starch 40 injection.

4. Discussion

Although our widely used infusion monitoring system involves regular pressure monitoring parameters, they cannot directly reflect changes in body volume. It has been reported that the classical indicators, such as CVP and pulmonary artery wedge pressure, could neither objectively reflect the volume condition under a state of general anesthesia nor identify the existence of tissue hypoperfusion.[5] Gastric tonometry is used to monitor the partial pressure of carbon dioxide (P_gCO_2) in the gastric mucosa, and this monitoring can aid in the early detection of hidden visceral hypoperfusion conditions.

It should be noted that regardless of the state of respiratory or metabolic acidosis, what P_gCO_2 and pHi reflect is no longer local mucosal acidosis; instead, these measurements reflect systemic acidosis conditions. Therefore, the hypercapnia caused by carbon dioxide pneumoperitoneum will inevitably affect the measurement accuracy of gastric tonometry. In our experiment, both P_aCO_2 and P_gCO_2 were changed, and the 2 were positively correlated, suggesting that the fluctuation of P_gCO_2 in this experiment was mainly caused by hypercapnia, rather than a paradigm of an impact on visceral perfusion. In addition, the good correlation between the 2 also showed that gastric mucosal cells had a good diffusion effect for CO_2, which, to a certain extent, indicated that the cell function had not been significantly affected.

Nowadays, many researchers suggest that $P_{g-a}CO_2$ is not affected by a systemic acid–base state and P_aCO_2; therefore, $P_{g-a}CO_2$ can more accurately reflect the mucosal ischemic condition and is the specific oxygenation indicator of the

gastrointestinal mucosa.[6] To this end, in this experiment, $P_{g-a}CO_2$ was the main parameter of the discussion. The data showed that $P_{g-a}CO_2$ started to decline after volume infusion in the 3 groups and that the trough value appeared at approximately the T5 time point, after which it slowly recovered to form a wave-like curve. In other studies, it has been reported[7] that $P_{g-a}CO_2$ increased significantly 60 min into pneumoperitoneum; however, the result of this experiment was very different. The explanation for this difference is that the descending branch of the curve in our result was mainly due to the increase in visceral blood infusion caused by volume infusion in the induction period, while the ascending branch indicated that the carbon dioxide concentrations in the mucosa and the arterial blood were approaching equilibrium. Thus, AHFI during the induction period improved the visceral perfusion to a certain extent. In addition, the differences in the gastric mucosal perfusion indicators between the 3 groups were not statistically significant (all $P > .05$), suggesting that various solutions used in the present experiment for AHFI could achieve a good visceral perfusion result during the early stage.

At present, the clinically used hypervolemic solutions are mainly isotonic fluid, including crystalloid and artificial colloid solutions. However, with their extensive clinical applications, the problems caused by them also garner more attention. Studies have found that hypertonic sodium chloride solution could rapidly increase blood volume, correct hypovolemia status, improve blood perfusion of organs and hemodynamics, and simultaneously effectively increase myocardial contractility.[8] Hypertonic sodium chloride hydroxyethyl starch 40 injection (HS) is a hypertonic artificial colloidal salt solution consisting of 4.2% sodium chloride and 7.6% hydroxyethyl starch 40, with a hypervolemic ratio of approximately 300% to 400%. Both animal experiments and clinical case observations have confirmed its clinical safety and practicality.[9]

The results of this study showed that the SVRI value after volume infusion in HS group was lower than those of Gel and RL groups, with a very clear trend. The blood pressure levels in RL and Gel groups underwent large changes before and after pneumoperitoneum, while the noninvasive hemodynamics in HS group at various time points was not significantly different. Many studies in the literature have reported that HS has a lowering effect on peripheral vascular resistance.[10] Because the peripheral circulation resistance will increase sharply after the establishment of pneumoperitoneum in laparoscopic surgery, the properties of hypertonic saline solution seem to help partially alleviate this problem.

The plasma Na^+ and Cl^- concentrations of a healthy person range between 135 and 145 mmol/L and 95 and 108 mmol/L, respectively. HS contains 4.2% sodium chloride, and the experiments in this study showed that the plasma Na^+ concentration in HS group increased significantly after the T2 time point, after which it was gradually restored, suggesting that mild hypernatremia and hyperchloremia existed after the use of HS. In addition, observations found that the HCO_3^- levels in RL and Gel groups continued to increase after the T2 time point all the way to the T7 time point and then decreased. Although HS group also experienced this type of trend, it was not as significant as the other 2 groups, and the difference was also not statistically significant. When simple respiratory acidosis occurs, the body's compensatory response to hypercapnia is to increase the plasma HCO_3^- level; therefore, all 3 groups exhibited increased HCO_3^-. The kidney will accelerate the excretion of K^+-HCO_3^- when the plasma sodium and chloride levels are high[11]; therefore, the increase in the plasma HCO_3^- level in HS group was not significant. At the same time, the BE value was lower than those of the other 2 groups, and the degree of a sudden decrease in the K^+ concentration was large. However, the differences in pH_a and P_aCO_2 values between the 3 groups at various time points were not statistically significant (all $P > .05$); therefore, even though there was a certain degree of hyperchloremia, its impact on acid–base homeostasis was not serious and was much less than the impact of the CO_2 pneumoperitoneum.

This study also found that in RL and Gel groups, elderly patients ≥65 years of age had more significant fluctuations in blood pressure. During the pneumoperitoneum, the CVP of patients <65 years was lower than that of patients ≥65 years. In Gel group, the peripheral circulation resistance of patients <65 years was higher than that of patients ≥65 years. In HS group, the differences in the hemodynamic parameters between the 2 subgroups were not statistically significant (all $P > .05$). In addition, the data showed that the CVPs of different solution groups increased significantly after the T3 time point and then decreased slowly; by the T7 time point, the CVPs abruptly decreased to levels before T3. This observation was directly associated with the establishment of the pneumoperitoneum, and the low head and lithotomy positions of the patient's body. Although the CVP can gradually decrease after pneumoperitoneum, changes in CVP should be closely observed to prevent severe cardiac arrest and pulmonary edema, particularly for elderly patients and patients with poor heart and lung functions.

In RL and HS groups, there were no significant differences in $P_{g-a}CO_2$ between the 2 subgroups (all $P > .05$), while in the Gel group, although the $P_{g-a}CO_2$ of patients ≥65 years was lower than that of patients <65 years, the $P_{g-a}CO_2$ levels of both subgroups always changed in parallel. This observation cannot be attributed to the difference of visceral perfusion, and its specific cause needs further investigation.

In summary, laparoscopic colorectal cancer surgery will have a certain amount of impact on the cardiopulmonary function and circulatory dynamics of patients, and AHFI during the induction period can alleviate the potential risk of gastric mucosal hypoperfusion and delay the occurrence of visceral ischemia. The use of different solutions for volume infusion can all achieve good results in the early stage. Longer surgical duration or age factors do not have significant impacts on gastric mucosal perfusion. In this type of surgery, HS can maintain more stable intraoperative hemodynamics, which are more suitable for elderly patients. However, because the use of HS can cause abrupt mild hypernatremia, it should be used with caution for patients who already have an intention of it preoperatively. Due to the limited amount of patients included in our study, there might be statistical bias in analysis. We hope this series of research could be expanded steadily.

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