Original

SPLANCHNIC PERFUSION DURING THE COMBINATION OF ACUTE HYPERVOLEMIC HEMODILUTION AND PROSTAGLANDIN E1-INDUCED HYPOTENSION UNDER SEVOFLURANE ANESTHESIA

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Abstract

We evaluated the effects of the combination of acute hypervolemic hemodilution and prostaglandin E1-induced hypotension under sevoflurane anesthesia on splanchnic perfusion. We determined the gastric intramucosal Poc_2 gradients and pH for assessing splanchnic perfusion using tonometry in 30 patients undergoing hip surgery. Patients were randomly assigned to two groups according to the maintainance of anesthesia. Anesthesia was maintained with nitrous oxide in oxygen supplemented with isoflurane (Group A; n=15) or sevoflurane (Group B; n=15). After induction of anesthesia, acute hypervolemic hemodilution (HHD) was produced by preoperative infusion of 1,000 mL of 6% hydroxyethylstarch without removing blood in each group and hematocrit value was approximately 26%. Controlled hypotension was induced with prostaglandin E1 (PGE 1) and mean blood pressure was maintained at approximately 55 mmHg for approximately 80 minutes. Gastric intramucosal Pco_2 ($Pmco_2$) was measured using tonometry, and intramucosal to arterical difference in Pco_2 (P [m-a] co_2) and intramucosal pH (pHi) in stomach were calculated. $Pmco_2$, concentration of serum lactate and arterial blood gas were measured before hemodilution, after hemodilution, 80 minutes after starting hypotension, 60 minutes after recovery from hypotension and on the first post-orerative day.

The values of P (m-a)co_2 and pHi did not change after hemodilution and during hypotension in either group. No intergroup differences were found.

In conclusion, the combination of HHD and controlled hypotension induced with prostaglandin E1 under sevoflurane anesthesia did not cause splanchnic hypoperfusion.

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—**Key words**—
Hemodilution, Induced Hypotension, Splanchnic Perfusion

Introduction

Preperative acute hypervolemic hemodilution (HHD) without removal of blood is a simple procedure for conserving autologous blood[1)2)]. Controlled hypotension combined with HHD may be more useful for avoiding allogenic blood transfusion. However, the combined method may cause the changes in systemic and regional hemodynamics because of the acute volume overload and the reduction of perfusion pressure resulting in redistribution within splanchnic perfusion, and it may be influenced by anesthesia.

Partial pressure of carbon dioxide (Pco_2) or calculated pH in gastrointestinal mucosa has been suggested to constitute an index of the adequacy of splanchnic perfusion and the indirect measurement by tonometry has been established as minimally invasive and sensitive means[3)~6)].

It has been reported that the combination of HHD and controlled hypotension induced with prostaglandin E1 (PGE 1) does not cause splanchnic hypoperfusion under isoflurane anesthesia[7)], however, there are no studies that have evaluated the perfusion in such situation under sevoflurane anesthesia in humans. This study was designed to evaluate the effects of PGE1-induced hypotension combined with HHD under sevoflurane anesthesia on splanchnic

perfusion using tonometry.

Methods

The subjects of this investigation were 30 ASA physical status I or II total hip arthroplasty patients, aged 50 to 69 years, weighing 46 to 68 kg, without hypertension, ischemic heart disease, cerebral infarction, hepatic and renal dysfunction and anemia (hemoglobin<11g/dL). All patients had no use of beta blockers. The protocol was approved by the Nagasaki Rosai Hospital Institutional Human Committee and written informed consent was obtained from each patient.

Premedication consisted of atropine sulphate 0.5 mg and hydroxyzine hydrochrolide 1 mg/kg, given intramuscularly 1 hour before the scheduled time of surgery. A dose of 50 mg of ranitidine was given intravenously 2 hours prior to anesthesia induction according to the recommendation by Heard et al[8]. Patients were continuously monitored with pulse oximetry (oxypal OLV -1,200, Nihon Kohden Co., Ltd., Tokyo, Japan) and 3-lead electrocardiogtram. A radial arterial catheter was inserted for continuous monitoring of arterial blood pressure (ABP) and for obtaining blood samples, and ABP and heart rate (HR) were automotically recorded (Bed side monitor BSM-8,500, Life Scope 12, Nihon Kohden Co., Ltd., Tokyo, Japan). Anesthesia was induced with intravenously thiamylal 5 mg/kg and fentanyl 2 mcg/kg. Tracheal intubation was facilitated with intravenously vecuronium bromide 0.1 mg/kg. After induction of anesthesia, patients were randomly divided by sealed envelope assignment into two groups according to the maintainance of anesthesia. Anesthesia was maintained with 60% nitrous oxide in oxygen supplemented with 1.0 to 1.8% end-tidal isoflurane (Group A; n=15) or 1.4 to 2.2% end-tidal sevoflurane (Group B; n=15). Intravenous fentanyl, 1 to 2 mcg/kg, and vecuronium, 0.05 mg/kg, were injected during surgery as required. Ventilation was controlled to maintain end-tidal corbon dioxide tension ($ETCO_2$) at approximately 35 mmHg. $ETCO_2$ and end-expiratory concentration of isoflurane or sevoflurane were continuously monitored and recorded by anesthetic gas monitor (Capnomac; Datex Instrumentarium, Helsinki, Finland). Acetated Ringer's solution was infused to the amount of 15 mL/kg prior to surgery during a 4hr period. The infusion was continued at a rate of 4 to 6 mL/kg/hr during surgery. Additional acetated Ringer's solution was infused to the amount three times the blood loss. HHD was produced by preoperative infusion of 1,000 mL of 6% hydroxyethylstarch solution (HES; molecular weight=70,000) without removing blood in each group. six% HES was infused at a rate of approximately 50 mL/min. Controlled hypotension was induced by prostaglandin E1 (PGE 1), and mean arterial blood pressure (MAP) was maintained at 55 to 60 mmHg for approximately 80 minutes during surgery. Autologous blood stored by a cell saver (Haemolight, Haemonetics, Corp., Boston, USA) during and after surgery was retransfused in each group. Measurements included systemic hemodynamics (MAP, HR and hematocrit), $Pmco_2$, arterial blood gas and concentration of serum lactate. A nasogastric tube with a silicone rubber balloon (TRIP-NGS catheter, Tonometrics Inc., Worcester, MA, USA) was used to measure $Pmco_2$ in stomach according to the method described by Fiddian-Green[9]. The tube was inserted into the stomach and exactly placed by roentgenography. The balloon of the tonometer was filled with 2.5 mL of normal saline solution. After the equilibration time of Pco_2 between the saline and the gastric lumen, the first mL of fluid obtained from the balloon was discarded to account for the dead space of the conduit, and the remaining 1.5 mL was measured for Pco_2. At the same time, samples of arterial blood were obtained for calculation of sodium bicarbonate (HCO_3^-) and measurement of serum lactate. The intramucosal to arterial difference in Pco_2 ($P[m\text{-}a]co_2$) and intramucosal pH (pHi) in stomach were calculated for the detection of splanchnic perfusion. Henderson-Hasselbalch equation was used for calculation of gastric pHi using arterial HCO_3^- value according to the recommendation by Fiddian-Green et al[9]. Arterial blood gas was analyzed by a blood gas analyzer (ABL-4, Radiometer Corp., Copenhagen, Denmark). Arterial lactate was measured by enzymatic analysis (Enzyme immunoassay kit, Determiner LA, Kyowa, Medix, Tokyo, Japan). Hematocrit (Hct)value was determined by centrifugatation. The measurements were made before hemodilution (T0), after hemodilution (T1), 80 minutes after starting hypotension (T2), 60 minutes after recovery from hypotension (T3), and on the first post-operative day (T4). The blood and the saline samples were analyzed immediately after collection in the operating room. The equilibration time of saline within the ballon of the tonometer was set as 30 minutes at T0 and T1, 80 minutes at T2 and 60 minutes at T3 according to the operative process, and 90 minutes at T4.

Data are expressed as means ± SD. Analysis of variance, Scheffe's test and Unpaired Student's t-test were used

for statistical analysis. A p-value less than 0.05 was considered statistically significant.

Results

The two groups were similar in demographic characteristics (gender, age, and weight), surgical period, hypotensive period, blood loss, urinary output, and infusion volume (Table 1.). Total dosage of PGE1 was 656 ± 114 mcg in group A and 679 ± 142 mcg in group B.

The changes of Hct and hemodynamic and arterial blood gas variables in groups A and B are shown in table 2. Hct value was 26 ± 2% in group A and 27 ± 2% in group B. During controlled hypotension, MAP was maintained at approximately 55 mmHg in each group. No differences in hemodynamic variables were observed between the two groups throughout the study.

The changes of lactate, P(m-a)co_2 and pHi in each group are shown in Figure 1. Arterial lactate concentrations showed no change throughout the time course. P(m-a)co_2 values showed no significant increase and pHi values showed no significant decrease at T1 and T2 in the two groups. Intergroup differences were found between the two groups. The mean pHi values both groups were more than 7.32 throughout the time course.

Discussion

The present study shows that the combination of HHD and PGE1-induced hypotension did not cause splanchnic hypoperfusion.

The high P(m-a)co_2 or low pHi gastric intramucosa indicates the insufficient tissue oxygenation due to gastrointestinal hypoperfusion[10]. Although commonly accepted abnomal value for P(m-a) co_2 in gastric mucosa has

Table 1 Patient Group Characteristics

	Group A	Group B
N（Male/Female）	15（1/14）	15（1/14）
Age（years）	60±9	62±7
Weight（kg）	56±10	55±12
Operative period（min）	104±21	102±18
Hypotensive period（min）	80±5	79±3
Intraoperative infusion volume（mL）	1,922±204	1,968±174
Postoperative infusion volume（mL）	1,345±202	1,277±169
Intraoperative blood loss（mL）	491±164	509±123
Postoperative blood loss（mL）	511±208	524±241
Intraoperative urinary output（mL）	365±168	390±182
Postoperative urinary output（mL）	449±262	423±216

Data are means±SD.
Group A=induced hypotension with acute hypervolemic hemodilution under isoflurane anesthesia ; Group B=induced hypotension with acute hypervolemic hemodilution under sevoflurane anesthesia.

Table 2 Changes in hematocrit and hemodynamic and blood gas valiables in Group A and Group B

Time	T0		T1		T2		T3		T4	
Group	A	B	A	B	A	B	A	B	A	B
HCT（%）	36±2	37±3	26±2†	27±2†	24±3†	26±3†	24±2†	25±3†	31±5	32±4
MAP（mmHg）	98±7	96±6	101±6	102±9	56±3††	56±2††	94±9	91±12	100±14	98±12
HR（beats/min）	73±9	69±10	68±8	66±7	77±6	75±8	71±8	70±6	65±14	68±12
pHa	7.458±0.039	7.464±0.029	7.454±0.035	7.448±0.042	7.443±0.032	7.439±0.040	7.438±0.038	7.441±0.034	7.443±0.039	7.437±0.036
Pao_2（mmHg）	196±28	193±30	188±25	190±27	186±16	184±18	182±22	189±24	179±45	182±42
$Paco_2$（mmHg）	38±4	37±3	36±3	37±3	37±4	35±3	36±3	37±4	40±4	39±3

Data are means±SD.
† $p<0.01$ vs. T0. †† $p<0.001$ vs. T0.
T0=before hemodilution ; T1=after hemodilution ; T2=80 minutes after starting hypotension ; T3=60 minutes after recovery from hypotension ; T4=first post-operative day ; HCT=hematocrit ; MAP=mean arterial pressure ; HR=heart rate ; pHa=arterial blood pH ; Pao_2=arterial oxygen partial pressure ; $Paco_2$=arterial carbon dioxide partial pressure.

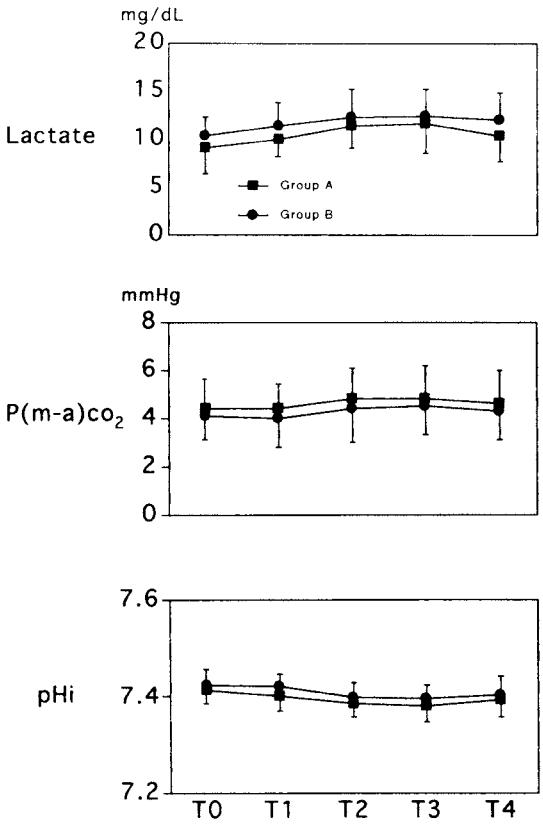

Fig. 1 Time course of changes in lactate, gastric P(m-a)co_2 and gastric pHi in groups A and B (means ± SD, n=15 for each point).
Group A=induced hypotension with acute hypervolemic hemodilution under isoflurane anesthesia, Group B=induced hypotension with acute hypervolemic hemodilution under sevoflurane anesthesia, T0=before hemodilution, T1=after hemodilution, T2=80 minutes after starting hypotension, T4=first postoperative day, P (m-a) co_2 =the intramucosal to arterial difference in Pco_2 in stomach, pHi=gastric intramucosal pH.
Within normal range: lactate 9 to 16 mg/dL, gastric, pHi>7.32.

not been established, it has been known that the lower limit of pHi in critically ill patients is between 7.32 and 7.35[3] and in perioperative studies is less than 7.32[11]. Sevoflurane is similar to isoflurane in its effect on cardiovascular responses[12)13)] and regional blood flow including liver and kindney[14)15)]. It has been reported that 1 minimum alveolar anesthetic concentration (MAC) of sevoflurane or isoflurane decreased gastrointestinal bloood flow in swine[14)15)], but 0.7 MAC of sevoflurane or isoflurane did not decrease in rats[16].

In the present study, HHD did not result in excessively high arterial blood pressure (SBP>180 mmHg) and low arterial oxygen partial pressure (PaO_2). Sevoflurane anesthesia could attenuate cardio-pulmonary vascular responses to HHD with acute large intravascular volume by inducing vasodilation. The mean values of P(m-a)co_2 and pHi showed no change after HHD under sevoflurane anesthesia and pHi value was greater than 7.35. The results indicate that HHD under sevoflurane anesthesia would preserve cardiac output and gastrointestinal perfusion for adequate intravacular volume. Diebel et al[17]. showed that as long as an adequate intravacular volume is maintained, hemodilution is well tolerated.

PGE1-induced hypotension combined with HHD under sevoflurane anesthesia showed no increase in gastric P(m-a)co_2 and no decrease in pHi. This results suggest that PGE1-induced hypotension during HHD under sevoflurane anesthesia would not impair gastrointestinal perfusion. PGE1 during hypotension may show several advantageous effects, e. g., positive inotropic action and increasing action in splanchnic blood flow[18)19)]. PGE1 also reduces systemic vascular resistance[18] and increases gastric mucosal blood flow[20]. PGE1-induced hypotension under sevoflurane anesthesia can preserve hepatic and renal function[21)22)] and may show increase of splanchnic blood flow[23]. Krejci et al[24]. have reported that the changes in the distribution of microcirculatory blood flow in the gas-

trointestinal tract during acute hemorrhagic shock under halothane anesthesia cannot be predicted from changes in systemic or regional hemodynamics in animals. However, Hamilton-Davies et al[25]. reported that the gastric Pco_2 gradient measured by tonometry proved an early, sensitive indicator of general hypoperfusion during hemorrhage in healthy volunteers. In the present study, it seems that the combination under sevoflurane anesthesia would not cause the inadequate distribution to gastrointestinal perfusion for the preservation of systemic and regional hemodynamics. The reaction could be similar in the combination under isoflurane anesthesia because gastric P (m-a) co_2 and pHi values were no different between the two groups.

Systemic hypoxia would not cause during the combination because the blood lactate concentrations showed no change.

In conclusion, HHD under sevoflurane anesthesia does not impair splanchnic perfusion and the combination of controlled hypotension induced with prostaglandin El would not aggravate the perfusion.

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セボフルレン麻酔下での急速高容量性血液希釈とプロスタグランジン E1による低血圧麻酔併用が腹腔内臓器潅流に及ぼす影響

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長崎労災病院麻酔科

―キーワード―
血液希釈，低血圧麻酔，腹腔内臓器潅流

セボフルレン麻酔下における急速高容量性血液希釈とプロスタグランジンE1による低血圧麻酔併用が腹腔内臓器潅流に及ぼす影響をイソフルレン麻酔下の場合と比較検討した．本研究の被検者として同意を得た30名の股関節予定手術をうける患者を対象とした．無作為にA群（イソフルレン麻酔，15名），とB群（セボフルレン麻酔，15名）の2群に分けた．各々麻酔導入後，脱血なしにヒドロキシエチルスターチ1,000mlの急速輸液による高容量性血液希釈を行い，術中はプロスタグランジン E1（PGE1）にて平均血圧を約55mmHg に約80分間維持した．腹腔内臓器潅流の指標として胃トノミータを留置後，間接的に胃粘膜内Pco_2を測定し，胃粘膜内―動脈血Pco_2較差（P[m-a]co_2）および胃粘膜内pH（pHi）を計算にて求めた．これらの指標を血中乳酸値とともに，血液希釈前，血液希釈後，低血圧麻酔開始80分後，低血圧麻酔終了60分後，術後1日目に測定した．これらの指標は2群とも時間経過において有意な変化はなく，両群間においても有意差は認めなかった．セボフルレン麻酔下での高容量性血液希釈とPGE1による低血圧麻酔併用は腹腔内臓器潅流を維持し，それはイソフルレン麻酔下と同等であろう．