Original Article

Regional and Systemic Hemodynamics During Isovolemic Hemodilution Alone and Combined with Halothane or Trimethaphan Induced Controlled Hypotension

Masao KOBORI　Hideru NEGISHI
Department of Anesthesiology, School of Medicine, Showa University
Masatoshi KUNO　Hiroyoshi YAMAZAKI　Kinuko GOTOH
Department of Anesthesia, School of Dentistry,Showa University

Abstract

We randomly divided adult mongrel dogs into 2 groups. The dogs were subjected to acute isovolemic hemodilution until the Hct value was reduced by approximately one-half in both groups. While in the hemodiluted condition, hypotension was induced by inspired concentration of halothane (group H) or intravenous infusion of trimethaphan (group T) to reduce mAP to 60 mmHg. Hemodilution combined with halothane-induced hypotension reduced mAP, CI, and LVSWI in comparison with control or hemodilution-alone values. However, hypotension induced with trimethaphan was associated with a marked reduction in mAP and LVSWI without a change in CI as compared with the control values. RBF decreased significantly during hemodilution combined with induced hypotension as compared with the control or hemodilution-alone values in both groups. However, LBF decreased significantly in group H, but not in group T, during hemodilution combined with induced hypotension as compared with the control or hemodilution-alone values.

These results indicate that trimethaphan is a safer hypotensive agent in terms of its effects on systemic and regional hemodynamics than halothane during combined hemodilution and induced hypotension.

Introduction

Hemodilution is accepted technique during major surgey because it reduces the need for homologous blood transfusion. Controlled hypotension is a well established technique to decrease blood loss and improve surgical visibility. Currently, trimethaphan induced hypotensive anesthesia is used widely during surgery. In addition, halothane causes a dose-dependent arterial hypotension. Preoperative hemodilution with self blood donation is being used increasingly in combination with controlled hypotension to conserve blood.

The objective of this experimental study was to evaluate systemic hemodynamic and regional blood flow responses during isovolemic hemodilution alone and combined with halothane- or trimethaphan-induced hypotension in anesthetized dogs.

Materials and methods

The experiments were performed on 12 adults male mongrel dogs weighing 12-16 kg allocated randomly to 2 groups of 6 dogs each: the halothane (H) group ; and the trimethaphan (T) group.

The experimental animals were anesthetized with sodium pentobarbital 30 mg/kg iv. Pancuronium bromide 0.2 mg/kg was administered after insertion of an endotracheal tube, and the dogs were

ventilated via a cuffed endotracheal tube with 0.5% halothane in 50% nitrous oxide using a Harvard respirator. Tidal volumes were adjusted to maintain end-expiratory ETCO2 at 30-40 mmHg, as monitored with an infrared CO2 analyzer. The animals were maintained in the supine position under anesthesia.

Bilateral femoral veins were cannulated for the infusion of 0.9% saline at the rate of 5ml/kg·h as a maintenance dose, for withdrawal of blood, and for volume replacement. The left femoral artery was cannulated for continuous systemic arterial pressure monitoring and for blood sampling. A 7.5– French balloon-tripped triple-lumen pulmonary catheter (Swan-Gantz catheter) was cannulated via the right external jugular vein and positioned in a branch of the pulmonary artery to measure hemodynamic variables. Cardiac output (CO) was determined using the thermodilution technique (5 ml of 0.9% saline at 0°C into the right atrium at end-expiration). The heart rate (HR) was calculated from lead II of an electocardiograph using a cardiotachometer.

Regional blood flow was determined by the hydrogen gas clearance method. Laparotomy was performed and hydrogen gas clearance electrodes were inserted into the kidney and liver.

The dogs were allowed to stabilize for at least 60 min after surgical preparation and then control physiological measurements, including hemodynamic and blood gases analysis (control values) were obtained. Hematocrit (Hct) values did not differ significantly between the 2 groups (H group, 41.8±3.2% ; T group, 38.1±7.5%). The animals were then subjected to acute normovolemic hemodilution, which was achieved by exchanging an equivalent volume of blood with 6% hydroxyethyl starch (MW 70,000) in saline until the Hct value was reduced by approximately one-half in both groups. After the hemodilution, the Hct values did not differ significantly between the groups (H group, 20.1±2.0% ; t group, 19.0±3.3%).

A second set of measurements was obtained after a 30 min stabilization period after the completion of the hemodilution. In the hemodiluted condition, hypotension was induced in the dogs by either inspired concentration of halothane (in the range of 1.6-3.4%) or intravenous infusion of trimethaphan (in the range of 0.4-1.4 mg/kg h) to reduce mean arterial pressure (mAP) to 60 mmHg. A third and fourth set of measurements was then obtained in the combined hemodilution and hypotension condition at 30 min and 60 min, respectively. Then the hypotension induced for 60 min. The hypotension was ceased and 30 min was allowed to recover before final measurements of all parameters were obtained.

The parameters measured in the 2 groups were: HR; mAP; CO; arterial oxygen partial pressure (PaO2); arterial carbon dioxide partial pressure (PaCO2); renal blood flow (RBF); and liver blood flow (LBF).The Hct value was measured by centrifuging sampled blood at 5,000 rpm for 5 min. The cardiac index (CI), systemic vascular resistance (SVR), and left ventricular stroke work index (LVSWI) were calculated using the standard formulas, respectively.

Data are expressed as mean±standard error (SE). Comparisons between the control or hemodilution-alone values and the experimental measurements in each group were made using Student's paired t-test, with $p<0.05$ considered statistically significant. Differences between the 2 groups were analyzed for variance using the unpaired t-test, with $P<0.05$ considered statistically significance.

Results

The control and isovolemic hemodilution-alone values did not differ significantly between the 2 groups.

[1] Hemodynamic variables

Hemodynamic varlables are shown in the Table. The change in HR was not

significant either group under hemodilution alone. However, HR decreased significantly during the course of the hypotensive and recovery periods as compared with the control or hemodilution-alone values in both groups. mAP decreased significantly during hemodilution alone and when hemodilution was combined with induced hypotension in all experimental periods in both groups. CI increased significantly due to hemodilution alone in both groups. However, CI decreased significantly in the H group during the hypotensive periods as compared with the control or hemodilution-alone values. No significant change in CI was observed during the trimethaphan induced hypotensive period as compared with the control value. SVR decreased significantly during all the experimental periods in both groups. However, no significant change in SVR was observed with hemodilution alone in either group. LVSWI did not change significantly due to hemodilution alone in 2 groups, although it decreased significantly during the hypotensive periods as compared with that of the control or hemodilution-alone. In addition, during the hypotensive and recovery period, the differences in LVSWI measured were statistically significant between the 2 groups.

[2] Respiratory variables

The control PaO2 and PaCO2 values did not differ significantly between the 2 groups. In group H, the mean PaO2 value was 172±12 mmHg and the mean PaCO2 value was 36.3±0.7 mmHg in control period. In group T, the mean PaO2 value was 183±9 mmHg and the mean PaCO2 value was 36.2±1.3 mmHg.

[3] Regional blood flows

The organ blood flows are shown in the Table. Hemodilution alone caused a significant decrease in RBF, but not in LBF. During the hypotensive and recovery period, RBF decreased significantly as compared with the control value in both groups, but the change was not significant when compared with hemodilution alone. RBF did not differ significantly between group H and T. On the other hand, during hypotensive period LBF in group H decreased significantly compared to the control or hemodilution-alone values. In contrast, LBF in group T did not differ significantly during hypotension compared with the control or hemodilution-alone values. However, LBF also did not differ significantly between group H and T.

Discussion

Acute isovolemic hemodilution entails collecting blood from a patient immediately prior to surgery with simultaneous colloidal fluid infusion to maintain the intravascular volume constant. This technique is advocated as a means to reduce the need for homologous blood transfusion during surgery.Compensation for the decrease in blood oxygen content due to hemodilution is supported by an increase in CO and more efficient extraction of oxygen from the blood. Crystal et al[1] have found that the blood flows in the renal cortex and liver were unchanged during hemodilution, but increased in the brain and myocardium. Generally, coronary and cerebral blood flows appear to be affected more than flow to the splanchnic organs when the Hct is reduced. In the present study, CO increased significantly during hemodilution. However, hemodilution caused a significant decrease in RBF.

The safety of any method for inducing hypotension is dependent on a number of factors, but the integrity of the cardiac pumping function is perhaps the most important in the maintenance of organ blood flow. The concentration of inspired anesthesia suppresses cardiac function in a dose-dependent manner. Prys-Roberts et al[2] reported that the greatest disadvantage of halothane for indication of hypotension is its dose-dependent reduction of CO and depression of the contractile force of

Table Systemic and Regional Hemodynamics

		Control	HD alone	HD/HP 30 min	HD/HP 60 min	Recovery
HR	H	162±13	142±9	117±4[ab]	116±6[ab]	120±5[ab]
	T	144±5	128±11	110±7[ab]	108±7[ab]	112±5[ab]
mAP	H	115±5	86±2[a]	56±1[ab]	60±1[ab]	76±3[ab]
	T	115±9	82±4[a]	59±1[ab]	60±1[ab]	80±3[a]
CI	H	1.62±0.13	1.95±0.15[a]	1.13±0.11[ab]	1.15±0.10[ab]	1.50±0.07[b]
	T	1.63±0.19	2.19±0.18[a]	1.47±0.19[b]	1.47±0.20[b]	1.87±0.20[b]
SVR	H	9556±976	5908±729[a]	6577±979[a]	6952±1003[a]	6448±682[a]
	T	10286±1415	5168±703[a]	5852±1014[a]	6032±1152[a]	6173±995[a]
LVSWI	H	15.0±2.3	14.2±1.7	5.9±0.7[abc]	6.8±0.8[abc]	11.6±1.1[ac]
	T	15.5±1.3	16.4±1.6	9.0±0.9[ab]	9.2±0.9[ab]	15.9±1.1
RBF	H	149±10	112±7[a]	97±3[a]	99±4[a]	107±4[a]
	T	137±13	109±4[a]	93±4[a]	98±4[a]	104±9[a]
LBF	H	49±5	49±3	35±5[ab]	35±5[ab]	46±4
	T	53±8	50±6	40±5	40±5	51±4

Data are expressed as mean±standard error(SE)
HR(heart rate;beats·min^{-1}), mAP(mean arterial pressure;mmHg), CI(cardiac index;l·min^{-1}·m^{-2}), SVR(systemic vascular resistance;dyn·sec·cm^{-5}), LVSWI(left ventricular stroke work index; g·m·beat^{-1}·m^{-2}), RBF(renal blood flow;ml·min^{-1}·100g^{-1}), LBF(liver blood flow;ml·min^{-1}·100g^{-1})
H:halothane group, T:trimethaphan group
HD:hemodilution, HP:hypotension
Control:control period, HD alone:30 min after HD, HD/HP 30 min:30 min after induction of HP
HD/HP 60 min:60 min after induction of HP, Recovery:30 min after cessation of hypotensive procedure
[a]$P<0.05$, from control
[b]$P<0.05$, from HD alone
[c]$P<0.05$, between group H and group T

the myocardium. Gelman et al[3] found that myocardial blood flow increased during isoflurane anesthesia and decreased during halothane. However, Merin et al[4] suggested that the dose-dependent negative inotropic effect of halothane resulted in a decrease in cardiac oxygen demand which was balanced with the decrease in oxygen delivery or increased in some instances. On the other hand, Scott et al[5] have demonstrated that trimethaphan does not have a direct myocardial depressant action.

In our results, hemodilution combined with halothane-induced hypotension reduced mAP, CI and LVSWI as compared with those in control or hemodilution period. In contrast, the same degree of arterial hypotension as induced with trimethaphan was associated with a marked reduction in mAP and LVSWI without any marked change in CI as compared with control value. Futhermore, LVSWI was significantly higher in group T than in group H during the hypotensive and recovery periods. The present study indicated that the concentration of halothane using the controlled hypotension might cause negative inotropic effects.

Gelman et al[3] found that LBF and oxygen supply to the liver were better maintained during isoflurane than during halothane anesthesia. In addltion, administration of trimethaphan results in a decause in splanchnic blood flow. Colley et al[6] suggested that blood flow to the kidney and liver were maintained at control levels during nitrogricerine-induced hypotension. Behnia et al[7] have reported that the oxygen tension value of the kidney was maintained during trimethaphan-induced hypotension. In the present study, RBF decreased significantly during hemodilution combined with induced hypotension as compared with the control values in both groups. RBF between group H and T were statistically indistinguishable. During hemodilution combined with

induced hypotension, LBF showed a significant decreased in group H, but not in group T, as compared with the control or hemodilution-alone values. While LBF did not differ significantly in both groups, LBF was tended better to maintain during trimethaphan- than during halothane-controlled hypotension.

In this study, the experimental animals underwent 60 min of isovolemic hemodilution combined with induced hypotension. Ahlgren et al[8] reported that LBF was reduced during long-term (120 min) halothane-induced hypotension with hemodilution and suggested that halothane may cause hepatic damage due to hepatic ischemia. Similary, Plewes et al[9] indicated that, at least for 30 min, hemodilution combined with trimethaphan-induced hypotension was a relatively safe technique. However, changes seen by 90 min could result in major decreases in oxygen delivery to important organs.

The findings in the present study suggest that trimethaphan is a safer hypotensive agent in terms of the hemodynamic and regional blood flow variables during combined hemodilution than halothane.

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