Original Article

Influence of isoflurane anesthesia on systemic and regional hemodynamics - Comparison of not hemodiluted and hemodiluted state -

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Abstract

We divided adult mongrel dogs into a not hemodiluted group (N group, hematocrit value 38±3%) and a hemodiluted group (H group, hematocrit value 20±1%).In both the groups, control measurements were taken at the isoflurane 1 MAC level. After this, the inspired concentration of isoflurane was increased to a 2 MAC level, and then further increased to a 3 MAC level. With an increased concentration of insplred isoflurane, in both groups a considerable reduction was seen in hemodynamic variables, renal, and liver tissue blood flow. However at the 3 MAC level the mean arterial pressure value and renal tissue blood flow were significantly higher in the N group.

Our results indicate that anesthesiologists should be attentive to hemodynamics and regional blood flow when administering concentrated isoflurane to patients undergoing surgery, particularly if it involves using an intraoperative hemodiluted technlque.

Introduction

Hemodilution and autologous blood transfusion eliminate the risk of hepatitis, reduce erythrocyte loss, and decrease demands on a blood bank. Compensatory responses, such as increased cardiac output, occure following hemodilution. Generally, coronary and cerebral blood flow appear to be more affected than flow to the splanchnic blood vessels when the oxygen carrying capacity of the blood is reduced. However, which hemodynamic and regional blood flow is suppressed by the anesthetic depends on the administered dose.

This study has investigated the effect of hemodilution in anesthetized dogs by measuring hemodynamic and regional blood flow before and after a hemodilution.

Materials and Methods

The experiments were performed on 7 adult male mongrel dogs weighing 10-14 kg. The animals were anesthetized with sodium pentobarbital (30mg/kg i.v.). Pancuronium bromide (0.2 mg/kg) was administered after insertion of an endotracheal tube, and the dogs were ventilated with a 1.15% of isoflurane in oxygen (1MAC) using a Harvard respirator. Tidal volumes were adjusted to maintain an end-tidal CO_2 (ETCO_2) of 30-40 mmHg, which was monitored with an infrated CO_2 analyzer. The animals were maintained in the supine position while under anesthesia.

The femoral veins were cannulated bilaterally for infusion of a lactated Ringer's solution at a rate of 5 ml/kg/h as a maintenance dose. Blood which was to be diluted was obtained from these cannulae. The left femoral artery was cannulated for continuous systemic arterial pressure monitoring and for blood sampling. A 7-French pigtail catheter was passed into the left ventricle via the right femoral artery. After positioning, this catheter was used for measurements of left ventricular pressure.

The maximum rate of the left ventricular pressure change (LV dp/dt max) was electrically derived from the signal of the left ventricular pressure wave by using an electronic differentiator.

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. This catheter permitted measurements to be made of a number of hemodynamic variables. Cardiac output (CO) was determined by the thermodilution technique (5 ml of 0.9% saline at 0°C injected into the right atrium at end-expiration). The heart rate (HR) was calculated from records obtained from lead II an electocardiogram, by using a cardiotachometer.

The hydrogen gas clearance method was used to determine the blood flow through organs. A laparotomy was performed so that the electrodes could be placed, and hydrogen gas clearance electrodes were inserted into the kidney and liver.

After the surgery was completed for dogs in the not hemodiluted group (N group) and a steady anesthetic state was maintained, samples and control measurements were taken of the isoflurane 1 MAC level. After this, by adjusting the vaporizer setting, the concentration of isoflurane inspired was increased to a 2 MAC level (2.30% of isoflurane in oxygen) and then further increased to a 3 MAC level (3.45% of isoflurane in oxygen). Measurements of all investigated variables were taken 30 min after attaining the increased isoflurane concentration at each MAC level (N group hematocrit value 38±3%).

Next the dogs were subjected to an acute isovolemic hemodilution. This was achieved by exchanging a blood volume equivalent, using 6% hydroxyethyl starch ((MW 70,000) in sallne, until the hematocrit value was reduced to approximately half (H group hematocrit value 20± 1%). For dog in the H group, after completion of the acute isovolemic hemodilution, measurements of all the investigated parameters were performed in the same manner as for the N group at the 1 MAC concentration of isoflurane. The same methods were also used for the 2 MAC and 3 MAC levels, i.e. 30 min after reaching each increased MAC level.

The parameters measured in both groups were as follows: heart rate (HR). mean arterial pressure (mAP), mean pulmonay arterial pressure (mPAP), pulmonary arterial wedge pressure (PAWP), central venous pressure (CVP), cardiac output (CO), left intraventricular pressure (LVP), partial arterial oxygen pressure (PaO2), partial arterial carbon dioxide pressure (PaCO2), renal tissue blood flow (RBF), and liver tissue blood flow (LBF). The hematocrit (Hct) value was measured by centrifuging sampled blood at 5,000 rpm for 5 min. The cardiac index (CI), maximum rate of the left ventricular pressure change (LV dp/dt max), and systemic vascular resistance (SVR) were calculated using standard formulas.

All data are expressed as mean±standard error (SE), and stastistical comparisons were made by using Student's paired t-test. Comparisons between values at 1 MAC levels and at 2 and 3 MAC, and between values at 2 MAC levels and at 3 MAC for each group of dogs were performed by an analysis of variance ($P<0.05$ considered as statistically significant). Differences between both groups were analyzed by using unpaired t-test, with $p<0.05$ considered as statistically significant.

Table Systemic and Regional Hemodynamics

		1MAC	2MAC	3MAC
HR	N	125±4	116±3^{a}	110±3^{a}
	H	121±4	113±6^{a}	101±7^{ab}
mAP	N	107±9	75±7^{a}	46±4^{abc}
	H	95±8	62±6^{a}	36±3^{ab}
mPAP	N	19±3	19±2	17±2^{a}
	H	21±3	17±2^{a}	16±1^{a}
PAWP	N	13±3	14±2	13±1
	H	15±2	13±2	14±1
CVP	N	7±1	8±1	9±1
	H	9±1	9±1	10±1
CI	N	1.85±0.15	1.26±0.09^{a}	0.81±0.06^{ab}
	H	2.04±0.15	1.37±0.12^{a}	0.74±0.09^{ab}
LV dp/dt max	N	1900±163	1029±106^{a}	629±68^{ab}
	H	1886±189	1100±184^{a}	514±70^{ab}
SVR	N	6326±329^{c}	6255±475^{c}	5257±756^{ac}
	H	5024±461	4606±421	4052±691^{a}
RBF	N	141±19	128±17^{a}	91±8^{abc}
	H	133±16	112±19^{a}	76±16^{ab}
LBF	N	60±8	36±6^{a}	19±3^{ab}
	H	45±7	27±5^{a}	14±2^{ab}

Values are a mean±standard error (SE)

HR (heart rate;beats·min^{-1}), mAP (mean arterial pressure;mmHg), mPAP (mean pulmonary arterialpressure;mmHg), PAWP (pulmonary arterial wedge pressure;mmHg), CVP (cetral venous pressure;mmHg), CI (cardiac index;l·min^{-1}·m^{-2}), LV dp/dt max (left ventricular maximum rate of pressure change;mmHg·sec^{-1}), SVR (systemic vascular resistance;dyn·sec·cm^{-5})

RBF (renal tissue blood flow;ml·min^{-1}·100g^{-1}), LBF (liver blood flow;ml·min^{-1}·100g^{-1})

N:no hemodiluted group,

H:hemodiluted group

$^{a}P<0.05$, versus 1MAC

$^{b}P<0.05$, versus 2MAC

$^{c}P<0.05$, between group N and group H

Results

1. Hemodynamic variables

The values of hemodynamic variables are shown in Table. The hemodynamic changes on increasing the amount of the isoflurane did not differ significantly in either group of dogs with respect to the PAWA and CVP values. But changes in the HR, mAP, mPAP, CI, LV dp/dt max, and SVR values were significant. With an increase in the concentration of inspired isoflurane, a remarkable reduction in the values of the hemodynamic variables was seen in both groups. However, the mAP value at the 3 MAC level was significantly higher in the N group than in the H group. In addition, SVR was signiflcantly greater in the N group than in the H group during the experimental period.

2. Respiratory variables

At the 1 MAC level of respiration, the control values of PaO2 and PaCO2 did not significantly differ between the N and H groups. In group N, the mean PaO2 value was 557±24 mmHg, and the mean PaCO2 value was 36±2 mmHg, whereas in the H group the mean PaO2 value was 545± 31 mmHg and the mean PaCO2 value was 38±2 mmHg.

3. Regional variables

The values of regional variables are shown in Table. With an increase in the concentration of the inspired isoflurane, an even greater reduction in all the blood flow of all organs was seen in both groups. Furthermore, there was a significant difference in RBF between group N and H at the 3 MAC level.

Discussion

The preoperative hemodilutional method is simple, does not require special instrumentation and can therefore be used on a routine basis in any type of hospital. Hemodilution entails collecting blood from a patient immediately prior surgery, with concurrent fluid infusion to maintain the intravascular volume so that it is constant. Many investigators[1-3] have reported, for reason of safety and practicability, colloid solutions rather than crystalloid solutions should be used when hemodilution is planned. Mirhashemi et al[4] have suggested that hemodilution is particularly effective for increasing oxygenation of ischemic tissue, while it has a comparatively small effect in normal conditions. Gelman et al[5] investigated myocardial blood flow and found it was increased during isoflurane inhalation (despite decreased blood pressure and cardiac output) and decreased during halothane anesthesia. In this regard, Kobori et al[6] have reported that the hemodynamic effects of halothane anesthesia appear to be more detrimental in both the normal and hemodiluted state compared to those during isoflurane anesthesia. However, pribe et al[7] have investigated the effects on coronary hemodynamics of isoflurane-induced hypotention when combined with coronary artery stenosis. Their data indicates that in the presence of coronary artery stenosis influrane-induced hypotension may cause regional myocardial dysfunction, suggestive of ischemia. In the present study, with an increase in the concentration of inspired isoflurane, a remarkable reduction in the values of the hemodynamic variables was seen in both groups. The effects of isoflurane anesthesia on the values of the hemodynamic variables were almost identical in both the N and H groups. However, Kobori et al[8] investigated that concentration of inspired isoflurane suppresses cardiac function in a dose-dependent manner.

Gelman et al[5] suggested that halothane preserved hepatic artery blood flow at the 1 MAC level and decreased it at 2 MAC, while isoflurane increased it at both levels of anesthesia. The reason for this may be because, isoflurane is a dilator of the hepatic artery vascular bed, and/or that autoregulatory ability of the liver to increase hepatic artery blood flow in response to decreased portal blood flow is better preserved during isoflurane than during halothane anesthesia. Contzen et al[9] found that the total hepatic and renal blood flow remained unchange from the control value (mean arterial pressure of 70 mmHg) but decreased to a mean arterial pressure of 50 mmHg during isoflurane anesthesia. In the present study, a decrease in the regional blood flow after an increase in the concentration of inspired isoflurane paralleled suppression of hemodynamic variables. The data suggests that the maintainance of regional blood flow under inspired isoflurane is produced by the stability of hemodynamic variables. However, contzen et al[10] observed that isoflurane significantly decreased total hepatic blood flow, whereas oxygen consumption of the splanchnic viscera remained unchanged.

With hemodilution and normal heart conditions, the cardiac output increases to conpensate for the reduced oxygen carrying capacity of the blood and so maintains oxygen delivery to the tissues. Factors that contribute to the increase in cardiac output are reduction in blood viscosity and cardiac sympathetic activity. In particular, sympathetic activity is suppressed by high concentrations of an inspired anesthetics. On the other hand, if there is an associated rise in oxygen requirement because reason of a low concentration of an inspired anesthetic, the margin of safety for hemodilution may be compromised[11].

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