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A519

TITLE:EFFECT OF HALOTHANE ON PLATELET INTERACTION WITH CORONARY CIRCULATION

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Platelets play an important role in the pathophysiolgy of coronary insufficiency. When activated by the atheroslerotic plaque, they aggregate and adhere to the vessel wall and release several spasm mediators. It has been shown that halothane inhibits the cyclic flow reduction induced by platelets in critically stenosed canine coronary arteries in vivo (1) and that it also reduces the aggregation of platelets in vitro(2). To further study the effect of halothane on platelet interaction with coronary circulation, we measured its effect on platelets deposition in coronary vessels and on the increase of coronary perfusion pressure (CPP) and left ventricular pressure (LVP) induced by platelets in isolated rat hearts.

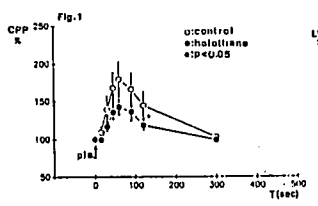
Rat hearts were continuously perfused by an oxygenated (O_2 95%, CO_2 5%) Krebs-Ringer solution at a constant flow of 9 ± 2 cc/min in a Langendorff system. The CPP and the LVP were continuously measured. Half the hearts were perfused with the Krebs-Ringer solution equilibrated with 1.1% halothane (1 MAC in rat). Human platelets obtained from healthy donors were washed and diluted in normal saline and added to the perfusion line of control and halothane-treated hearts for 60 seconds, at 0.25 cc/min, to reach a final concentration of $17 \pm 2 \times 10^9$ pl/L. Platelet counts were obtained for both the affluent and effluent solutions. The data were analyzed using ANOVA and unpaired t-test with $p < 0.05$ as significant.

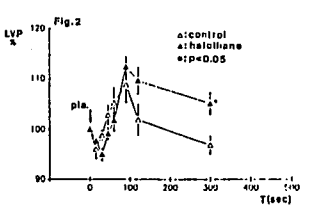
Platelets increased the CPP by a mean of $79.18 \pm 23.08\%$ and had a biphasic effect (decrease of $3.94 \pm 1.91\%$ and increase of 8.86 ± 3.45 %) on LVP. These effects were attenuated by halothane (Fig 1-2). Halothane also reduced platelet trapping in coronary circulation as shown by a platelet recovery of $40.8 \pm 1.3\%$ in the control group and $56.6 \pm 7.9\%$ in the halothane group($p < 0.05$).

These data confirm halothane's effect on platelet interaction with coronary circulation and myocardial function, in a model where only the heart was treated with halothane. We could expect a larger effect when both platelets and heart are pre-treated with halothane. The results suggest that halothane is a good anesthetic agent for patients with coronary artery diseases.

References:

1. Anesthesiology, 1989, pp 96-102.
2. Anesthesiology, 1990, A586.





A520

TITLE:DO HALOTHANE AND ISOFLURANE INHIBIT THE RELEASE OF 5-HYDROXYTRYPTAMINE AND THROMBOXANE A_2 FROM HUMAN PLATELETS.

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We have previously shown that halothane, but not isoflurane, decreases the contractile response of isolated canine coronary artery rings to activate platelets in vitro. Others have shown that halothane reduces, more so than isoflurane, platelet aggregation in vitro.[1] Activated platelets release several vasoactive compounds, such as 5-hydroxytryptamine(5-HT) and thromboxane A_2 (TA_2), which induce vascular spasm and amplify platelet aggregation. Reducing the release of these compounds by the platelets could inhibit their vasoactive effect. This study was done to determine if halothane and isoflurane can inhibit the release of 5-HT and TA_2 by activated platelets.

Human platelets were activated by isolated canine coronary rings. Rings were prepared from canine coronary arteries and suspended between 2 stirrups in 25 cc organ chambers filled with oxygenated (95% O_2, 5% CO_2) Krebs-Ringer solution. Some of the organ chambers were treated with either halothane or isoflurane. Human platelets were prepared from blood samples of healthy donors as follows: a mixture of 30 cc of blood and 3 cc of citrate was centrifuged and the resulting platelet-rich plasma was re-centrifuged to obtain a platelet concentrate. After a platelet count was made, a small amount of platelet concentrate was introduced into the organ chambers until a final platelet concentration of 70×10^9 pl/l was reached. Five minutes later, a 1cc aliquot of K-R solution was taken to determine 5-HT and TA_2 levels.

Serotonin and TA_2 concentrations were determined by HPLC and radioimmunoassay respectively as previously described.[2] ANOVA was used to analyse the results, with $P < 0.05$ as significant

Platelets added to the organ chambers released 5HT and TA2; pretreatment of the organ chambers with the anesthetics attenuated the the amount of mediators released; however the results were significant only for the effect of halothane on TA_2 release (table 1)

Halothane has a greater interference than isoflurane with platelets function. These results suggest that one of the ways halothane affects platelet function could be by inhibiting their release reaction. In these experiments, only the organ chambers were pre-treated with the volatile agents. An even greater inhibition might have occured if platelets had been pre-treated with the anesthetics as well.

References:

1. Anesthesiology, 1990, A586.
2. J Clin Invest, 1986, pp 539-544.

Table 1:

	5-HT (ng/cc) Mean ± SEM		TA_2 (pg/cc) Mean ± SEM	
Control	4.145 ± 1.64	ns	739.52 ± 153	ns *
Isoflurane (2.3%)	1.76 ± 0.57	ns	417 ± 73	
Halothane (1.3%)	2.46 ± 0.60		410 ± 50	

* $p < 0.05$