

Anesthesiology  
1997; 87:1016  
© 1997 American Society of Anesthesiologists, Inc.  
Lippincott-Raven Publishers

## Platelet Aggregation Inhibited by Sevoflurane, or by Ethanol?

*To the Editor:*—In their recent report entitled "Sevoflurane Inhibits Human Platelet Aggregation and Thromboxane A<sub>2</sub> Formation, Possibly by Suppression of Cyclooxygenase Activity" (Hirakata H *et al*, ANESTHESIOLOGY 1996; 85:1447–53), the authors demonstrate deterioration in platelet functions by a low concentration of sevoflurane, 0.5%. Such a strong inhibitory effect on platelet aggregation is inconsistent with the fact that clinically serious hemorrhagic complications have never been observed in sevoflurane anesthesia. Although their study is well done and informative, we have one concern about their methodology. They used ethanol in the platelet samples to dissolve inhalation anesthetics. Ethanol has been generally recognized to inhibit platelet aggregability.<sup>1</sup> Moreover, the reporter findings that similar concentration of ethanol did not affect platelets were obtained using rabbits and rats. The platelet reaction to the aggregating agents differs with the species.<sup>2</sup> For example, rabbit and rat platelets show essentially the primary aggregation alone in an adenosine diphosphate (ADP)-induced aggregation study.<sup>2,3</sup> In a human *in vitro* study using ADP, platelet aggregation was inhibited even with ethanol at less than 100 mM<sup>3,4</sup> (they used 0.5% v/v of ethanol, which corresponds to approximately 100 mM). Thus, the inhibitory effect they demonstrated might be attributed to ethanol. We found that platelet aggregation in healthy volunteers (n = 5) is inhibited by ethanol at the same concentration as they used on platelet aggregation. We conclude that the inhibitory effect of sevoflurane on platelet aggregation they reported is attributed to the presence of sevoflurane and ethanol.

**Hiroshi Aoki, M.D.**  
**Toshiki Mizobe, M.D., Ph.D.**  
Department of Anesthesiology  
Kyoto Prefectural University of Medicine  
Kawaramachi-Hirokoji  
Kamigyo-ku  
Kyoto, Japan 602  
Email: aoki@koto.kpu-m.ac.jp

### References

1. Rubin R: Effects of ethanol on platelets (Editorial). *Lab Invest* 1990; 63:729–32
2. Macmillan DC, Sim AK: A comparative study of platelet aggregation in man and laboratory animals. *Thrombosis Diathesis Haemorrh* (Stuttg) 1970; 24:385–94
3. Rand ML, Packham MA, Kinlough-Rathbone RL, Mustard JF: Effects of ethanol on pathways of platelet aggregation *in vitro*. *Thromb Haemostas* 1988; 59:383–7
4. Mikhailidis DP, Jeremy JY, Barradas MA, Green N, Dandona P: Effect of ethanol on vascular prostacyclin (prostaglandin I<sub>2</sub>) synthesis, platelet aggregation, and platelet thromboxane release. *BMJ* 1983; 287:1495–8

(Accepted for publication June 19, 1997.)

Anesthesiology  
1997; 87:1016–7  
© 1997 American Society of Anesthesiologists, Inc.  
Lippincott-Raven Publishers

*In Reply:*—We appreciate the interest shown by Drs. Aoki and Mizobe in our manuscript.<sup>1</sup> However, we believe that the effect of ethanol used to dilute the anesthetics can not explain our finding with sevoflurane. We used the same range of ethanol to dilute all the concentrated anesthetics (including halothane, sevoflurane and isoflurane) and isoflurane with ethanol did not affect platelet aggregation (fig. 1). The concentration of ethanol stated in the manuscript (less than 0.5%) was the possible maximal concentration, and was calculated basing on the total volume of ethanol divided by the volume of platelet-containing solution in the test tubes. Because of the presence of a gas space in the parafilm-sealed tube, the concentration of ethanol in the liquid phase could have been lowered as that in the gas phase increased during incubation at 37°C. In contrast, the concentration of volatile anesthetics mentioned was, of course, that in the liquid phase, confirmed by gas chromatography. This may

explain why ethanol did not affect platelet aggregation during our experimental conditions.

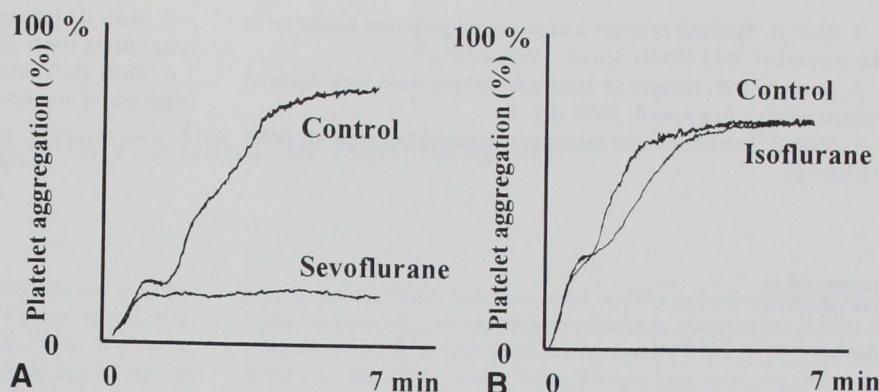
As Drs. Aoki and Mizobe pointed out, no clinical report has ever suggested increased blood loss or blood transfusion during general anesthesia with sevoflurane. This situation can also be extended to halothane anesthesia, although many investigators have reported suppressive effects of halothane on platelet aggregation.<sup>2–4</sup> The fact that the amount of hemorrhage during surgery depends on the surgical technique or skill of the surgeon probably makes clinical studies in this field difficult.

**Hideo Hirakata, M.D.**  
**Kumi Nakamura, M.D.**  
Department of Anesthesia  
Kyoto University Hospital  
Kyoto 606-01, Japan  
Email: H-Hirakata@msn.com



## CORRESPONDENCE

Fig. 1. Effects of sevoflurane and isoflurane on platelet aggregation. (A) Sevoflurane (0.13 mm), with 0.225% ethanol, completely suppressed epinephrine ( $4 \mu\text{M}$ )-induced secondary aggregation. (B) Isoflurane (0.56 mm), with 0.5% ethanol, did not affect epinephrine ( $3 \mu\text{M}$ )-induced platelet aggregation.



## References

1. Hirakata H, Ushikubi F, Toda H, Nakamura K, Sai S, Urabe N, Hatano Y, Narumiya S, Mori K: Sevoflurane inhibits human platelet aggregation and thromboxane  $A_2$  formation, possibly by suppression of cyclooxygenase activity. *ANESTHESIOLOGY* 1996; 85:1447-53
2. Ueda I: The effects of volatile general anesthetics on adenocine

diphosphate-induced platelet aggregation. *ANESTHESIOLOGY* 1971; 34:405-8

3. Dalsgaard-Nielsen J, Gromsen J: Effect of halothane on platelet function. *Thromb Haemost* 1980; 44:143-5

4. Weber A, Hohlfeld T, Schror K: ADP-induced second wave aggregation in platelet rich plasma from hypercholesterolemic rabbits. *Thromb Res* 1991; 64:703-12

(Accepted for publication June 19, 1997.)

Anesthesiology

1997; 87:1017-8

© 1997 American Society of Anesthesiologists, Inc.  
Lippincott-Raven Publishers

## Postdural Puncture Headache and Epidural Blood Patch

*To the Editor:*—The case report by Borum *et al.*<sup>1</sup> illustrates the difficulty in the differential diagnosis of headache in a parturient. Postpartum headache may be due to dural puncture, eclampsia, meningitis, or cortical vein thrombosis. Epidural blood patch is a recognized treatment for postdural puncture headache (PDPH). However, in the other conditions, injection of blood in the epidural space may cause complications.

Prolonged leakage of cerebrospinal fluid (CSF) may occur after a dural puncture. Before performing a blood patch, it is advisable to demonstrate this leakage. Cerebrospinal fluid rarely emerges from the needle when an epidural is performed in a patient with PDPH. In a series of 50 patients with PDPH, the CSF emerged from the epidural needle in only 8 patients (16%).<sup>2</sup> However, insertion of an epidural catheter and gentle aspiration revealed CSF in the epidural space of all these patients.<sup>2</sup>

The compliance of the dura depends on the volume and pressure of CSF contained within it. The CSF pressure is low in patients with PDPH.<sup>3</sup> The compliance of the dura decreases when the CSF pressure is low. Reduction in the compliance of the dura lowers the epidural pressure.<sup>2</sup> The epidural pressure gives a rough estimate of the prevailing CSF pressure.<sup>4</sup> The mean epidural pressure of parturients is approximately 15 cm  $H_2O$  in the lateral posture.<sup>5</sup> However, it decreases

in patients with PDPH. In 50 patients with PDPH the mean epidural pressure was 6.4 cm  $H_2O$ .<sup>2</sup>

Demonstration of free CSF in the epidural space and a low epidural pressure assists in the differential diagnosis of PDPH in the parturient. Before performing a blood patch, it is advisable to demonstrate free CSF in the epidural space and a low epidural pressure. Epidural pressure is easily measured using a 16-gauge (1.1 mm OD) epidural catheter as a simple manometer.<sup>2,4</sup> Injection of blood through a 16-gauge epidural catheter is easy and safe.<sup>2,6</sup>

J. L. Shah, M.D.

Department of Anaesthetics  
City Hospital NHS Trust  
Dudley Road  
Birmingham, B18 7QH  
England

## References

1. Borum SE, Naul LG, McLeskey CH: Postpartum dural venous sinus thrombosis after postdural puncture headache and epidural blood patch. *ANESTHESIOLOGY* 1997; 86:487-90