Prevention of Postanesthetic Shivering with Intravenous Administration of Aspirin

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There have been many reports of postanesthetic shivering (PAS); however, the causes have not been defined clearly, and the reported methods of inhibiting PAS are not always available clinically. In the present study, we assessed the effect of the intravenous administration of aspirin on the prevention of PAS in 62 patients undergoing oral or maxillofacial surgery, anesthetized with enflurane-nitrous oxide. Thirty of the patients were randomly selected, and received intravenous aspirin DL-lysine 900 mg (equivalent to aspirin 495 mg) before the end of surgery. No significant differences were noted in the rectal temperatures between the group given aspirin and the control group. Shivering was observed in 17 of the 32 patients of control group. In contrast, shivering was observed in 5 of the 30 patients who received aspirin. This was a statistically significant difference ($P < 0.01$). These data indicate that intravenous administration of aspirin significantly inhibited PAS. The finding suggests that PAS is related to prostaglandin synthesis or to the formation of derivatives of arachidonic acid, since aspirin inhibits both the synthesis of prostaglandins and the formation of derivatives of arachidonic acid.
(Key words: enflurane-nitrous oxide anesthesia, aspirin, postanesthetic shivering, rectal temperature)

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Postanesthetic shivering (PAS) is a frequent complication of anesthesia that should be prevented. Various methods and drugs to inhibit PAS have been reported, including methylphenidate[1], warmed humidified anesthetic gases[2], meperidine[3], putative inhibitory neurotransmitter taurine[4] and radiant heat[5]. However, these are not always practical because of the special equipment required, limited effectiveness, or unsuitability of the drug for use during general anesthesia.

Our clinical experience showed that the incidence of PAS was less in patients who received intravenous aspirin to inhibit postoperative hyperthermia. In this study, therefore, the effect of intravenous administration of aspirin on the prevention of PAS was assessed in patients following general anesthesia.

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Patients and Methods

Sixty-two ASA Physical Status 1 or 2 patients undergoing oral or maxillofacial surgery were selected after institutional approval and informed consent. Patients with a known allergy to aspirin, with abnormal bleeding tendencies, or who had received a blood transfusion during surgery were excluded. The series consisted of 38 males and 24 females. Ages ranged from 17 to 78 years.

Table 1. Patient data

	Sex ratio	Age (years)	Weight (kg)	Height (cm)	Duration of anesthesia (min)
Control group (n = 32)	21M/11F	46.7 ± 17.7	60.4 ± 10.4	162.2 ± 6.5	252.7 ± 136.4
Aspirin group (n = 30)	17M/13F	42.5 ± 16.6	57.4 ± 10.4	161.1 ± 10.1	264.7 ± 142.9
Difference P	NS	NS	NS	NS	NS

NS = No significant M/F = Male/Female (Mean ± SD)

After premedication with intramuscular administrations of atropine 0.3–0.5 mg, hydroxydine 25–75 mg (1 mg·kg^{-1}) and famotidine (H_2-blocker) 20 mg, anesthesia was induced with benzodiazepine (flunitrazepam 2 mg or diazepam 10–20 mg), butorphanol 2–3 mg, nitrous oxide (50%) and oxygen (50%), and enflurane (1.0–3.0%) was added if necessary. Either vecronium 0.1 mg·kg^{-1} or pancuronium 0.1 mg·kg^{-1} was administered to facilitate endotracheal intubation, and added during surgery at need. In all patients, anesthesia was maintained with a mixture of enflurane (1.0–3.0%), nitrous oxide (33–50%) and oxygen (50–66%). Atropine 0.5–1.0 mg and neostigmine 1.0–2.0 mg were administered for reversal of muscle relaxation.

The rectal temperature in 54 patients was measured with a thermistor probe at 30 min intervals after intubation, and at the end of surgery. The probe was accurate to 0.1°C on the temperature range studied. The operating room temperature was maintained at 23 ± 1°C. All patients were covered with a cotton sheet. All intravenous fluids and inspired gases were at room temperature. During surgery, patients did not receive any warming measures. After discontinuance of anesthetics, the patient was covered with warmed blankets over the body. Temperatures of the operating room after surgery and the recovery room were controlled at a mean ambient temperature of 25 ± 1°C.

Thirty of 62 patients were randomly selected, and received a bolus dose of aspirin DL-lysine 900 mg (dissolved in 0.9% normal saline 20 ml) intravenously 43.3 ± 30.9 (SD) min before the end of surgery. Aspirin DL-lysine is a water soluble salt of aspirin (acetylsalicylic acid). Aspirin DL-lysine 900 mg is equivalent to aspirin 495 mg. The other patients served as the control group.

In this study, shivering was defined as generalized and visible spontaneous shaking after discontinuance of anesthetics. The presence or absence of shivering was recorded up to 60 min after surgery. The investigators who judged the presence or absence of PAS blinded to which patients received aspirin. No attempt was made to quantify the degree of shivering.

Statistical significance was determined for parametric data by Student's t-test, and for non-parametric data by the χ^2-test. Statistical significance was defined as $P < 0.05$.

Results

There were no significant differences in sex, age, weight, height and duration of anesthesia between the group given aspirin (Aspirin group) and the control group (table 1). No significant differences were noted in the mean rectal temperature after intubation, in the mean lowest value during surgery and in the mean rectal temperature at 1 hr before the end of surgery and at the end of surgery between the groups (table 2).

Postanesthetic shivering was observed in 17 of the 32 patients in the control group. In contrast, shivering was observed in only 5 of the 30 patients in the Aspirin group (table 3). There was a statistically significant difference between the groups ($P < 0.01$).

Table 2. Rectal temperatures after intubation (T-pre), the lowest value during surgery (T-lowest), at 1 hr before the end of surgery (T-1hr before) and at the end of surgery (T-end) in two groups

	T-pre	T-lowest	T-1hr before	T-end
Control group (n = 26)	36.51 ± 0.51	35.97 ± 0.67	36.16 ± 0.84	36.22* ± 0.84
Aspirin group (n = 28)	36.65 ± 0.56	36.26 ± 0.55	36.43 ± 0.66	36.49** ± 0.77

Mean ± SD (°C)

*Significantly different ($P < 0.01$) from the T-lowest
**Significantly different ($P < 0.05$) from the T-lowest

Table 3. Incidence of shivering

	Shivered	Not shivered
Control group (n = 32)	17*	15
Aspirin group (n = 30)	5*	25

*Significant difference ($P < 0.01$ χ^2 analysis)

These data indicate that intravenous administration of aspirin significantly inhibited PAS. There was no correlation between the effectiveness and sex, age, weight, height or duration of anesthesia.

In both groups, the rectal temperature tended to decrease after intubation, but rose again by the end of surgery in 28 of the 54 patients. The mean rectal temperature at the end of surgery was significantly ($P < 0.01$) higher than the mean lowest rectal temperature during surgery in both groups (table 2). However, there were no differences at any points between the groups.

The incidence of side effects associated with intravenous administration of aspirin was not obtained. There were no significant differences in blood loss during surgery and the time for awakening from anesthesia between the groups.

Discussion

Postanesthetic shivering has been attributed to various causes, including acute thermogenesis in response to the difference between "set point" and core temperature during surgery[2], alteration of central nervous system activity[1,6,7], postoperative hypothermia[8] and stimulation by reduced skin temperature[4]. In some[2,7,9], there was no correlation between the incidence of PAS and core temperature.

In a recent study of PAS, electromyographic patterns in patients recovering from anesthesia usually differed from those of normal thermogenic shivering[6]. The authors suggested that spontaneous tremor (PAS) was caused by spinal reflex hyperactivity that resulted when descending cortical control was inhibited by residual anesthetic, rather than by a thermoregulatory mechanism. Murphy et al.[4], using the putative inhibitory neurotransmitter taurine, suggested that PAS resulted primarily from cold thermal stimulation. Their study showed that mechanisms involved in PAS included activation of central heat production pathways. Sessler et al.[6], combining their findings with the results of Murphy's study, concluded that stimulation of cutaneous cold receptors enhanced spinal cord reflexes and resulted in trigger of postanesthetic tremor (PAS). However, since there was no correlation between the incidence of PAS and skin temperature in some investigators[2,9,10], factors other than stimulation of cutaneous cold receptors are thought to enhance spinal cord reflexes and result in the trigger of PAS.

Aspirin and aspirin-like drugs inhibit synthesis of prostaglandins[11]. Prostaglandins have been shown to produce hyperthermia associated with shivering[12]. Laburn et

al.[13] showed that sodium arachidonate, a prostaglandin precursor, also resulted in hyperthermia. They suggested that a derivative of arachidonic acid was pyrogenic and that aspirin-like drugs prevented formation of all of the pyrogenic derivatives of arachidonic acid. Therefore, the finding that aspirin was effective in preventing PAS suggests that the causes of PAS are related to prostaglandin synthesis or to the formation of pyrogenic derivatives of arachidonic acid. This finding raises the possibility that prostaglandins or the pyrogenic derivatives may enhance spinal cord reflexes and result in one of the triggers of PAS.

The data in our study showed that mean rectal temperature tended to increase by the end of surgery. Holdcroft[10] showed that regardless of the incidence of PAS, both core temperature and skin temperature increased significantly during the recovery period after surgery. During and after surgery, there may be activation of central heat product pathways induced by prostaglandin synthesis or by the formation of pyrogenic derivatives of arachidonic acid. Furthermore, the activation may depend upon either release of endogenous pyrogens during surgery or the anesthetic itself since synthesis and release of prostaglandins can be induced by pyrogen[14].

Murphy et al.[4], using an endogenous antipyretic, α-melanocyte stimulating hormone (α-MSH), showed that PAS was not inhibited by α-MSH and concluded that PAS does not depend upon release of endogenous pyrogens. However, α-MSH does not alter hyperthermia induced by prostaglandin and sodium arachidonate, and the antipyretic action of α-MSH occurs subsequent to the release of endogenous pyrogen and prior to the release of arachidonic acid[15]. Therefore, α-MSH would not inhibit shivering induced by prostaglandin after it had occurred. The finding that the causes of PAS are related to prostaglandins or to pyrogenic derivatives of arachidonic acid is not incompatible with the result of the Murphy's study.

For aspirin to be effective in preventing PAS, it must be administered at the time during surgery when prostaglandins are synthesized because aspirin does not inhibit activation of prostaglandins themselves. However, the fact that most aspirin-like drugs must be administered orally limited the use of these drugs during anesthesia. Therefore, intravenous administration of aspirin is most useful and effective in preventing PAS.

Previous studies[16–18] showed that intravenous administration of aspirin was safe and effective for providing pain relief after surgery. Aspirin is known to influence platelet function and to prolong bleeding time. However, comparison of blood loss during surgery between the two groups indicated that administration of aspirin was not clinically associated with significantly greater blood losses.

The results of our study indicate that intravenous administration of aspirin is significantly effective in preventing PAS. This finding suggests that PAS is related to prostaglandin synthesis or to the formation of pyrogenic derivatives of arachidonic acid since aspirin inhibits them. Although causes of PAS have not been defined clearly, we propose the hypothesis that PAS can be caused by spinal reflex hyperactivity enhanced by either prostaglandins or pyrogenic derivatives of arachidonic acid during surgery.

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