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Comparison between alfentanil, pethidine and placebo in the treatment of post-anaesthetic shivering

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Summary

We have compared the effects of pethidine, alfentanil and placebo in the treatment of post-anaesthetic shivering. Ninety patients who shivered after routine surgery were allocated randomly to receive normal saline ($n=30$), alfentanil 250 μg ($n=30$) or pethidine 25 mg ($n=30$). After 10 min, 26 patients had stopped shivering in the pethidine group which was significantly more than the incidence in the two other groups (placebo = 7; alfentanil = 12) ($P<0.0002$). Alfentanil was not significantly different from normal saline in affecting shivering. We conclude that alfentanil 250 μg was not effective in the treatment of post-anaesthetic shivering. (*Br. J. Anaesth.* 1997; **79**: 541–542).

Key words

Complications, shivering. Analgesics opioid, alfentanil. Analgesics opioid, pethidine.

Post-anaesthetic shivering is a common problem in the recovery room, with detrimental effects including increased oxygen consumption and hypoxaemia.[1] Pethidine has been shown to be one of the most effective treatments for post-anaesthetic shivering.[2–4] Although its mechanism of action is not completely understood, a study using naloxone indicated that pethidine may act via kappa rather than mu opioid receptors. The anti-shivering action of pethidine is inhibited by high-dose naloxone which blocks mu and kappa receptors but not by low-dose naloxone which blocks only mu receptors.[3] Previous work on the efficacy of mu opioid receptor agonists in the treatment of shivering has been conflicting.[2 4] However, in an audit of postoperative shivering it appeared that intraoperative administration of the mu opioid receptor agonist alfentanil was associated with a reduced incidence of postoperative shivering.[1]

In order to investigate further the importance of mu opioid receptors in the treatment of shivering, we have compared the actions of alfentanil and pethidine. Alfentanil 250 μg was used as this is equi-analgesic to pethidine 25 mg,[5] the dose often used to treat shivering.[2] As alfentanil is a more specific mu agonist than pethidine, an equi-analgesic dose should have at least as great an effect on mu receptors. It should also follow that if pethidine acts principally via mu receptors in the treatment of shivering, this dose of alfentanil should be at least as effective.

Methods and results

The study was approved by the local hospital Ethics Committee. We studied 90 patients of both sexes, aged 18–70 yr, who developed shivering in the recovery room. All patients were ASA class I or II and had undergone routine general, orthopaedic, gynaecological or ENT surgery. As a consequence of the patients being selected as they recovered from anaesthesia, their consent was not considered valid and with agreement from the hospital Ethics Committee, informed consent was not obtained. Patients with any contraindications to the use of alfentanil or pethidine were not included.

Routine care for patients in this hospital suffering from postoperative shivering consists of oxygen 4 litre min^{-1} by Hudson mask and covering with a heat reflective blanket. In addition, each patient received an i.v. bolus dose of saline, pethidine 25 mg or alfentanil 250 μg in a total volume of 5 ml. Syringes containing the drug were prepared by recovery room staff after written instructions removed from a sealed envelope. The envelopes were inserted in a random order generated by microcomputer using a shuffling technique.

The investigator giving the i.v. injection was unaware of the treatment received by the patient and assessed the shivering grade before treatment according to a five-point scale: 0 = no shivering; 1 = one or more of the following: piloerection, peripheral vasoconstriction, peripheral cyanosis without other cause, but without visible muscular activity; 2 = visible muscular activity confined to one muscle group; 3 = visible muscular activity in more than one muscle group; and 4 = gross muscular activity involving the entire body. Tympanic membrane temperature was measured (First Temp

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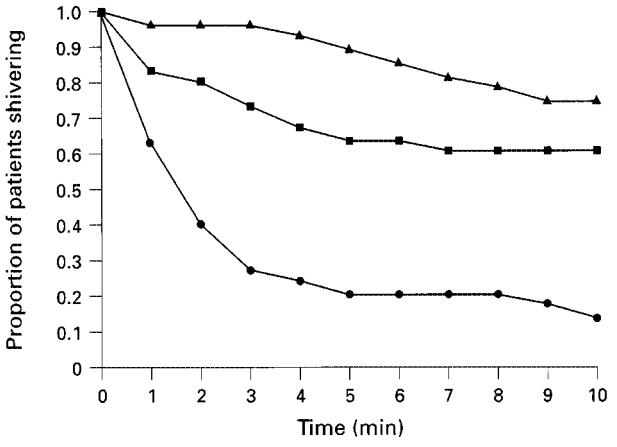

Figure 1 Proportion of patients who continued to shiver at each time in the placebo (▲), pethidine (●) and alfentanil (■) groups ($n=28$ for the placebo and $n=30$ for the two other groups). Chi-square analysis at 10 min showed that pethidine was significantly more effective than the two other groups ($P<0.0002$).

Genius Thermometer) immediately before giving the drug and shivering was assessed every minute for 10 min.

From previous work we estimated that a group size of 28 patients was sufficient to detect a 40% reduction in the incidence of shivering relative to placebo with a power of 0.85 at the 5% level.

All three groups had a median shivering grade at entry of 3 (range 2–4). Mean temperature at the time of treatment was similar in all three groups: 36.2 (SD 0.7) for placebo, 36.6 (0.8) for the pethidine group and 36.3 (0.7) for the alfentanil group. None of the patients recommenced shivering after they had stopped. Two patients in the placebo group were excluded as they received morphine for pain relief during the study.

After 10 min, four patients who had been given pethidine continued to shiver compared with 18 in the group given alfentanil and 21 in the placebo group (fig. 1). Chi-square analysis showed that pethidine was significantly more effective than both of the other treatments ($P<0.0002$). Alfentanil did not differ significantly from saline.

Comment

We have shown that alfentanil 250 μg was not significantly different from placebo in the treatment of post-anaesthetic shivering. However, fewer people shivered in the alfentanil group compared with the saline group at every time studied, indicating the possibility that a higher dose may have been more effective. This has been found to be the case with fentanyl; 25 μg (i.e. 0.36 μg kg^{-1} for a 70-kg man) did not reduce post-anaesthetic shivering[2] whereas 1.7 μg kg^{-1} (i.e. five-fold greater) was as efficacious as pethidine.[4] As indicated above there is evidence that pethidine may act via kappa opioid receptors in the treatment of this condition. Fentanyl also binds to kappa receptors, although five-fold more weakly than pethidine when binding to mu opioid receptors is used as a reference.[6] It is possible, therefore, that fentanyl, when given in a relatively high dose, acts via kappa receptors to stop post-anaesthetic shivering. This may also be the case for other mu agonists such as alfentanil.

In conclusion, we found that alfentanil 250 μg did not differ from placebo in the treatment of post-anaesthetic shivering. Our results are consistent with the hypothesis that kappa opioid receptors are more important than mu opioid receptors in the treatment of this condition.

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