Effects of sub-hypnotic doses of propofol on the side effects of intrathecal morphine

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Summary
We have studied the effect of propofol on the side effects associated with intrathecal morphine in 40 patients undergoing major arthroplasty. Patients received spinal anaesthesia with plain 0.5% bupivacaine 20 mg mixed with preservative-free morphine 0.3 mg. Before injection of the local anaesthetic, the patients were allocated randomly to receive either a bolus dose of propofol 10 mg followed by an infusion of 30 mg/24 h or equal volumes of 10% Intralipid (control group). The number of patients without postoperative nausea and vomiting (PONV) was similar in both groups. However, the incidence of nausea and vomiting was lower in the propofol (13 and 22, respectively) than in the control (34 and 36) group (P < 0.01 and P < 0.05, respectively). Severe vomiting episodes were less frequent in the propofol group (1 vs 11; P < 0.05). Four patients in the propofol group and 12 patients in the control group had itching (P < 0.05). The incidence of urinary retention was similar in both groups. There was no additional sedation attributable to propofol. In conclusion, sub-hypnotic doses of propofol protected significantly against itching and had a modest effect on PONV after intrathecal morphine.

Key words

Propofol has antiemetic properties, especially when used for total i.v. anaesthesia [1]. Borgeat and colleagues [2] have recently shown that sub-hypnotic doses of propofol relieved postoperative nausea and vomiting (PONV) after general anaesthesia. They also found that sub-hypnotic doses of propofol were effective against pruritus induced by intrathecal morphine [3]. Intrathecal morphine provides good postoperative pain relief but its use is associated with unpleasant side effects including nausea, vomiting, urinary retention and itching [4]. We have investigated the efficacy of prophylactic sub-hypnotic doses of propofol given as a continuous infusion on the side effects induced by intrathecal morphine.

Methods and results
The study was approved by the local Ethics Committee and patients gave informed consent. We studied 40 ASA I–III patients, aged 51–83 yr, undergoing arthroplasty surgery of the lower extremities under spinal anaesthesia. All patients were premedicated with oral diazepam. Spinal anaesthesia was performed with plain 0.5% bupivacaine 20 mg mixed with preservative-free morphine 0.3 mg. The patients were allocated randomly to receive either a single dose of propofol 10 mg (Diprivan, ICI, Pharmaceuticals, UK) followed by an infusion of 30 mg/24 h (propofol group) or equal volumes of 10% Intralipid (Kabi Pharmacia, Sweden) (control group) in a double-blind design. Lignocaine 10 mg was given into the same vein before the test drugs in all patients to prevent possible pain induced by propofol. Oxygen 2–3 litre min⁻¹ was delivered via a nasal catheter during surgery. Decreases in arterial pressure (> 30% from baseline) were treated with ephedrine 5 mg i.v. and bradycardia (heart rate < 45 beat min⁻¹) with atropine 0.5 mg i.v.

Postoperative side effects (nausea, vomiting, itching and urinary difficulties), pain and sedation were noted by the authors and trained nurses during the patients' stay in the operating theatre and in the recovery room, and also in the ward by trained nurses for 24 h after induction of spinal anaesthesia. The investigators interviewed all patients at 24 h. Nausea and vomiting were assessed as 0 (no symptoms), + (moderate symptoms) or ++ (severe symptoms). For analyses, episodes of nausea and vomiting were grouped at 3-h intervals. Droperidol 1.25 mg i.m. was given to treat persistent nausea or vomiting. After operation, naloxone 0.2 mg i.m. was given for urinary retention and thereafter catheterization was performed, if necessary.

Pain and analgesic requirements were assessed on an arbitrary scale: 0 = no pain, 1 = mild pain (opioids not needed), 2 = pain (opioids needed), 3 = severe pain (opioids needed immediately) after operation during the 24-h study period. Oxycodone 0.1–0.14 mg kg⁻¹ i.m. was given to treat persistent nausea or vomiting. After operation, naloxone 0.2 mg i.m. was given for urinary retention and thereafter catheterization was performed, if necessary.

Data were analysed by the chi-square test or Fisher's exact test where appropriate.

Patient characteristics and perioperative data in

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Although there are several reasons for PONV after major orthopaedic surgery (opioids, surgery, transfusions, methylmethacrylate, etc.), it seems likely that the high incidence of PONV here was caused by intrathecal morphine.

It has been demonstrated that propofol protects against emetic sequelae after total i.v. anaesthesia [1]. In addition, sub-hypnotic doses of propofol were found to have a direct therapeutic effect on established PONV after general anaesthesia [2]. In our study an antiemetic effect of propofol was also demonstrated: the number of episodes of both nausea and vomiting decreased and severe vomiting occurred only once in the propofol group. Unfortunately, the number of patients without PONV was unchanged. It is probable that our dose was not sufficient, although it was chosen on the basis of the study of Borgeat and colleagues [2]. A continuous infusion of propofol was used in order to produce persistent effects.

The emetic effect of intrathecal morphine is thought to result from slow migration to the chemoreceptor trigger zone [4]. There may also be a vestibular and a gastrointestinal component. However, after the relatively small dose of intrathecal morphine used (0.3 mg), the blood concentrations of morphine may have been too small to produce systemic effects. The mechanism of the antiemetic effect of propofol is not clear but it may result at least partly from its significant brain depressant effects [6].

Propofol decreased significantly the incidence of itching in comparison with the control group (20% vs 60%). Opioid-related pruritus is thought to be a result of local stimulation, particularly in the spinal cord. Propofol has been shown to produce marked spinal depression and probably exerts its antipruritic action through inhibition of posterior horn transmission [6].

The incidence of PONV was high (60% and 65%) in this study, confirming previous studies in which intrathecal morphine was given with bupivacaine spinal anaesthesia [5]. Although there are several

the two groups were comparable. The median level of pinprick analgesia at 60 min was T6 in the propofol group and T7 in the control group.

The number of patients who had no PONV was similar in both groups: eight patients in the propofol group and seven in the control group. In the propofol group there were significantly fewer episodes of nausea and vomiting at 3-h intervals compared with the control group (P < 0.01 and P < 0.05, respectively) (table 1). Severe vomiting (+ +) occurred more frequently in the control than in the propofol group (11 episodes vs 1; P < 0.05). The intensity of nausea was similar in both groups. Fourteen doses of droperidol were given to 10 patients in the propofol group and 25 doses to 11 patients in the control group (ns).

The difference in the incidence of itching was statistically significant between groups; four patients in the propofol group had itching and 12 patients in the control group (P < 0.05). The incidence of urinary retention was similar in both groups (table 1).

Nine patients in the propofol group and eight patients in the control group had no pain (grade 0) during the study. Eleven patients in the propofol group were given 18 doses of oxycodone and 12 patients in the control group received 29 doses because of pain (grade 2, in one patient in both groups grade 3) (ns). Clinically disturbing sedation was not noted in either group.

Comment

We have found that sub-hypnotic doses of propofol given as a continuous infusion had a modest but definite effect on PONV and protected significantly against pruritus associated with the use of intrathecal morphine.

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References