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The efficacy of pre-emptive tramadol in orthopaedic day-surgery☆

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Abstract

It has been suggested that there may be some advantage in pre-emptive administration of analgesics, which may be of some relevance in day-surgery. Post-operative pain control is often difficult due to the reluctance to use potent analgesics, whose side effects include nausea and vomiting, which are an important cause of delayed discharge.

In order to test the potential beneficial effects of pre-emptive analgesia, 110 day-surgery patients were randomly allocated to receive either pre-emptive tramadol or a placebo pre-operatively. Per and postoperative complications were recorded following administration of a standard anaesthetic, comprising intravenous induction with propofol and maintenance with isoflurane. Post operative analgesia and anti-emetics were administered as required. Patients who received tramadol had a slightly lower incidence of postoperative pain, but at the expense of increased nausea; all differences were not significant.

Keywords: Anaesthesia; Day-case anaesthetic; Analgesia; Complication; Postoperative nausea and vomiting

1. Introduction

Postoperative nausea and vomiting (PONV) and pain are the commonest complications following day-surgery, and may result in either delayed discharge or even overnight admission [1]. Standard analgesia such as paracetamol or non-steroidal anti-inflammatory drugs are routinely used in orthopaedic day-surgery but occasionally stronger analgesia, such as morphine, may be required. More potent analgesics such as morphine are generally not regarded as a first line treatment in this setting, because of their side-effect profile, which includes respiratory depression, sedation and PONV [2].

Tramadol, a centrally acting analgesic with both opioid and non-opioid mechanisms of action is reputed to be relatively free from such side effects and therefore may be of potential use in the day-surgery setting [3–5]. In addition there has been some evidence that the administration of analgesics given prior to a painful stimulus may be more efficacious than if given after the event [6,7]. We decided therefore, to investigate the potential benefit of pre-emptive tramadol, in particular, improvements in postoperative analgesia with a corresponding reduction in postoperative analgesic requirements and the resulting side effects.

2. Methods

After local research ethics committee approval and gaining informed written consent, 110 ASA I and II patients aged 16–70 years scheduled for day-case arthroscopy were randomly allocated to receive either an IM injection of tramadol 1–1.5 mg kg^{-1} or, a placebo IM injection of normal saline 1 h preoperatively. A preoperative history was taken which included details of previous PONV/motion sickness and smoking habits. Weight and blood pressure were also recorded.

In the anaesthetic room a pulse oximeter was attached to each patient and intermittent non-invasive blood pressure monitoring was commenced. Intravenous access was established followed by intravenous induction with propofol 2–4 mg kg^{-1} and fentanyl 1–1.5 μg kg^{-1}. A laryngeal mask airway was inserted and gentle manual ventilation was continued until the return of spontaneous ventilation.

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Table 1
Postoperative pain and nausea scoring systems

Pain	None	Mild	Moderate	Severe	Excruciating
Score	0	1	2	3	4
Nausea	None	Mild	Moderate	Severe	
Score	0	1	2	3	

Anaesthesia was maintained with isoflurane in a 66% nitrous oxide in oxygen mixture. A fresh gas flow of 4 l min^{-1} was used with a semi-closed circle system. Intraoperatively, electrocardiogram (ECG), oxygen saturation levels (SpO_2) and end-tidal carbon dioxide concentration ($FetCO_2$) were monitored continuously. Blood pressure was monitored at 5 min intervals. Details of any complications or adverse events involving the cardio-respiratory system were also recorded. In particular, the occurrence of bradycardias (heart rate <50 beats min^{-1}), hypotension (systolic blood pressure <80 mmHg.), low oxygen saturation (SaO_2 <90%), hypercapnia ($ETCO_2$ >6.0 kPa) and coughing were noted.

Postoperative pain, where it occurred, was treated with oral codeine/paracetamol and/or rectal diclofenac. Pethidine (1–1.5 mg kg^{-1}) was used as a second line treatment if required.

Postoperative nausea was treated initially with IM prochlorperazine 12.5 mg and cyclizine 50 mg IM was used for persistent symptoms. Both the intensity and treatment of these symptoms were recorded.

When patients' symptoms were adequately controlled and they were deemed in other respects stable by recovery staff, they were returned to the day ward. Here, further analgesia and anti-emetics were administered if necessary. Prior to discharge patients were asked to complete a questionnaire detailing any postoperative complications such as PONV or pain which they had experienced. Pain was scored on a four-point scale, PONV on a five-point scale (Table 1).

A priori statistical analysis suggested that 50 patients in each group would be needed to demonstrate a 20% difference in the number of patients who required analgesia (with 80% power at the 5% level). For categorical and continuous data a χ^2- test and *t*-test were used, respectively. A probability value of <0.05 was considered to be statistically significant. The study was not powered for outcomes other than analgesia.

3. Results

There were a total of 56 patients in the tramadol group and 54 in the placebo group. The two groups were similar both in terms of demographic data and intravenous anaesthetic requirements (Table 2). There were more patients with a history of PONV and/or motion sickness in the tramadol group (3 versus 1, NS). The patients in the tramadol group received a slightly lower percentage of isoflurane (NS). Perioperative complications are presented in Table 3. In the tramadol group a higher number of adverse events were seen; only bradycardia approached statisical significance ($P = 0.06$, Fisher's exact test).

Table 2
Demographic data values are mean (S.D.) where appropriate

	Treatment ($n = 56$)	Placebo ($n = 54$)
Age (year)	38.9 (11.2)	37.6 (13.9)
Weight (kg)	79.4 (12.1)	78.4 (13.6)
Sex ratio (male/female)	40/16	39/15
History of PONV/motion sickness (*n*)	3	1
Duration of anaesthesia (min)	26.7 (13.0)	27.9 (12.2)
Smokers (*n*)	14	15
Propofol dose (mg kg^{-1})	257 (44.2)	265 (47.5)
Fentanyl dose (μg kg^{-1})	99.6 (3.31)	98.1 (13.48)
Isoflurane concentration (%)	1.61 (0.39)	1.92 (0.18)

All differences are not significant.

Table 3
Perioperative complications

	Treatment	Placebo
Coughing	5	3
Hypercapnia	1	1
Hypotension	0	0
Bradycardia[a]	5	0
Desaturation	0	0
Overnight stay	2	1
Total	13	5

All differences are not significant.
[a] $P = 0.06$; Fisher's exact test.

Fewer patients in the treatment group received anti-emetics in recovery compared with the control group (4% versus 11%, NS)(difference 7%. 95% CI; −3 and 19%). Prochlorperazine 12.5 mg IM was the only anti-emetic used in recovery.

There was no statistical difference in analgesic requirements during recovery. In all, 77% of patients in the treatment group required no analgesia in recovery compared with 67% of control patients. (difference 10 and 95% confidence interval; −6 and 26%), NS ($P = 0.29$). In the placebo group six patients required additional pethidine, although this was not statistically significant. Following discharge from recovery to the day ward, analgesic requirements were very

Table 4
Nausea scores

Nausea score	Treatment ($n = 56$)	Placebo ($n = 54$)
0	47	47
1	5	4
2	3	2
3	1	1
Total nauseated	9 (16%)	7 (13%)
Average nausea scores, mean (S.D.)	0.25 (0.63)	0.20 (0.59)
Total vomited	3 (5%)	2 (4%)

Table 5
Pain scores

Pain score	Treatment($n = 56$)	Placebo($n = 54$)
0	20	17
1	26	20
2	8	13
3	2	4
4	0	0
Total in pain	36 (64%)	37 (69%)
Average pain score, mean (S.D.)	0.80 (0.74)	1.07 (0.92)

similar in the two groups, and most patients in each required no analgesia at all (treatment 75% versus control 74%, NS).

The questionnaire at discharge revealed small differences in nausea or vomiting between the groups (16% versus 13%, NS) (3% difference, CI; −11 and 17%) (Table 4). Reports of pain were also not statistically different (Table 5).

4. Discussion

Pain, nausea, and vomiting are the most common postoperative complications, which prevent the scheduled discharge of day-surgery patients. However, the use of potent analgesics is generally avoided whenever possible, especially long acting opiates such as morphine, which are associated with prolonged PONV and delayed ambulation.

Pre-emptive analgesia has received considerable attention during the last decade [6,8].

Following acute injury, changes take place in the nervous system both centrally and peripherally involving sensitization of nociceptors with corresponding hyperalgesia at the site of injury [8]. However, rapid analgesic intervention may prevent this so-called wind-up (upregulation) of the nociceptive system within the central nervous system [9]. Tramadol's action is dependent upon both opioid and non-opioid pathways [10] and should, in theory, exhibit pre-emptive analgesic effects. In order to test the hypothesis that pre-emptive analgesia might be associated with a better outcome, a placebo-controlled study was adopted, as this was anticipated to provide the best discrimination between treatment and control groups [11], while allowing placebo failure to be treated by administration of analgesics in the conventional manner.

The results of this study demonstrate that there was a small, nonsignificant reduction in analgesic requirements in the recovery unit in the treatment group (23% versus 33%, $P = 0.29$), but also no significant difference in pain scores.

There was a higher incidence of nausea in the treatment group (16% versus 13%) and slightly higher average nausea scores (0.25 versus 0.20), although none were statistically different. Paradoxically, fewer patients from the treatment group were given anti-emetic medication in the recovery ward as compared to the control group (4% versus 11%), though anti-emetic requirements and administration in the day ward were identical in both groups (2%). The incidences of PONV corresponded well with previously published data in similar patient populations [12]. We have shown a non-significant difference in the incidence of side effects between the two groups, particularly the occurrence of bradycardias in the treatment group. Bradycardia is not per-se a side effect of tramadol [13] though opiates in general are known to be associated with bradycardia especially if anaesthesia depth is profound.

In conclusion this study has shown that the use of tramadol as pre-emptive analgesia in day-case arthroscopy patients does not significantly reduce postoperative pain scores or requirements for analgesia. In addition, the higher incidence of perioperative bradycardia together with PONV suggests that its use in this group of patients is of questionable benefit. It is conceivable that using a larger study population would identify an improvement in pain scores.

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