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ORIGINAL ARTICLE

Postoperative analgesia with tramadol and indomethacin for diagnostic curettage and early termination of pregnancy

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ABSTRACT

Background: The postoperative analgesic effects of rectal indomethacin and tramadol were compared in patients undergoing elective termination of first trimester pregnancy and diagnostic dilatation and curettage.

Methods: Eighty-one American Society of Anesthesiologists class I and II women undergoing first trimester termination of pregnancy or diagnostic dilation and curettage were randomly allocated to receive rectal suppositories of either tramadol 100 mg ($n = 41$) or indomethacin 100 mg ($n = 40$) 90 min before induction of anesthesia. Pain scores and side effects were evaluated until discharge. Intraoperative anesthetic and postoperative analgesic consumption was also recorded. Intravenous metamizole 1 g was employed for postoperative rescue analgesia.

Results: When compared to the indomethacin group, the tramadol group required less intraoperative propofol [136 mg ±28 vs. 160 mg ±35 ($P = 0.001$)], less rescue analgesia [2.4% vs. 22% ($P = 0.005$)] and lower visual analogue pain scores [2.4 ±8 vs. 23 ±22 ($P = 0.005$)]. The incidence of postoperative nausea and vomiting was similar in both groups.

Conclusion: When compared to indomethacin 100 mg, preoperative administration of tramadol 100 mg provides superior postoperative analgesia with minimal adverse effects.

Keywords: Termination of pregnancy; Analgesia; Tramadol; Indomethacin

Introduction

Inadequate treatment of postoperative pain is associated with patient suffering, prolonged hospitalization, higher health care costs and increased morbidity and mortality rates.[1] Improved pain management can result in reduced postoperative sequelae for day-surgery patients, including fewer hospital admissions.[2] Opioids, often used for postoperative pain management, can be associated with respiratory depression, drowsiness, nausea, and delayed discharge. By contrast, non-steroidal anti-inflammatory drugs (NSAIDs) and anti-pyretic analgesics are usually sufficient to provide analgesia after ambulatory surgery.[3,4]

Introduced into clinical practice in 1978, tramadol is a synthetic 4-phenylpiperidine analogue of codeine with two optical isomers: one having opioid-like effects and the other antagonizing the neuronal uptake of noradrenaline and serotonin in the nerve terminals,[5] displacing serotonin stores in the spinal cord, and facilitating descending inhibitory pain pathways.[6,7] Houmes et al. showed that tramadol was as effective and safe as morphine for postoperative pain relief with potential advantages of longer duration of action and limited respiratory depression.[8] Maximum analgesic effect occurs at 1–2 h after intravenous administration;[5,9] therefore, tramadol should be given before or during anesthesia to provide adequate postoperative pain relief.

In this study, the postoperative analgesic effect of tramadol and indomethacin suppositories administered before minor gynecological procedures was compared.

Methods

After obtaining institutional ethics committee approval and written informed consent, 81 American Society of Anesthesiologists class I and II women scheduled for

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day-case diagnostic curettage or first trimester termination of pregnancy at the Wolfson Medical Center were recruited into this prospective, randomized, double-blind study. Patients with known hypersensitivity to the study medications, history of asthma, epilepsy, renal failure, peptic ulcer, drug addiction and alcohol abuse were excluded.

Patients were randomly allocated to receive rectal suppositories of either indomethacin 100 mg or tramadol 100 mg. Randomization was made with the aid of random numbers tables. The study medication was stored in a separate sealed envelope. A researcher blinded to the study groups attached the envelopes to the medical records and the attending nurse, also blinded to the study groups, administered the drugs rectally 90 min before induction of anesthesia. The suppositories were identical in appearance.

Before induction of general anesthesia, all patients received intravenous fentanyl 1 μg/kg. Anesthesia was induced with intravenous propofol 2 mg/kg and maintained with nitrous oxide in 40% oxygen and 30–50 mg boluses of propofol as required, to maintain surgical anesthesia. Postoperative rescue analgesia was provided with intravenous metamizole 1 g and administered when pain intensity was $>$ 30 mm on a 100-mm visual analogue scale (VAS) (0 = no pain; 100 = worst possible pain). Nausea was treated with intravenous metoclopramide 10 mg.

Patient assessments were performed during surgery and in the postoperative period until discharge. These measurements included: blood pressure, heart rate, oxygen saturation, and respiratory rate which were recorded at baseline (5 min before induction of anesthesia) and every 2 min during anesthesia. In the postoperative period measurements were performed at 5, 15, 30, 60 and 120 min. Total intraoperative propofol consumption was recorded. Pain intensity was assessed by VAS on arrival in the recovery room and every 15 min until discharge and again 24 h later by telephone interview. In addition, the presence of nausea and/or vomiting, dry mouth, dizziness and shivering were also recorded. Respiratory depression was assessed by measurement of respiratory rate.

Statistical analysis

Data analysis was carried out using SPSS 9.0 statistical analysis software (SPSS Inc., Chicago, IL, USA, 1999). For continuous variables such as age and hemodynamic values, descriptive statistics were calculated and reported as mean ±standard deviation (SD). Normality of distribution of continuous variables was assessed using the Kolmogorov–Smirnov test (cut off at $P = 0.01$). Categorical variables, such as treatment group and symptoms, were described using frequency distributions and are presented as frequency (%). The t test for independent samples was used to compare continuous variables, such as blood pressure, heart rate. The χ^2 test was used to assess associations between treatment group and other categorical variables. All tests were two-sided and considered significant at $P < 0.05$. With a sample size of 40 subjects in each treatment assignment, the present study was designed to have 80% power to detect a true, by-treatment group VAS score difference of 13 points (SD 20) in mean scores of pain 1 h after surgery using the t test for independent samples, assuming a two-sided alpha of 0.05.

Results

Eighty three patients were recruited; 41 were assigned to the indomethacin group and 42 to the tramadol group. Two patients, one in each group, were excluded because of protocol violation leaving 81 patients completing the study; 40 receiving indomethacin and 41 tramadol. Patient characteristics are presented in Table 1. The two groups were comparable in age, weight, gestational age, type of surgical procedure and duration of surgery.

Neither indomethacin nor tramadol caused changes in blood pressure, oxygen saturation and respiratory rate (Table 2). The total propofol dose required to maintain anesthesia was lower in the tramadol group – 136 mg ±28 vs. 160 mg ±35 ($P = 0.001$). There was a significant difference in heart rate between the groups at one and two hours after surgery; those in the indomethacin group being lower. Patients receiving tramadol had significantly lower VAS at 30 min (12 ± 18 vs. 36 ± 28), 60 min (2.4 ± 8 vs. 23 ± 22) and 24 h (0.2 ± 1.0 vs. 5.6 ± 8.0) after surgery when compared to those receiving indomethacin ($P = 0.001$) (Table 3). Only one (2.4%) patient receiving tramadol required additional analgesia compared to nine (22%) in the indomethacin group ($P = 0.005$). The discharge times and the incidence of adverse effects were similar for each group.

Table 1 Patient demographics and surgical procedure variables

	Indomethacin ($n = 40$)	Tramadol ($n = 41$)	P value
Age (years)	29 ± 7	31 ± 7	0.10
Weight (kg)	65 ± 7	66 ± 6	0.25
Gestation (weeks)	9.4 ± 1.7	9.1 ± 2.0	0.46
Termination of pregnancy	25 (62%)	18 (43%)	0.06
Diagnostic D&C	15 (38%)	23 (57%)	0.06
Duration of surgery (min)	6 ± 2	6 ± 3	0.94
Total propofol dose (mg)	160 ± 35	136 ± 28	0.001

Data are mean ±SD or number (%); D&C: Dilation and curettage.