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Preemptive analgesia with controlled-release oxycodone is successful in prevention of post-inguinal herniorrhaphy pain

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Abstract

In a double-blind randomized study, controlled-release (CR) oxycodone (OxyContin ®) administration was assessed against placebo to ascertain the extent of postinguinal herniorrhaphy pain control. Patients received a single dose of CR oxycodone (40 mg orally) or placebo 40 min before surgery.

When post-surgical pain was first reported, a visual analogue scale (VAS) was used to assess pain score. Postoperative pain-free time, dolestin (opiod) and dipyrone (antipyretic) consumption were assessed 24 h after the surgery. Postoperative pain-free time in the CR oxycodone group (Group I) was 655 ± 548 min versus 112 ± 71.5 min in the placebo group (Group II) ($P < 0.02$). Postoperative 24 h dolestin consumption was 8.3 ± 19.5 mg (Group I) versus 120.1 ± 89.2 mg ($P = 0.004$) (Group II). Postoperative 24 h dipyrone consumption in Group I was 0.58 ± 0.67 g versus 1.42 ± 1.0 g in Group II ($P = 0.004$). Accordingly, 41.7% of patients in Group I demonstrated a need for postoperative analgesic drugs was versus 100% of the patients in Group II ($P = 0.037$). *Conclusions:* Preemptive administration of a single 40 mg oral dose of CR oxycodone significantly reduced both postoperative pain and consumption of analgesic agents, without causing side effects, and may be useful in an ambulatory surgery setting.

Keywords: Preemptive analgesia; Postoperative pain; Oxycodone

1. Introduction

The present study assesses the effectiveness of controlled-release (CR) oxycodone controlled-release medication in providing postoperative pain control after unilateral inguinal herniorrhaphy versus lactose as placebo treatment.

Although uncontrolled pain is a known impediment to postoperative recovery, strategies to ensure patient comfort have yet to be extensively integrated into clinical practice. In the face of expanding numbers of operations, optimal postoperative management becomes increasingly important as a medico economic and public health concern [1,2].

Preemptive analgesia includes the introduction of an analgesic regimen prior to a surgical procedure with the goal of attenuating pain postoperatively or even preventing pain throughout the entire perioperative period [2]. Additionally, since preemptive analgesia reduces the need for post surgical analgesic, patients return to normal activities earlier [3]. Preemptive use of controlled-release medication attenuates postoperative pain by providing stable serum concentrations, thus avoiding the erratic serum drug level fluctuations seen in administration of immediate-release formulations [1].

A search of the literature has found a number of studies published concerning the effect of controlled-released opioids on postoperative pain [2,4]. In contrast to immediate release analgesics, controlled-released opioids are capable of maintaining relatively constant serum levels. One such new opioid preparation available in tablet form is controlled-release oxycodone, which was designed to provide controlled delivery of oxycodone over 12 h. Onset of pain relief is seen within 1 h of administration [5], patient recovery accelerates, and both the need for subsequent opioids injections and for nursing care are reduced [1], a significant economic advantage. The technique may be implemented in an ambulatory surgery setting as well as in a inpatient hospital setting [5].

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Table 1
Influence of preemptive administration of CR oxycodone on postoperative pain severity

Parameters	CR oxycodone group	Placebo group	*P*
Mean age (±S.D.)	55 ± 17	56 ± 14	>0.05
Postop pain-free time (M ± S.D.)	655 ± 548 min	112 ± 71.5 min	<0.02
Dosage of dolestin (M ± S.D.)	8.3 ± 19.5 mg	120.1 ± 89.2 mg	=0.004
Number and percentage of patients requiring post surgerical dolestin	1/1216.7%	12/12100.0%	=0.02
Dosage of dipyrone (M ± S.D.)	0.58 ± 0.67 g	1.42 ± 1.0 g	=0.004
Number and percentage of patients receiving post surgerical analgesics	5/1241.7%	12/12100.0%	=0.037

Some authors have reported that preoperative administration of CR oxycodone was useless in the control of postoperative pain [1,6–9] while in other studies, high efficacy of postoperative pain control was noted [5,10,11]. Most of these earlier studies however, have used a low (10 mg) preoperative dose of CR oxycodone in contrast to the present study which used a 40 mg dose.

2. Methods

The study was conducted in the Surgical Department of Sieff Hospital, Safed, Israel, between 1 February 2002 and 30 August 2002. The trial was randomized, double blind and placebo-controlled. Approval was received from the institutional review board and written informed consent was obtained from patients, aged 30–65 years. All patients were in Groups ASA 1–2 and were scheduled for elective unilateral inguinal herniorrhaphy under spinal anesthesia L3–4 using heavy bupivacaine 10 mg. A total of 24 male patients were screened. Patients using chronic analgesics were excluded.

Two patient groups, namely CR oxycodone and placebo groups, were age-adjusted. Average age in CR oxycodone and placebo groups (M ± S.D.) was similar, 55 ± 17 and 56 ± 14 years, respectively ($P > 0.05$). Twelve patients received 40 mg tablets of controlled-release CR oxycodone orally 40 min before surgery. At the same time 12 patients in the placebo group received lactose tablets.

Assessment of pain severity was performed using a visual analogue scale (VAS) of self-patient method (with 0: no pain to 10: the worst imaginable pain). Postoperatively, all patients received IM dolestin (opioids) or oral dipyrone. When the patient initially complained of pain after operation, he received IM 50 mg of dolestin if the pain was more than 4 by VAS. If the pain score by VAS rose above 4 again, the patient received IM dolestin 1 mg/kg but not more often than one injection every 4 h. When the pain score was less than 4 by VAS, 1 g of liquid dipyrone was administered orally.

For each patient we assessed:

(1) Pain-free time from spinal injection to onset of pain.
(2) Total dolestin (opioid) consumption during 24 h after surgery.
(3) Total dipyrone (antipyretic) consumption during 24 h after surgery.
(4) Side effects such nausea, vomiting, and pruritus as reported by both patients and nurses at any time. *Note*: Patients were interviewed during rounds. Attending nurses were interviewed at the end of their shift.

Selected parameters of postoperative pain intensity were compared between the CR oxycodone and placebo groups. Statistical processing of data was done by Kruskal–Wallis analysis, Npar test, Mann–Whitney *U*-Wilcoxon rank test, and Fisher's exact test.

3. Results

In the CR oxycodone group, postoperative pain-free time was longer versus the placebo group ($P < 0.02$) (Table 1). Only two of the 12 (16.7%) patients in the CR oxycodone group required IM injection of dolestin during the 24 h after surgery, whereas all 12 patients (100%) in the placebo group received 1.9 ± 0.4 doses of dolestin daily ($P = 0.02$) (Table 1). The total daily dose of dolestin in the CR oxycodone group was significantly lower than in the placebo group ($P = 0.004$). In addition, the total daily dose of dipyrone in the CR oxycodone group was much lower than in the placebo group ($P = 0.004$). In the CR oxycodone group five patients (41.7%–5/12) received analgesics (dipyrone or dolestin), whereas all patients in the placebo group did ($P = 0.037$) (Table 1).

No side effects such pruritus, nausea, vomiting, drowsiness, sedation or respiratory depression were noted in either group.

4. Discussion

Unfortunately, opioids such as morphine sulfate or meperidine hydrochloride can produce mental and respiratory depression. They may also cause circulatory impairment that can increase postoperative morbidity when given in doses sufficient to produce postoperative pain relief [12]. These side effects are less characteristic of immediate-release oral opioids.

Immediate-release oral opioids should be given every 4–6 h on patient's request in order to control postoperative pain. These preparations are generally effective in relieving

moderate to severe pain although they can fail in postoperative pain control, thus delaying recovery [1,5,13].

Preemptive analgesia with controlled-release opioids, recently introduced into clinical practice, differs markedly from the current practice of using "as-needed" opioids or nonsteroidal anti-inflammatory drugs (NSAIDs). Controlled-release morphine successfully controlled pain when given 2 h prior to abdominal hysterectomy [7]. The present study demonstrates the efficacy of CR oxycodone administration 40 min before herniorrhaphy.

Some authors have found that preoperative administration of controlled-release opioids or NSAIDs not only reduces postoperative need for analgesic drugs but also the cost of treatment [1,2,5,14]. Positive results of the use of controlled-release opioids were noted in different clinical conditions; for example, controlled-release morphine sulfate tablets in abdominal hysterectomy and cesarean section provided full analgesic effects, whereas side effects such as mild to moderate drowsiness were minimal [15].

Patients who undergo unilateral inguinal herniorrhaphy often experience intense postoperative pain. Pain appears to be inadequately treated in about a half of all surgical procedures [2,16]. Preoperative administration of CR oxycodone reduced postoperative pain intensity both at rest ($P = 0.07$) and during movement ($P > 0.05$). The need for postoperative administration of both dolestin ($P = 0.02$) and dipyrone ($P = 0.004$) was reduced, and the number of patients who needed analgesics was significantly reduced ($P = 0.037$). Thus, patients utilized fewer health-care resources both in terms of medication and in terms of nursing care. None of the patients in either group reported any side effects. This may be due to the fact that most side effects are experienced in the first 2 h after ingestion and during that time the patients were being operated.

5. Conclusion

A single 40 mg dose of CR oxycodone administered preemptively 40 min prior to unilateral inguinal herniorrhaphy significantly decreases postoperative pain and consumption of "as-needed" dolestin and dipyrone, without causing side effects, and may be useful in an ambulatory surgery setting.

References

[1] Cheville A, Chen A, Oster G, McGarry L, Narcessian E. A randomized trial of controlled-release oxycodone during inpatient rehabilitation following unilateral total knee arthroplasty. J Bone Joint Surg 2001;83:572–6.
[2] Gottschalk A, Smith DS. New concepts in acute pain therapy: preemptive analgesia. Am Fam Phys 2001;63:1079–84.
[3] Dionne R. Preemptive vs. preventive analgesia: which approach improves clinical outcomes? Compend Contin Educ Dent 2000;21:51–4.
[4] Kissin I. Preemptive analgesia. Anesthesiology 2000;93:1138–43.
[5] Reuben SS, Connelly NR, Maciolek H. Postoperative analgesia with controlled-release oxycodone for outpatient anterior cruciate ligament surgery. Anesth Analg 1999;88:1286–91.
[6] Speranza R, Martino R, Laveneziana D, Sala B. Oxycodone versus paracetamol in cholecystectomy. Minerva Anesthesiol 1992;58:191–4.
[7] Cruickshank RH, Spencer A, Ellis FR. Pretreatment with controlled-release morphine for pain after hysterectomy. Anaesthesia 1996;51:1097–101.
[8] Rasanayagam R, Harrison G. Pre-operative oral administration of morphine in day-case gynaecological laparoscopy. Anaesthesia 1996;51:1179–81.
[9] Simpson KH, Dearden MJ, Ellis FR, Jack TM. Premedication with slow release morphine (MST) and adjuvants. Br J Anaesth 1988;60:825–30.
[10] Richmond CE, Bromley LM, Woolf CJ. Preoperative morphine preempts postoperative pain. Lancet 1993;342:73–5.
[11] Poyhia R. Opioids in anaesthesia: a questionnaire survey in Finland. Eur J Anaesth 1994;11:221–30.
[12] Pflug AE, Bonica JJ. Physiopathology and control of postoperative pain. Arch Surg 1977;112:773–81.
[13] Bourke M, Hayes A, Doyle M, McCarroll M. A comparison of regularly administered sustained release oral morphine with intramuscular morphine for control of postoperative pain. Anesth Analg 2000;90:427–30.
[14] Rowe WL, Goodwin AP, Miller AJ. The efficacy of pre-operative controlled-release indomethacin in the treatment of post-operative pain. Curr Med Res Opin 1992;12:662–7.
[15] Bloomfield SS, Cissell GB, Mitchell J, Barden TP, Kaiko RF, Fitzmartin RD, et al. Analgesic efficacy and potency of two oral controlled-release morphine preparations. Clin Pharmacol Ther 1993;53:469–78.
[16] Carr DB, Jacox AK, Chapman CR, Ferrell B, Fields HL, Heidrich G, et al. Clinical practice guidelines for acute pain management: operative or medical procedures and trauma. Washington, DC: Agency for Health Care Policy and Research; 1992. DHHS publication no. 95-0034.