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Intrathecal morphine reduces postoperative tramadol consumption in patients undergoing radical retropubic prostatectomy: a randomized trial

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Abstract. – BACKGROUND: Intrathecal (IT) morphine provides prolonged analgesia after major surgery.

AIM: The aim of our study was to assess the impact of intrathecal morphine 200 µg on patient-controlled analgesia (PCA) tramadol consumptions and postoperative pain in patients who underwent radical retropubic prostatectomy (RRP) under general anesthesia.

MATERIALS AND METHODS: In this prospective trial, 56 men who underwent radical retropubic prostatectomy (RRP) were randomized into 2 groups. Group M received intrathecal morphine (200 µg) before the induction of general anesthesia. Group C did not receive intrathecal morphine. Postoperative analgesia was provided with tramadol PCA. Pain scores, tramadol consumption, adverse effects, rescue analgesia were recorded.

RESULTS: Total tramadol consumption at 24 hours and pain scores during 12 hours postoperatively were significantly lower in Group M compared with Group C ($p < 0.05$). Rescue analgesia and postoperative nausea were lower in Group M than in Group C ($p < 0.05$).

CONCLUSIONS: Intrathecal morphine 200 µg provided a significant reduction in tramadol consumption, postoperative pain scores, rescue analgesia, and postoperative nausea after RRP without serious adverse effects.

Key Words:
Radical retropubic prostatectomy, Intrathecal morphine, Postoperative analgesia and tramadol.

Introduction

Intrathecal (IT) morphine without local anesthetic can be added to a general anestetic to provide prolonged analgesia after major surgery. Studies showed that benefit and risk of IT morphine as well as dose response should be evaluated for different surgical procedure[1]. Radical retropubic prostatectomy (RRP), which is the most common treatment for prostate carcinoma, causes severe postoperative pain[2]. This procedure is performed under general anesthesia and there are few studies evaluating the efficacy of intrathecal analgesia for postoperative pain after RRP[2-4]. These studies used IT morphine combined with clonidine and bupivacaine[2,4]. The aim of this report was to assess the efficacy and safety preincisional IT morphine alone for postoperative pain after RRP.

Materials and Methods

We enrolled 56 patients aged between 30-80 years, (ASA physical status I-II) undergoing RRP under general anesthesia in this study. This prospective, randomized study was approved by the Ethical Committee of Ege University School of Medicine, and written informed consent was obtained from all patients. Patients with allergy to local anesthetics or morphine, coagulation abnormalities, mental disturbance, diabeteS mellitus, cardiac or renal failure, neurological disease or patients who could not receive general anesthesia were excluded from the study. Patients were randomly allocated to one of two groups, according to a computer-generated list of random numbers: Group morphine (n=28) received IT morphine (200 µg) before the induction of general anesthesia. Group control (n=28) did not receive IT morphine. No premedication was given to the patients. After routine monitoring and intravenous (iv) access were established, patients in the morphine group received 200 µg morphine (0.5 mL) intrathecally. Injection was performed in the sitting position at the L3-L4 interspace via a midline approach with a 25-gauge Quincke needle. A standard anesthesia was given to both groups. Anesthesia was induced with atropine 0.5 mg/kg^{-1} iv,

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propofol 2 mg/kg^{-1}, remifentanil 1 μg/kg^{-1} and rocuronium 0.65 mg/kg^{-1} and maintained with O_2-air-sevoflurane and remifentanil infusion (0.25-1.0 μg/kg/min). At the end of anesthesia, neuromuscular block was reversed with standard doses of atropine and neostigmine. Postoperatively, all the patients received tramadol via a patient controlled analgesia (PCA) device with the following settings: bolus dose 50 mg followed by 20 mg on demand with a lockout interval of 15 min with a maximum allowable dose of 200 mg in 4 h. Rescue analgesia was paracetamol 1 g iv, if inadequate diclofenac sodium 75 mg intramuscularly (im). Postoperative pain was assessed after surgery using a visual analog scale (VAS: 0 no pain, 10 maximally tolerable pain) at 0, 15 min, 30 min, 45 min, 60 min, 2 h, 4 h, 6 h, 12 h, 24 h. Primary outcome measure was PCA tramadol consumption The secondary endpoints included the evaluation of pain at rest (VAS), rescue analgesia, adverse effects. Adverse effects were evaluated as present/absent: pruritus, postoperative nausea and/or vomiting, respiratory depression (respiratory rate < 8 breaths/min). At 24 hours, patient satisfaction about postoperative pain management was evaluated as good, neutral, or bad.

Statistical Analysis

Assuming a difference of 30% total tramadol consumption between the groups, it was calculated that 24 patients in each group would have been required with 80% power and 0.05 significance level. Data are presented as means ± SD or numbers for categorical variables. Data were analyzed using SPSS 16.0 for Windows (SPSS, Inc., Chicago, IL, USA). Chi-Square Test was used for the comparison patients satisfaction, Fisher's Exact Test was used for ASA, side effects. Demographic data were analyzed using Independent Samples Test and other data (duration of surgery, tramadol consumption) from two groups were compared using the Mann-Whitney U test. A p value < 0.05 was considered significant. Differences between two groups according to VAS scores was evaluated by Mann Whitney U test.

Results

56 patients completed the study. Groups were comparable with respect to demographic data and duration of surgery (Table I). VAS scores were significantly lower in IT morphine group compared to the control group in the first 12 h postoperatively ($p < 0.05$) (Figure 1). Tramadol consumption and the appearance of postoperative nausea were lower in IT morphine compared to the control group ($p < 0.05$) (Table II). Less patients in IT morphine required rescue analgesia than the control group ($p < 0.05$) (Table II). Only three patients recorded mild pruritus in the IT morphine group. No respiratory depression was reported. Patient satisfaction was higher in the IT morphine group ($p < 0.05$) (Table II).

Discussion

Our study shows the effectiveness of IT injection of 200 μg morphine for postoperative analgesia in patients undergoing RRP under general anesthesia. The decrease in postoperative pain intensity, less use of tramadol with lesser appearance of nausea resulted in higher patient satisfaction. Thus, single shot preincisional IT 200 μg morphine alone may be an effective and simple method for postoperative pain control after RRP in the first postoperative day.

In recent years clinical investigation on the use of IT morphine in the perioperative period has centered on finding the optimal dose of IT morphine for different surgical procedures[5]. Rathmell et al[6] found that after total hip replacement IT morphine 200 μg provided excellent analgesia. Gehling et al[7] reported that IT morphine in a dose of 200 μg provided effective postoperative analgesia and decreased the need for systemic opioids in orthopedic patients. Lower doses intrathecal morphine for major orthopedic procedures have also been studied by Frassanito et al in two studies[8,9]. In the first study the Authors compared the efficacy of intrathecal analgesia (morphine 100 μg, fentanyl 15 μg and hyperbaric bupivacaine 15 mg) and psoas compartment block in patients scheduled for primary hip

Table I. Demographic data.

	Group M (n=28)	Group C (n=28)
Age (y)	63.4 ± 5.7	62.6 ± 8.1
Weight (kg)	78.2 ± 14.3	80.6 ± 9.9
Height (cm)	173 ± 5.9	172 ± 5.9
ASA (1/2)	11/17	8/20
Duration of surgery (min)	115 ± 25.1	130 ± 33.7

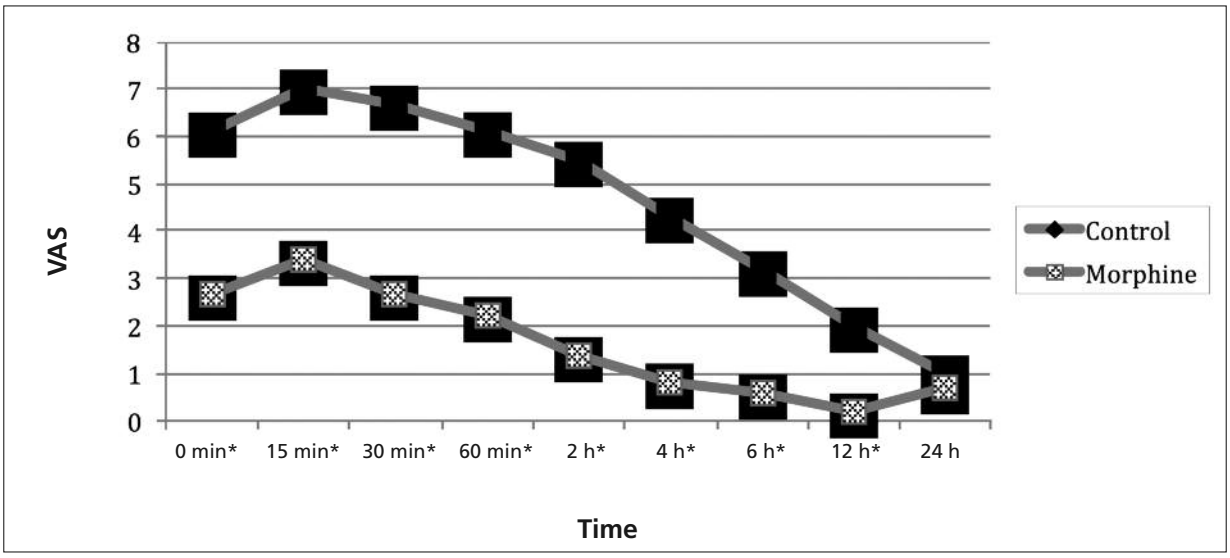

Figure 1. Postoperative pain scores in PACU. (*$p < 0.05$)

arthroplasty under general anesthesia. They found that in the setup receiving intrathecal morphine 100 µg, the patients had lower pain scores during the first 24 hours. They concluded that intrathecal morphine, fentanyl, bupivacaine and single shot psoas compartment block provide efficient postoperative pain control. In the another study, they compared intrathecal morphine 100 µg and femoral block in patients scheduled for total knee arthroplasty under spinal anesthesia. They found that intrathecal morphine provided better analgesia than femoral nerve block especially within the first 24 hours postoperatively. Massicotte et al[10] found that IT morphine 150 µg with 15 µg fentanyl decreased postoperative pain and morphine consumption by PCA without adverse reactions after abdominal hysterectomy.

IT morphine in higher doses has also been studied as an analgesic for pain after spinal procedures, and more extensive surgery such as thoracotomy or abdominal aortic aneurysm[11-14]. Available evidence suggests that the prevalence of side effects increases in proportion to the dose administered with doses greater than 300 µg producing nausea, vomiting, pruritus, urinary retention and respiratory depression[5,15]. Based on these findings we used IT morphine in a dose 200 µg and found that postoperative pain scores were significantly lower in patients receiving IT morphine than the control patients in the first 12 hours postoperatively. 200 µg IT morphine was found safe because no respiratory depression was observed and only three patients reported mild pruritus associated with IT opioid.

IT analgesia with morphine to control postoperative pain after RRP has been investigated in a few studies[2,3]. Brown et al[3] investigated the effect of IT analgesia and recovery from RRP. They tested the IT administration of bupivacaine 15 µg, clonidine 75 µg, and morphine 200 µg to general anesthesia with regard to postoperative pain control and recovery of functional status. They

Table II. Tramadol consumption and for rescue analgesia.

	Group M (n=28)	Group C (n=28)	*p* value
PCA tramadol consumption (mg)	172.3 ± 138.8	258.7 ± 111.2	0.01*
Side effects			
Nausea (yes/no)	1/27	11/17	0.001*
Pruritis (yes/no)	3/25	0/28	0.08
Rescue analgesic (yes/no)	6/22	23/5	0.000*
Patient satisfaction (good/neutral/bad)	22/6/0	9/19/0	0.001*

*$p < 0.05$.

found that IT analgesia decreased pain and supplemental iv morphine use over the first postoperative day. Since patients receiving IT analgesia required more iv fluids and vasopressors intraoperatively, the authors suggested that the benefits of improved analgesia must be weighed against other factors including the increased need for vasopressors.

In another report Adrieu et al[2] assessed the impact of IT morphine with or without clonidine on morphine consumption after RRP. Patients were allocated to receive IT morphine 4 μg/kg, IT morphine and clonidine 1 μg/kg or only PCA in their study. They found that morphine consumption in the first 48 h was decreased in the morphine and morphine + clonidine groups. Pain scores were lower in the morphine group until the 18th postoperative hour and until the 24th postoperative hour in the morphine and clonidine group. The authors did not report any respiratory depression nor pruritus during the study. The authors concluded that IT morphine provided a significant reduction in morphine requirements after RRP and the addition of clonidine to IT morphine reduced intraoperative sufentanil use and further prolonged analgesia.

Our work differs from the above-mentioned two studies because we used IT morphine alone for postoperative analgesia in RRP. We used the same dose as Brown et al[3] and found that 200 μg IT morphine is a safe and effective dose for postoperative analgesia after RRP. Brown et al[3] did not find any advantage of adding local anesthesia and clonidine to IT analgesia because of the perioperative deterioration in the hemodynamic variables they observed during the preoperative period.

Our postoperative pain data in the morphine group are in accordance with the findings of Adrieu et al[2] because we have also found that in the group receiving single IT morphine, pain scores were lower in the early postoperative period compared to the control group. However, our 200 μg IT morphine dose is smaller than their dose which 4 μg/kg.

Conclusions

IT administration of morphine can provide pain relief after a wide range of surgical procedure and single-shot preincisional IT morphine 200 μg is an effective and safe method for postoperative analgesia after RRP in the early postoperative period.

Conflicts of Interest

None.

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