ORIGINAL PAPER
Submitted: 24.05.2008 • Corrected: 27.05.2008 • Accepted: 28.05.2008

Intrathecal morphine for postoperative analgesia in patients with rheumatoid arthritis and osteoarthritis who underwent orthopedic surgery

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Summary

Introduction. The aim of this study was to evaluate the analgesic and side effects of intrathecal morphine in patients with rheumatoid arthritis (RA) and osteoarthritis (OA) underwent orthopedic surgery. ***Material and methods.*** Eighty ASA physical status I-II patients scheduled for elective hip arthroplasty under spinal anesthesia due to primary diagnosis of RA or OA were included in this study. All patients received intrathecal 0,5% hyperbaric bupivacaine (20 mg) with morphine in dose either 0,3 or 0,5 mg. Patients were divided into two groups:

Group OA – patients with osteoarthritis, Group RA - patients with rheumatoid arthritis. The duration of analgesia was measured from the time of intrathecal morphine administration to the time of the first injection of morphine SC. The total consumption of morphine SC was recorded during the first 48 hours after surgery. Sedation was assessed with using sedation score: 1 = awake, 2 = mostly sleeping.The intensity of adverse effects (respiratory depression, nausea, vomiting, pruritus and urinary retention) was evaluated at the following time at 1, 6, 12, 24, 48 h after the surgery. ***Conclusions.*** The patients with RA demonstrated more intensity of postoperative pain with shorter lasting analgesia compared to patients with OA. The total, postoperative consumption of morphine turned out to be higher in patients with RA. Eventually, these data indicate that intrathecal morphine produced dose – dependent analgesia and incidence of side effects, particularly pruritus. Nonetheless, we suggest that the factor such as disease aethiology merits consideration in the planning of analgesic regimens. *Anestezjologia i Ratownictwo 2008; 2: 116-123.*

Keywords: intrathecal morphine, rheumatoid arthritis, osteoarthritis, orthopedic surgery

Introduction

Spinal anesthesia is known as standard for lower limbs orthopedic surgery.

The addition of morphine to intrathecal bupivacaine improves patient comfort during orthopedic surgery and provides effective postoperative pain relief without sensory and motor blockade [1,2]. Morphine (mf) is commonly chosen for intrathecal (IT) application because of its relatively long duration of action (water soluble opioid), low cost and extensive history of effective clinical use. Unfortunately, neuraxial morphine is associated with side effects including nausea, vomiting, pruritus and respiratory depression [3-5].

Morphine administered into the subarachnoid space interacts with opioid receptors which are concentrated within the spinal cord gray matter, particularly in the dorsal horn, and the greatest densities are in substantia gelatinosa [6].

The present study was designed to compare the analgesic effectiveness and side effects of intrathecal morfine in patients with rheumatoid arthritis (RA) and osteoarthritis (OA) undergoing orthopedic surgery.

The study was approved by the Medical Ethical Committee of our hospital. All patients were informed about the study and written informed consent was obtained one day before the operation.

Material and methods

Eighty ASA physical status I-II patients scheduled for elective hip arthroplasty under spinal anesthesia due to primary diagnosis of RA or OA were included in this study. Exclusion criteria included age <24 or >75, an ASA physical status greater than II, allergy to morphine and local anesthetics, contraindications to spinal anesthesia, weight >100 kg.

All patients were premedicated with midazolam 7,5 mg orally, 1 h before surgery.

Prior to the spinal injection, Ringer's solution 7 ml/kg was infused through either a 14G or 16G intravenous cannula. Spinal anesthesia was performed in the lateral decubitus position, depending on the operation side and the injection was made into space L3-4 or L4-5 using a 25–gauge needle. All patients received intrathecal 0,5% hyperbaric bupivacaine (20 mg) with morphine in dose either 0,3 mg or 0,5 mg. Patients were placed supine after spinal injection.

If a tranquillizer was required, midazolam 1-3 mg was given intravenously (IV).

Blood pressure was noninvasively monitored every 5 min throughout surgery and every 1 h after surgery (24 h) and at the same time when the intensity of side effects was controlled (at 1, 6, 12, 24, 48 h after surgery). A decrease in systolic blood pressure more than 20% less than preanesthetic baseline value was treated by 5 mg IV dose of ephedrine. ECG and oxyhemoglobin saturation (SpO_2) were continuously monitored throughout surgery and 24 h after surgery. Supplemental oxygen was not placed routinely, however, whenever evaluation revealed oxygen saturation<94% oxygen 3-5 l/min via either a nasal canula or a face mask was added.

Operation and recovery in all patients went without any complications including respiratory, urine tract and wound infection. Postoperatively, patients did not receive any oral analgesic drugs. Postoperative analgesia consisted of subcutaneous (SC) morphine in dose 10 mg every 4-6 hours and IV paracetamol 1000 mg every 8 hours.

Pain was assessed during rest using the 10-cm Visual Analogue Scale VAS (0 = no pain; 10 cm = the worst possible pain) at the following times after the surgery: at 1, 6, 12, 24, 48 h.

The duration of analgesia was measured from the time of intrathecal morphine administration to the time of the first injection of morphine SC.

The total consumption of morphine SC was recorded during the first 48 hours after surgery.

Sedation was assessed with using sedation score: 1 = awake, 2 = mostly sleeping

The patients were divided into two groups:

- Group OA - patients with OA
- Group RA - patients with RA

Additionally, each patient received randomly either 0,3 or 0,5 mg intrathecal morphine.

The intensity of adverse effects (respiratory depression, nausea, vomiting, pruritus and urinary retention) was evaluated at the following times: at 1, 6, 12, 24, 48 h after the surgery.

The intensity of nausea, vomiting, pruritus was evaluated using a 3-point scale from 0 to 2 (none, weak, strong).

The respiratory depression (RD) was defined as saturation ≤90 and respiratory rates <10 breaths/min.

The data was analysed using the Statgaphics test (version 4.1) and Fischer's exact test.

p-value <0,05 was considered significant. The SPSS for Windows (version 14.0 PL) was used. Data are presented as mean ± SD.

Results

The study group was composed of 12 (15%) men and 68 (85%) women. The mean age of the patients was 58 years (56 for RA, 61 for OA). There were no significant differences between the groups of patients with respect to age, weight and duration of surgery. No failure in the spinal anesthesia was noted. No patients suffered from headaches in the following days and no complications related to spinal anesthesia were observed in either group. No difference was found between groups concerning the degree of sensory blockade which was assessed with the pinprick test bilaterally 10 minutes after the injection of local anesthetic with morphine. Variations in cardio-respiratory details were small and not significantly different in the two groups of patients.

The results of study have shown that the patients with RA experienced more intensive pain (1,9 ± 2,3)

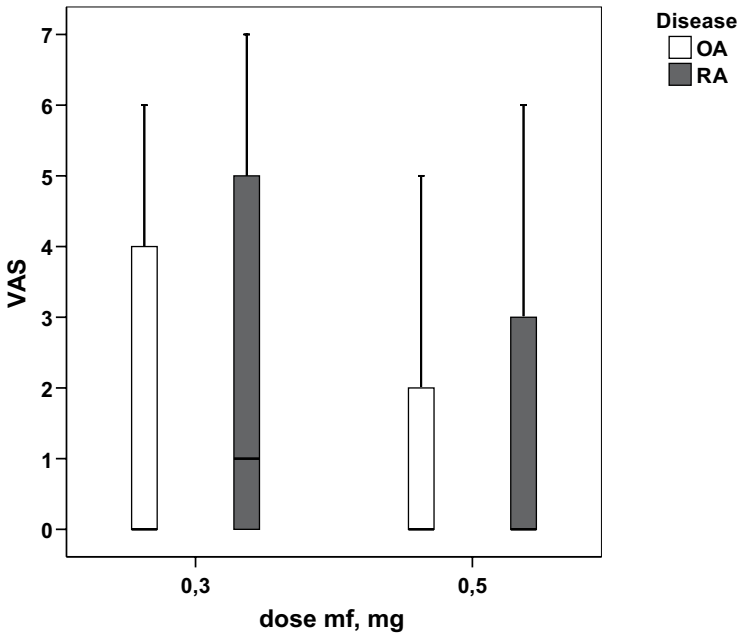


Figure 1. VAS scores for pain in patients with OA or RA who received either 0,3 or 0,5 mg of IT morphine

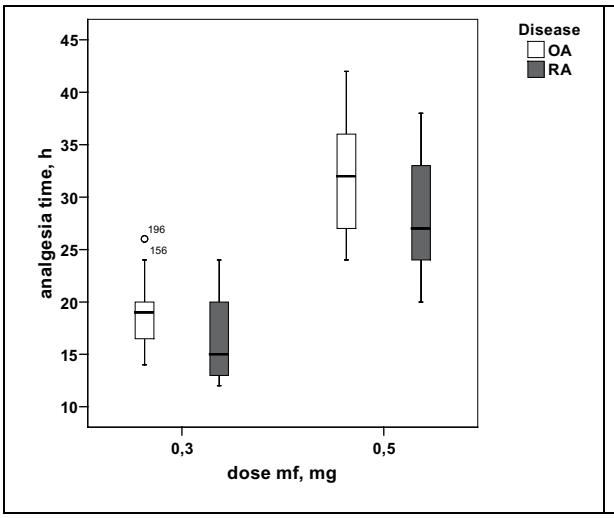


Figure 2. The effect of intrathecal morphine on time of analgesia (hour) in patients with OA and RA

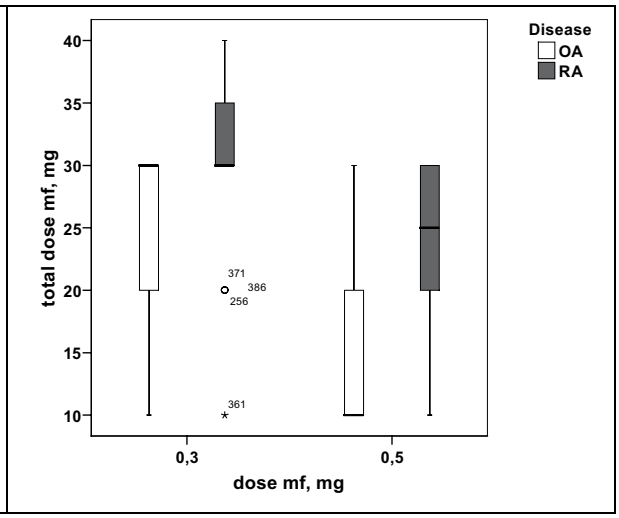


Figure 3. The effect of intrathecal morphine on total dose of morphine SC which was given to patients with AO and RA in the first 48 hours after surgery

than the patients with OA (1,4 ± 1,9). VAS scores were higher in the RA group than in the OA group (Figure1.) irrespectively of intrathecal morphine dose. The difference between groups of patients was statistically significant (p = 0,04)

The analgesic effect of IT morphine was significantly better in patients with OA (Figure 1.) and the time of IT morphine analgesia was also longer in these patients (25,4 ± 7,6) than in the others (22,3 ± 7,8). The difference between groups of patients was statistically

significant (p<0,005). The differences between doses administered to these two groups of patients were significant (p<0.005). The patients with RA demonstrated a shorter time of IT morphine analgesia irrespective of IT mf mg (Figure 2). However, the patients who had taken 0,5 mg IT mf presented a longer time of analgesia than the other patients. The mean time of postoperative analgesia was respectively: OA (0,5 mg) 31,55 ± 5,2, OA (0,3 mg) 19,15 ± 3,4, RA (0,5 mg) 28,4 ± 5,5, RA (0,3 mg) 16,2 ± 3,9.

The mean total dose of SC morphine application was significantly greater in patients with RA (26,5 ± 8,6) than in those with OA (19,5 ± 8,1). The difference between groups of patients was statistically significant (p<0,005). All patients who had received 0,3 mg IT morphine needed a higher dose of SC morphine to relieve postoperative pain (Figure 3.). The differences between doses of IT mf were statistically significant (p<0,005).

The sedation score was in the normal range and none experienced deep sedation with a difficulty to waken. However, patients who received 0,5 mg IT morphine had significantly higher sedation scores (p<0,05) than the other patients. A significant difference between groups of patients has not been found.

Side effects

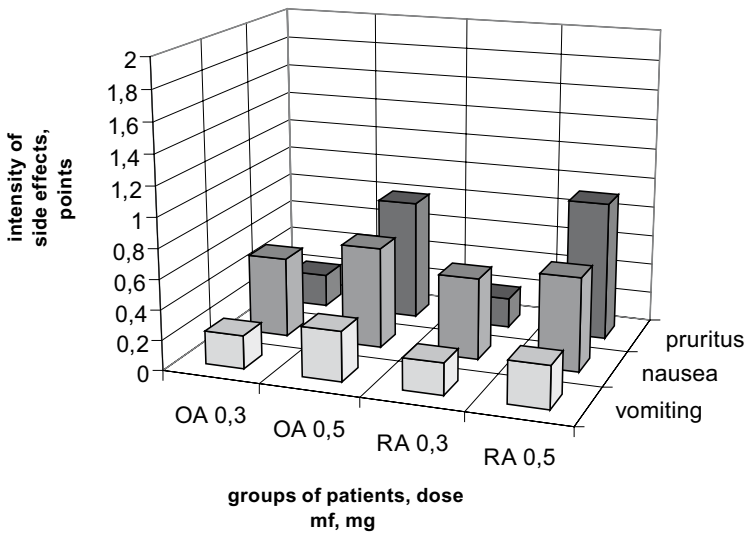
The intensity of side effects including nausea, vomiting and pruritus did not differ between the groups of patients related to disease. We have found a significant statistical difference between doses of IT morphine related to pruritus (p<0.05). The intensity of pruritus turned out to be the strongest in the patients who were given 0,5 mg morphine intrathecal (Figure 4.).

In all patients, the urine catheter was continued for 36-hrs after surgery and after removing it nobody complained of urinary retention.

We did not observe symptoms of respiratory depression (saturation ≤90 and respiratory rates <10).

Discussion

Hip joint replacement is a major operation leading to significant postoperative pain and associated analgesic regiments and opioids are commonly chosen for



	OA 0,3	OA 0,5	RA 0,3	RA 0,5
vomiting	0,22	0,33	0,21	0,28
nausea	0,53	0,67	0,54	0,62
pruritus	0,22	0,80	0,20	0,92

Figure 4. The intensity of side effects in patients with OA or RA who received either 0.3 mg or 0.5 mg IT morphine

pain relief. An alternative technique to pain controlled analgesia and peripheral nerve block may be intrathecal administration of opioids. Intratecal administration of opioids is frequently used to provide excellent pain control without either sensory or motor blockade.

Although the efficacy and side effects have been demonstrated in many studies, none presented them in the context of disease aethiology.

Our study demonstrated that patients with RA experienced more intensive pain irrespective of intrathecal morphine dose and finally, the time of postoperative analgesia is shorter so as these patients needed more analgesics to relieve pain.

One possible explanation for this observation may be the role of interleukin 6 in pathogenesis of RA – the chronic, progressive, systemic inflammatory disorder affecting synovial joints and typically producing symmetrical arthritis [7-10].

Persistent overproduction of IL-6 has been observed in response to the increased IL-1 at the arthritic joints suggesting a principal role of IL-6 in RA [11-13].

Patients with RA showed a high level of serum proinflammatory cytokines, which is usually connected with this disease severity [14,15].

Cytokines play a part in the modulation of pain and this modulation may result from changes in proteins involved in the pain pathway. Their activation plays a role in the induction of neuronal sensitization, a process underlying prolonged painful states characteristic of chronic inflammation. This important role in nociception is ascribed to IL-6, which modulates the action of several pain mediators and alters the perception and responses to pain stimuli [16].

Another explanation may be the chronic inflammation which is also characterized by the release of proinflammatory substances. The chronic inflammation that characterizes both diseases may also lead to increased pain sensitivity. Although both diseases are characterized by joint destruction, their symptoms are different. In patients with OA the inflammation is limited to the joint being stricken by a disorder. In contrast rheumatoid arthritis affects many joints and causes changes in many organs. Therefore, the severity of uncontrolled inflammation is significantly greater in patients with RA as compared with OA.

Additionally, the association between cyclooxygenase-2 (COX-2) genotypes and risk and severity of rheumatoid arthritis is known. These results of studies suggested that COX-2 genotyping might be useful in predicting the risk and severity of RA in individuals without the shared epitope, however, the radiologic severity of RA was not associated with COX-2 polymorphisms [17,18]. In peripheral sensitisation, local tissue injury or inflammation results in local production of COX-2, which converts arachidonate to prostaglandins (PGs). Elevated PGs sensitise primary afferent neurons and lead to the transmission of pain stimuli to the dorsal horn. Central sensitisation is a complication of ongoing pain or inflammation; COX-2 and prostaglandin levels are increased in the CNS in response to both peripheral inflammatory stimuli and the direct action of inflammatory cytokines [19,20]. It can result in an increased sensitivity to painful stimuli or painful perception in patients with strong chronic inflammation such as RA.

We found that the mean time of analgesia in all patients was 24 hrs. In our work intrathecal morphine produced analgesia lasting more than 25 hrs (for pts with OA), which was longer than the results shown in other studies [2,21]. Compared with these studies the duration of analgesia in our patients was longer because we recorded the time to the first request for analgesic in a different way. Our criterion was the time of administering the first morphine dose SC and not the VAS score, as was the case in other studies. Furthermore, these studies included patients having another type of orthopedic procedure, which might be associated with higher analgesic demand. In addition the intensity of pain in one study was measured in movement at shorter intervals.

In RA group the mean total consumption of morphine was 26,5 mg compared with 19,5 mg in the other group, and we think that the difference is appreciable and correlates with pain severity sensation in patients with RA. The obtained results of mean VAS values are in accordance with the data were presented in other studies (where such groups were not differentiated) [22,23].

We chose the evaluation of intensity of side effects instead of frequency in contrast to the other authors [24,25]. This approach seemed to be better for showing nuisances.

The dose – dependent intensity of pruritus was similar in both group of patients but it was shown significantly stronger with 0,5 mg of IT morphine. The intensity of nausea has been found to be similar in all patients irrespectively of disease. We have found

a correlation between the IT morphine dose and the intensity of nausea that is consistent with our previous study and the results presented by other authors [26]. In contrast to our study those authors evaluated the frequency of side effects.

Postoperative itching and nausea after intrathecal morphine are undesirable side effects and are caused by many complex mechanisms. The central mechanism of opioid-induced pruritus and nausea may be related to cephalad spread of the drug. Our patients have been treated with naloxon in a low dose (0,1 mg) and this classic μ-receptor antagonist turned out to be effective in preventing or treating opioid-induced nausea and pruritus. We did not find an increase of postoperative pain after naloxon. The drugs that may reduce pruritus and nausea without affecting the μ-receptor were also used to prevent them. Anti-emetic prophylaxis was also provided by intravenos torecan and metoclopramid with good results. Many authors suggested that ondansetron was effective in treating pruritus [27-30] but similarly to others we preferred to use it in preventing and treating nausea and vomiting [31]. We found that ondansetron is not significantly effective against pruritus and our suggestions are consistent with those of other authors [32].

No symptoms of respiratory depression were observed.

The term "respiratory depression" has no clear definition from a review of the literature on ITmf use for postoperative analgesia. While defining RD with bradypnea is superior to having no definition, this is still inadequate [33]. Therefore we decided to define RD with bradypnea (respiratory rates <10 breaths/min) and low saturation ($SaO_2 \leq 90\%$).

Although it is known that intrathecal morphine can predispose to respiratory depression [34-36] which has been shown to be dose-related and mediated via a central effect. Therefore we suggest that all patients who received treatment with morphine should stay in the postoperative ward and should be monitored for 24 hrs after the last dose administration.

No patients experienced urinary retention and similar results were demonstrated by other investigators [37,38]. The lack of urinary retention problems might be explained by the time of keeping the urinary catheter which was removed after 36 hours.

Conclusion

The patients with RA demonstrated more intensity of postoperative pain with shorter lasting analgesia compared to patients with OA. The total, postoperative consumption of morphine turned out to be higher in patients with RA. Eventually, these data indicate that intrathecal morphine produced dose – dependent analgesia and incidence of side effects, particularly pruritus. Nonetheless, we suggest that the factor such as disease aethiology merits consideration in the planning of analgesic regimens.

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