



## Intra articular intraoperative morphine causes increased postoperative demand and after total knee replacement

**Khaled Awwad Al-issa\*, Raid Hamad Al-smadi, Ethar Najeeb Ibrahim , Anan Hassan Qabha**

Department of anesthesia, intensive care and pain management, KHMC, Amman, Jordan.

### Abstract

Objective of the study was to assess the postoperative pain relief influence of intraoperative intra-articular morphine after total knee replacement. This prospective, double-blind and randomized study included 103 patients of both sexes, aged 46-75 years, classed I-III physical status by the American society of anesthesiologists and scheduled for total knee replacement for chronic osteoarthritis at Prince Hashim hospital, Zarqha, Jordan, during the period April 2014-March 2015. Patients were assigned randomly into two groups. Group I (n=60), patients received a mixture of 10 mg of morphine (1 ml) and 9 ml of normal saline(0.9%) and group II (n=43), patients received 10 ml of normal saline (0.9%). Postoperative morphine administered in the first 24 hours was registered. Postoperative pain was evaluated using the visual analog pain scale 0-10, at 1 and 24hours after surgery. Student's t test and Chi-square test were used to test statistical significance where P value less than 0.05 was considered significant. There were no significant differences between the two groups regarding the period of admission in hospital or the pain score at postoperative 1 or 24 hours. Patients in group I, received significantly more morphine in the first postoperative 24 than in group II. Intra-articular intraoperative morphine administration has no significant analgesic postoperative effect.

**Keywords:** Intra-articular, intraoperative, knee replacement, morphine, pain, postoperative.

\*Corresponding Author: Dr Khaled Awwad Al-issa, Department of anesthesia, Intensive care and pain management, KHMC, Amman, Jordan. Email: mnezel@gmail.com

Received: February 18, 2015 Accepted: April 23, 2015. Published: May 20, 2015. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

### Introduction

Analgesic actions of intra-articular administration of morphine after arthroscopic knee surgical technique was investigated by others in the past [1]. It was demonstrated that only small amounts are needed to treat pain effectively. The perfect analgesic must reduce pain with minimum adverse effects. When composing a management plan, it is important to imagine what causes pain perception and correlated distress. The international association for the study of pain defines pain as unpleasant sensory

and emotional experience correlated with actual or potential tissue damage or described regarding such insult. The degree of tissue damage and perception of pain are not associated [2]. Pain perception is a complicated feature, engaging sensory, emotional and cognitive features. While analgesic agents are potent in reducing acute and chronic pain, other factors may be discussed.

Patients continue to experience pain although there are a wide range of analgesics in the surgical theatre. When composing a management plan for acute setting, the balanced or multimodal analgesia is excellent. These define the administration of mixed agents acting by various mechanisms or at various locations in the pain tract [3]. Analgesics mixtures can be additive or synergistic regarding their way of action leading to dose-sparing actions with decrease in adverse effects. Optimal and recurrent evaluation of patients is crucial in defining adequate analgesic protocol. The aim of our investigation was to assess the postoperative pain relief influence of intraoperative intra-articular morphine after total knee replacement.

**Materials and Methods**

This prospective, double-blind and randomized investigation included 103 patients of both sexes, aged 46-75 years, classed I-III physical status by the American society of anesthesiologists and scheduled for total knee replacement for chronic osteoarthritis at Prince Hashim hospital, Zarqha, Jordan, during the period April 2014-March 2015 after obtaining written informed consent from all participants and approval from the ethical and research Jordanian board review committee. Patients with history of hypersensitivity to morphine were excluded from the study.

General laryngeal mask airway anesthesia was used in 80 patients and subarachnoid block anesthesia was used in 23 patients .Induction of general anesthesia included Propofol 2mg/kg, Fentanyl 3mg/kg and rocuronium 0.5 mg/kg. Subarachnoid block anesthesia included 3ml (0.5%) of plain bupivacaine. After skin closure, different solutions were administered intra-articularly of the knee. Patients were assigned randomly and double-blindly into two groups. Group I (n=60) patients received a mixture of 10 mg of morphine (1 ml) and 9 ml of normal saline (0.9%) and group II (n=43) patients received 10 ml of normal saline (0.9%). Postoperative morphine administered in the first 24 hours was registered. Postoperative pain was evaluated using the visual analog pain scale 0-10, at 1 and 24hours after surgery [4]. As another indicator of pain, morphine as intravenous required incremental doses of 2 mg was administered in the first 24 hours after surgery and was registered. Student’s t test and Chi-square test were used to test statistical significance where P value less than 0.05 was considered significant.

**Results**

There were 73 females and 30 males, distributed almost equally in both groups. The mean age in the whole study group was 60.5 years (46 to 75, SD ± 12.5) (Table I). In group I there were 20 males and 40 females with a mean age of 65.5 years while in group II, there were 15 males and 28 females with a mean age of 57.5 years.

There were no significant differences regarding the patients pain score at 1(p >0.05) and 24 hours (p >0.05) between the two groups and the period of admission in hospital (p >0.05) (Table II). Patients in group I received significantly more

morphine (p <0.05, mean 36.8 mg) than patients in group II who received a mean of 30.4mg) in 24 hours. Table II.

	Group I (n=60)	Group II (n=43)
<b>Age(yr)</b> 46-75 (mean 60.5, SD ± 12.5)	56-75 (65.5 ± 13.6)	46-69 (57.5 ± 10.2)
<b>ASA</b>		
<b>I</b>	30	24
<b>II</b>	20	12
<b>III</b>	10	7
<b>SEX</b>		
<b>M</b>	40	31
<b>F</b>	20	12
<b>Anesthesia</b>		
<b>General</b>	47	33
<b>Subarachnoid</b>	13	10
<b>Intra-articular</b>	Morphine	Saline

**Table I:** Demographic features of study subjects.

	Group I	Group II
<b>Mean period of admission (days)</b> (Mean ± SD)	7.3 ± 1.5	7.6 ± 1.3
<b>Mean postoperative pain Score (Mean ± SD )</b> <b>at:</b>		
<b>1hour</b>	4.4 ± 0.8	4.3 ± 0.6
<b>24hours</b>	2.8 ± 0.5	2.7 ± 0.6
<b>Mean amount of morphine used(mg)</b> (Mean ± SD) in 24 hours	36.8 ± 17.2	30.4 ± 16.5

**Table II:** Postoperative outcome profile. Whole study group.

In the 80 patients who had total knee replacement performed under general anesthesia, there was no significant difference in postoperative pain score between the two groups (Table II) at 1(p >0.05) and 24 hours (p>0.05) (Table III). If morphine had been administered into the knee at skin closure, patients received more intravenous morphine at 24 hours (p<0.05). There was a significant difference in the amount of morphine used at 24 hours by patients in groups I and II (p<0.05). No significant difference was recorded in patients who had total knee replacement performed under subarachnoid block

Awwad Al-issa K, Al-smadi RH, Ibrahim EN, Qabha AH. (May 2015). Intra articular intropoperative morphine causes increased postoperative demand and after total knee replacement. *Jour of Med Sc & Tech*; 4(2); Page No: 145 – 147.

anesthesia at 1(p>0.05) and 24 hours (p >0.05).Table IV.

	Group I	Group II
<b>Intra-articular</b>	Morphine (n=47)	Saline (n=33)
<b>Postoperative pain score at:</b>		
<b>1hour</b>	4.3	4.4
<b>24 hours</b>	2.8	2.7
<b>Mean amount of morphine (mg) at 24hours</b>	38.3	32.0

**Table III:** Postoperative outcome in patients with general anesthesia.

	Group I	Group II
<b>Intra-articular</b>	Morphine (n=13)	Saline (n=10)
<b>Pain postoperative score at:</b>		
<b>1hour</b>	2.9	3.0
<b>24hours</b>	2.4	2.8
<b>Mean amount of morphine (mg) at 24hours</b>	18.0	18.7

**Table IV:** Postoperative outcome in patients with subarachnoid block anesthesia.

## Discussion

Our results were the opposite to the results of others [1]. Patients who received intra-articular morphine at skin closure used more morphine in the first postoperative 24 hours than patients who had been administered saline. Our conclusion doesn't match the recommendations of Stein et al [1] that morphine administered intra-articularly at skin closure has an excellent postoperative pain relief influence after total knee replacement.

Opiates are the most commonly administered analgesics for the management of moderate to intense pain. Nevertheless, there are great fallouts in our information in terms of clinical pharmacology as the selection of agent and dose is empirical [5]. Opiates can be extremely potent but control of dynamic pain on movement or incident pain can be weak with extreme adverse effects. Opiate included synthetic and natural agents acting on opiate receptors. Opiates are natural opioids coming from the opium poppy *Papaver somniferum*, of which is morphine.

Knowing the exact physicochemical and pharmacokinetic characteristics is crucial to define the adequate path of agent administration to attain an effective receptor location concentration for an estimate duration of

action. All opiates are weak bases. The relative percentages of free and ionized parts depend on plasma PH and the PKa of the opiates [6]. The volume of opiate diffusing to the location of action (diffusible part) depends on lipid solubility, concentration gradient and degree of binding.

Postoperative pain score was almost comparable between the whole study group results and the general anesthesia group results. This was 4.4 and 4.3 in group I and was 4.3 and 4.4 in group II, at postoperative 1hour. This was not the case in subarachnoid anesthesia where the visual analog pain score was 2.9 in group I and 3 in group II. This illustrates the concept that spinal block was more efficient than general anesthesia in this type of surgery. There were significant differences between the general anesthesia and whole study groups and the spinal group but this difference disappeared at postoperative 24hours when the mean visual analog pain score was 2.8, 2.8 and 2.4 in group I while it was 2.7, 2.7 and 2.8 in group II. Subarachnoid block reduced the need for postoperative morphine as it was 18mg in both groups but it was 36 and 38 mg in group I in whole study and general anesthesia groups while it was 30 and 32 mg in group II in both previous groups. These results were similar to Ritter et al [7].

## Conclusion

Intra-articular intraoperative morphine administration has no significant analgesic postoperative effect. Instead, it increased the postoperative needs for morphine in the GA group. We emphasize that subarachnoid block is efficient in those operations.

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