



## Postoperative analgesic effect of intraoperative loading dose of morphine in caesarean section

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### General Note



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### ABSTRACT

**Objective:** evaluate the effect of intraoperative morphine intravenous (IV) in addition to tramadol and NSAIDs on post-operative analgesia in cesarean sections. **Methods:** This is a prospective comparative study done at Baghdad teaching hospital & nursing house at medical city complex from January 2017 to January 2018, including 100 patients scheduled for elective cesarean section. Patients are divided into two groups, one group receives morphine intraoperatively, and the other group is control group. Postoperative pain was assessed at specific time interval using numerical analogue scale. **Results:** Effect of morphine on pain score at awakening and after 15 minutes show significant difference otherwise no significant difference in the later 16 hours. Time of recovery is significantly

increased in morphine group. **Conclusions:** Intraoperative morphine administered after baby delivery in cesarean section decrease pain significantly at 0, 15 minutes postoperatively but did not affect pain score in the later 16 hours.

**Keywords:** Intraoperative morphine, postoperative analgesia, morphine in caesarian section, Preemptive analgesia

## 1. INTRODUCTION

With advancement of pain management and increase awareness toward pain management, there still more room for postoperative analgesia improvement (Gan *et al.*, 2014a). Postoperative pain continues to be inadequately managed in a surprising proportion of patients (Gan, 2017, Sommer *et al.*, 2008), this is most notably found in gynecological and orthopedic surgeries. Several risk factors existed that increased the incidence of postoperative pain, like woman sex, young people, etc (Murray and Retief, 2016). The main therapeutic option for post-op pain management is morphine (and other opioids), however there use require more adjustment to achieve an acceptable balance between effective pain control and harmful side effects (Gan, 2017; Bavarsadkarimi *et al.* 2020), and this is may be one of important reasons that patients experiencing moderate or severe pain received only 46% of their prescribed morphine in developing countries (Murray and Retief, 2016; Abdulla *et al.*, 2020).

Morphine is strong opioid that can be given in different routes of administration. It is easily titrated, provides a lasting analgesic effect and is inexpensive. Intravenous morphine can be safely used in older patients with intact cognitive function (Sommer *et al.*, 2008). Owing to its low lipid solubility, morphine have a relatively slow onset of action thus does not allow rapid titration to effect, this means that even following intravenous administration, peak analgesic effect will not be achieved for some time (Pathan and Williams, 2012; Gan *et al.*, 2014b). Early administration of morphine in the course of surgery to control postoperative pain may reduce the time required to control pain and increase patient satisfaction, however, results of preemptive analgesia remain equivocal and uncertain (Ong *et al.*, 2005). In our study we will evaluate preemptive morphine administration in cesarean section to control pain postoperatively.

## 2. PATIENTS AND METHODS

### Study design and setting

This was randomized prospective comparative study done at Baghdad teaching hospital and nursing house at medical city complex (from January 2017 to January 2018) including 100 patients scheduled for elective caesarean section (CS).

### Inclusion criteria

Elective CS  
Age between 18 to 45 years old undergo caesarian section  
Weight of patients between 50-100 kg

### Exclusion criteria

Emergency CS  
Level 3 to 4 ASA grade  
Any patient with allergy to any drug  
Any patient with chronic pain disease  
Patient with chronic analgesic use

### Study protocol

All patients receive anesthesia as follow: Preoxygenation for 5 minutes, Induction: Propofol dose (2-2.5 mg/kg), Ketamine (0.5 mg/kg), Dexamethasone (8mg), Rocuronium (0.6mg/kg) maintained on oxygen & Isoflourane 0.75-1.5%. Intubation done confirmed by auscultation, IPPV & standard. While monitoring for all patients which include: SPO<sub>2</sub>, NIBP, and ECG. After delivery of baby, Fentanyl (1 mcg/kg), oxytocin (10 unit direct IV and 20 unite by infusion), tramadol (1 mg/kg) IV, Diclofenac (1mg/kg) IM were administered. At the end of operation reversal agent administrated (neostigmine2.5mg+atropine1mg). All the 100 patients were allocated randomly into 2 groups: Group 1 (M) contain 50 females receive morphine (0.1 mg/kg) by 15mg morphine ampoule diluted in 5 ml normal saline after delivery of the baby. Group 2 (C) which contain 50 females receive equipotent volume from 5 ml syringe filled with normal saline.

### Pain scoring

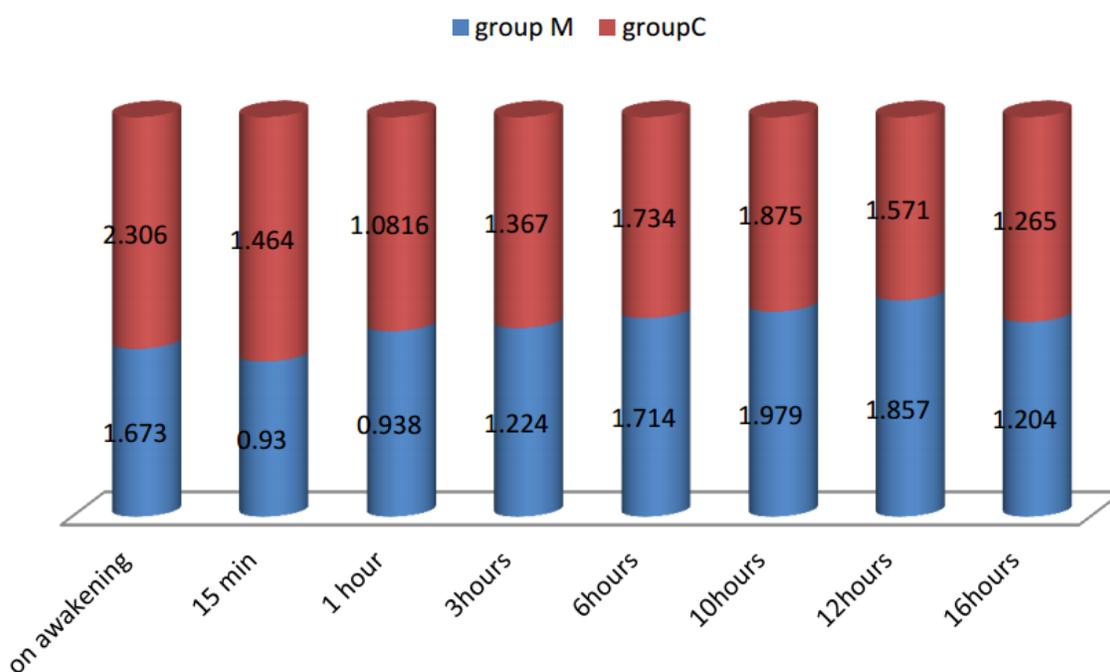
Pain scoring for all patients recorded by using numerical analogue scale. Pain recorded at awaking, 15 min and 1, 3, 6, 12, and 16 hours. If patient have pain on recovery period, she receives morphine intravenously (0.05 mg/kg). Both groups in the ward received the recommended doses of Tramadol and Diclofenac. If patient have pain in the ward, she receives paracetamol infusion (1000 mg) SPO2 also recorded postoperatively to see if there is any attack of respiratory depression. We also recorded duration of recovery from giving reversal to extubation.

### Statistical analysis

Categorical variables were assessed using Fisher exact test, while independent t-test used for analysis of continues variables. Kaplan-Meier Survival and ANOVA analysis were performed using Graph Pad 5.0 Software.

## 3. RESULTS

Effect of morphine on pain score at awakening & after 15 minutes show significant difference  $p= (0.005)$ ,  $p= (0.0012)$  respectively. The effect of morphine on pain score at 1, 3, 6, 10, 12, and 16 hours show no differences as  $p$  values (0.150), (0.197), (0.457), (0.255), (0.04), (0.292) respectively as illustrated in figure (1).



**Figure 1** pain score for group M and group C

### Respiratory depression

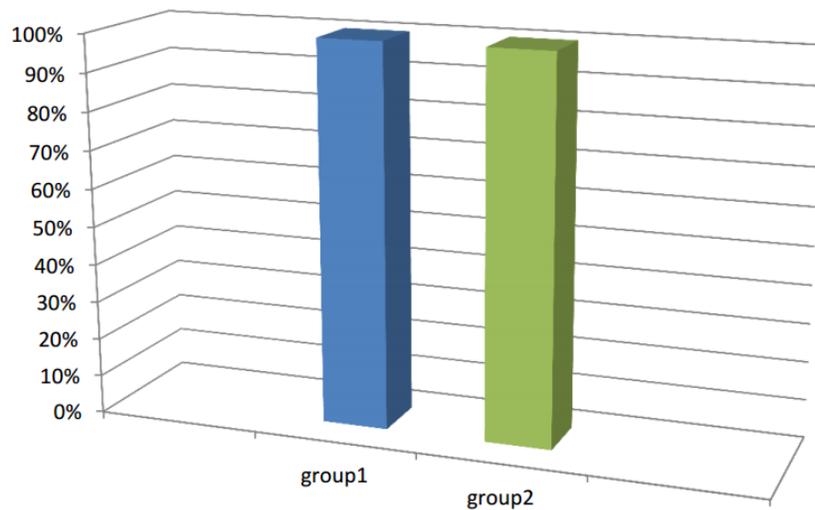
Only one patient suffers from respiratory depression in group M While group C no patient suffer from that problem.

### Spo2 recordings

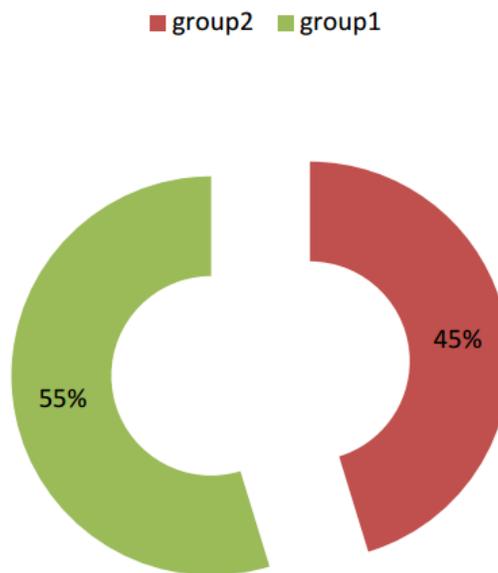
For group M the median result for spo2 recordings post operatively was 94.16%, while group C the results was 95% as illustrated in figure 2.

### Duration of recovery

Time of recovery was recorded in both groups, group C median time was 2.73 minutes, while group M was 3.3 minutes It was significantly affected by morphine ( $p=0.0089$ ) as illustrate in figure 3& 4.



**Figure 2** the medians for SPO<sub>2</sub> recordings for 100 patients, also the SPO<sub>2</sub> saturation show no difference  $p = (0.07)$ . For group M the median result for SPO<sub>2</sub> post operatively is 94.16%, while group C is 95%.

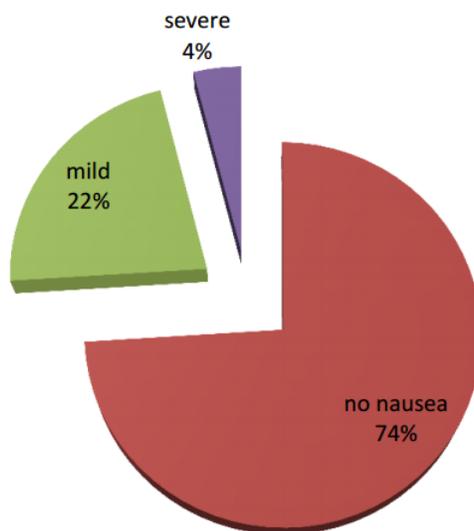


**Figure 3** the time of recovery difference between both groups. Duration of recovery is significantly affected by morphine ( $p=0.0089$ ). Group C median time was 2.73 minutes Group M was 3.3 minutes.

#### 4. DISCUSSION

In our study both groups were received intraoperative Fentanyl, Tramadol, and Diclofenac. Morphine was added to group M by loading of 0.1mg/kg after baby delivery. We observed that intraoperative morphine was only effectively decrease pain score in 0 minute and 15 minutes postoperatively. The patients still need titration of morphine to reach an efficient level of analgesia in the recovery period in our study. A larger dose of morphine (0.15 mg /kg) as loading at the end of surgery slightly decrease VAS but did not reduce time to pain relief or morphine consumption within the 24 hours postoperatively as shown by (Aubrun *et al.*, 2007) in their study in which analgesia maintained intraoperatively with only sufentanil (Aubrun *et al.*, 2007). It is consistent with our observation that only mild decrease in VAS in immediate postoperative period when morphine is added intraoperatively. Doses higher than 9 mg of morphine intraoperatively associated with 30 days read missions in ambulatory surgery as shown by (Long *et al.*, 2018). Also, adjusting morphine dose to sufficient level enough to control pain, while minimize the sedative effect of it post-

operatively will maximize the benefit and reduce side effect (Jain *et al.*, 2012). We showed in our study that titrating morphine dose in recovery period, and use of postoperative Tramadol, Diclofenac and Acetaminophen was good option to relieve pain to avoid higher dose of morphine to decrease unnecessary adverse effects.



**Figure 4** group M patients suffer from nausea

Fletcher and colleagues show that despite using intraoperative bolus of morphine, an additional dose of morphine was required in the postoperative period and in PACU, VAS decreased slightly with increased incidence of adverse effect. In consistency with our study it show that decrease pain score was in immediate postoperative period only (Fletcher *et al.*, 2000). More thorough studies needed to clarify the role of intraoperative morphine on different surgical operations to control postoperative pain with less sedation and adverse effect. Our study showed that intraoperative use of 1mg /kg Tramadol i.v and 1 mg / kg Diclofenac i.m was a good substitute as the pain score post operatively was generally accepted.

## 5. CONCLUSION

Intraoperative 0.1 mg/kg morphine in cesarean section after baby delivery significantly decrease pain score at 0 and 15 minutes postoperatively while no significant difference at 1,3,6,10,12,16 hours. Time of recovery was significantly affected by morphine. We recommend to not using morphine intraoperatively to control postoperative pain and the use of Tramadol and Diclofenac is a good option instead.

### Author contribution

Iyad Abbas Salman: Conception and design of the work, the acquisition, analysis, and interpretation of data for the work, and Drafting the work.

Hawazen Mohammed El-moraeb: Conception and design of the work, interpretation of data for the work, and revising it critically for important intellectual content

Haider Abbass Hassen: Conception and design of the work, and Drafting the work and finally revising it critically for important intellectual content

### Funding

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### Conflict of Interest

The authors declare that they have no conflict of interest.

### Informed consent

Written informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

### Ethical approval for human

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards (Code: 2017/A113).

### Data and materials availability

All data associated with this study are present in the paper.

### Peer-review

External peer-review was done through double-blind method.

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