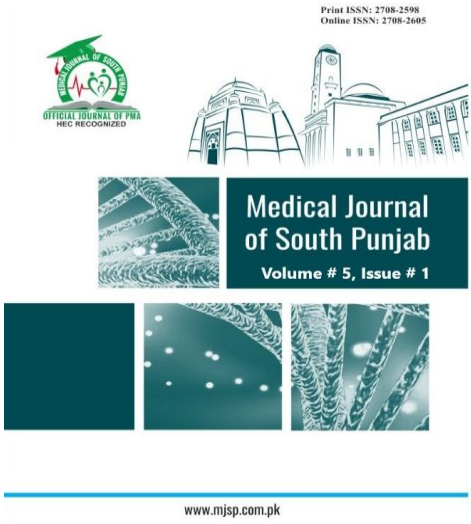
ISSN (E): 2708-2601
ISSN (P): 2708-2598

Medical Journal of South Punjab
Article DOI:10.61581/MJSP.VOL05/02/12

Volume 5, Issue 2, 2024



Association of intraoperative opioid administration with postoperative pain and opioid use

Publication History

Received: Jan, 27, 2024 Revised: May 23, 2024
Accepted: June 01, 2024 Published: June 30, 2024

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Conflict of Interest:

Author(s) declared no conflict of interest.

Acknowledgment:

No Funding received.

Citation: Ali A, Hameed J, Mairaj A , Khattak AH, Batool HT, Bukhari SF . Use of intraoperative Opioid and its effect on postoperative pain and Opioid use. Medical Journal of South Punjab. 2024 June 30; 5(2):69-74.

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An official publication of
Medteach Private Limited, Multan, Pakistan.
Email: farman@mjsp.com.pk, Website: https://mjsp.com.pk/index.php/mjsp

Medical Journal of South Punjab
Volume 5, Issue 2, 2024; pp: 69-74
Original Article

Association of intraoperative opioid administration with postoperative pain and opioid use

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ABSTRACT

Objective: *The primary goal of this study is to examine the impact of incentive spirometry and peak expiratory flow meter on risks of cardiopulmonary sequelae following valve surgery.*

Methods: *The study was conducted on 36 patients operated under general anaesthesia at Lady reading hospital Peshawar. We analyzed whether the total intraoperative opioid dose predicts 30-day hospital readmission after controlling for various patient-, anaesthetist-, and case-specific factors.*

Results: *Ambulatory surgical patients who received high intraoperative opioid doses had a substantially increased risk of readmission within 30 days after discharge. The largest adjusted risk of readmission was seen in patients receiving high doses of opioids (OR: 1.75; P <0.001). A dose–response trend was observed across quintiles (P for trend <0.05) and they also tended to return early (postoperative days 0–2 vs 3–30; P <0.001).*

Conclusion: *High intraoperative opioid dose is a modifiable anaesthetic factor that varies in the practice of individual anaesthetists and affects postoperative outcomes. Conservative standards for intraoperative opioid dosing may reduce the risk of postoperative readmission, particularly in ambulatory surgery.*

Keywords: *Intraoperative Opioids ,Postoperative Pain Management ,Opioid Consumption ,Opioid Analgesia*

1. INTRODUCTION

Opioids are amongst the most frequently prescribed drugs for acute pain like during surgical procedures and chronic debilitating pain seen in cancers. While opioids are very potent analgesics, they also have numerous downsides including the development of tolerance when used for long periods of time. In addition, opioid-induced hyperalgesia makes systemic pain feel more intense and therefore large doses of opioids have to be administered so that moderate pain relief can be achieved at lower amounts. The use of opioid analgesics overdose leads to physical dependence, psychological dependence and actual reduction in lifespan. Moreover, tolerance and hyperalgesia can occur within the short period after fentanyl and remifentanil which are usually given as anesthetics during operations. A certain level of opioid-induced hyperalgesia and tolerance may develop in the early postoperative phase together with other side effects such as nausea or respiratory depression resulting from an overdose.

Fentanyl, an analgesic opioid which is frequently prescribed for management of acute pain in the course and after sulTry surgery, has been reported to cause postoperative hyperalgesia with elevated doses. For instance, it was seen that patients who were administered with 100 µg/kg intraoperative fentanyl in cardiac surgery patients were having hyperalgesia more frequently than the patients included in the moderate dose group of only 10 µg/kg of fentanyl. Also, the research carried out under involving healthy adults showed that pain sensitization could be achieved just by using the 10 µg/kg dose of fentanyl. Thus analgesia during surgery using remifentanil has taken the advantage of applying it in a continuous method due to the use of short acting remifentanil that enables patients to recover from respiratory depression within 3-5 minutes. However, as with fentanyl, increased intraoperative dose of remifentanil is also found to increase postoperative pain because of hyperalgesia.

This opioid is given frequently in combination with fentanyl but the way in which it is administered is not always well supported. This is normally based on the notion known as preemptive analgesia whereby enough doses of opioids are given prior to actual surgical invasion to minimize subsequent pain. However, if one administered a higher dose of fentanyl together with continuous remifentanil, then the cases of opioid-induced hyperalgesia will be on the high end and this will actually increase postoperative pain sensation instead of alleviating pain.

2. METHODOLOGY

Randomized controlled trial within which 80 patients of both sexes who underwent abdominal surgery in Lady Reading Hospital Peshawar between January 2019 and October 2020 would be included. This study has adhered to the principles laid down in the Declaration of Helsinki and medical ethics committee publication on human health and medical research. All subjects have given permission for conducting this research and publication of its outcomes. Patients to be selected included those undergoing laparoscopic surgery under general anesthesia and were classified as I or II according to American Society of Anesthesiologists' (ASA). Exclusion criteria comprised pregnancy/breastfeeding, convulsions, critical head injury, dementia affecting assessment for pain, heart disease where opioids are not allowed, and previous use of opioid pain relievers for postoperative management within one month before surgery. There was no weight cut off for participants; however, weight was set at

whatever was lesser between actual weight/ideal weight with ideal weight = 22 × height(in meter)² kg. Participants were being sustained until they reached an acceptable number from among themselves

The same intraoperative protocol was followed for both the groups. However as point in this study opioids were only given as much as was necessary. The effect site targeted controlled Propofol infusion at the targeted effect site concentration of 3-4 micrograms/ml was used for anaesthetic induction and maintenance in this study. Heymann: «Intervals: Intravenous rocuronium was used only on an as needed basis to augment skeletal muscle relaxation. » As Regards to the placing of endotracheal tubes, That was followed by mechanical ventilation with air and oxygen. The depth of general anesthesia was monitored using the BIS fused index. From the beginning acetaminophen in a postoperative period was dosed at 15 m/kg (maximum dose of 1000 mg) and was administered by I. V. infusion. In addition, 20 mL of O.

analytical chemistry, nuclear chemistry 5% ropivacaine was used for the local infiltration anesthesia at the end of the surgical operation while giving local infiltration around the wound. Intravenous sugammadex was then given after surgery to antagonise the neuromuscular blocking agent and all the drugs infusions including opioids were discontinued. The anesthesiologist then ascertained spontaneous breathing and then liberated the patient from the endotracheal tube after anesthetic awakening. During the day the patient was observed in the recovery section before being taken to the hospital room. Postoperative pain was treated with flurbiprofen axetil at a dosage of 50 mg, acetaminophen at 1000 mg or pentazocine at 15 mg if necessary.

Patients' pain was measured by Numeric Rating Scale (NRS) which measures pain along a scale of 0–10; 0 meaning no pain and 10 meaning the worst pain. The NRS score needed to be collected from the patients on the day before surgery, as well as 3 hours as well as I day after the surgery. Further, at 3 hours from separation, the patients were asked about the highest NRS that they felt throughout the 0 to 3 hours interval after surgery.

For descriptive analysis of quantitative data mean was used and for descriptive analysis of categorical data frequency was considered while, standard deviation was the measure used for numerical data. P value less or equals to 0 is taken. However, .05 level of significance was considered.

3. RESULTS

Among the 46 patients, 23 (50%) were placed in Group A and 23 (50.0%) were put in Group B. Statistics showed that age, sex, weight, height and ASA status were distributed quite evenly in both study groups and there was a statistically insignificant difference ($p>0.050$). (Table. 1). In Group A, the average time for anesthesia was 264.13±14.15 minutes while that of Group B was 185.96±5.16 minutes ($p < 0.001$). The mean operative duration in Group A also surpassed the one for Group B which had a value of 191.87±12.05 minutes against 131.52±9.30 minutes respectively ($p < 0.001$). In addition to this, average amount of fentanyl administered in Group A greatly exceeded that of Group B as they were: 2.58±0.54 g/kg/h vs 1.09±0.26 g/kg/h; ($p < 0.001$). During surgery, fentanyl's estimated site concentration averaged significantly higher in Group A than in Group B at 8.00±1.13 ng/mL compared to 1.77±1.08 ng/mL respectively ($p < 0.001$). At the end of surgical procedures, however, fentanyl's estimated site concentration was approximately equal in Groups A and B (1.31 ± 0.80

ng/mL and 1.27 ± 0.59 ng/mL respectively). (p > 0.050). Table. 2).

Comparison of pre and postoperative NSR score and postoperative analgesic use between the study groups were exhibited in the table. 2. Mean preoperative NRS score in Group A and Group B was 0.54±0.15 and 0.53±0.10, respectively. (p>0.050). Mean NRS score after 1 hour in Group A and Group B was 8.03±0.99 and 7.96±1.16, respectively. (p>0.050). Mean NRS score after 6 hours in Group A and Group B was 5.23±1.22 and 5.04±1.19, respectively. (p>0.050). Mean NRS score after 24 hours in Group A and Group B was 4.48±1.05 and 4.37±0.64, respectively. (p>0.050). Use of postoperative analgesic medications at ≤3 hours in Group A and Group B was 10 (43.5%) and 12 (52.2%), respectively Wo wmuch did the postoperative analgesic medications use comparison show among groups A and B? This is the best way to start your exploration of the data presented in the table. Whereas postoperative analgesic use at 4-24 hours in Group A and Group B was 13 (56.5%) and 11 (47.8%), respectively (Table. 3).

Table. 1
Demographic and baseline characteristics between the study groups

Characteristic	Group A 23 (50.0%)	Group B 23 (50.0%)	P-value
Age (years)	39.22±6.28	44.57±7.46	0.062
Sex			
Male	14 (60.9)	15 (65.2)	0.760
Female	9 (39.1)	8 (34.8)	
Weight (kg)	68.83±7.97	73.13±8.25	0.541
Height (cm)	145.95±11.48	155.69±5.31	0.071
ASA status			
I	15 (65.2)	13 (56.5)	0.546
II	8 (34.8)	10 (43.5)	
N (%), Mean±standard deviation			

Table. 2
Duration of surgery and estimated effect site concentration of fentanyl between the study groups

Variable	Group A 23 (50.0%)	Group B 23 (50.0%)	P-value
Duration of anesthesia (minutes)	264.13±14.15	185.96±5.16	<0.001
Duration of surgery (minutes)	191.87±12.05	131.52±9.30	<0.001
Opioid amount (g/kg/h)	2.58±0.54	1.09±0.26	<0.001
Effect site concentration of fentanyl (estimated) (ng/mL)			
During surgery maximum	8.00±1.13	1.77±1.08	<0.001
End of surgery	1.31±0.80	1.27±0.59	0.852
Mean ± standard deviation			

Table. 3
Comparison of pre and postoperative numeric rating scale score, and postoperative analgesic use between the study groups

Numaric rating scale score/analgesic use	Group A 23 (50.0%)	Group B 23 (50.0%)	P-value
Preoperative NRS	0.54±0.15	0.53±0.10	0.817
NRS after 1 hour	8.03±0.99	7.96±1.16	0.808
NRS after 6 hours	5.23±1.22	5.04±1.19	0.610
NRS after 24 hours	4.48±1.05	4.37±0.64	0.676
Postoperative analgesic use			
≤3 hours	10 (43.5)	12 (52.2)	0.555
4-24 hours	13 (56.5)	11 (47.8)	
N (%), Mean ± standard deviation			

4. DISCUSSION

Recent studies have found a paucity of general knowledge about the source of variation in focused studies on the impacts of intraoperative opioid use. Therefore, available evidence remains inconclusive for whether intraoperative opioid use is associated with surgical

outcomes or an increased risk for aberrant opioid use post surgery12. References 41-45 however stress further studies about the intraoperative qualitative and quantitative use of opioids particularly on postoperative pain treatment and opioid consumption13.

Health adults have also been obtaiFrey et al21 sounds rather vague and out of place within the context of the rest of the document ba over opioid mu or kappa receptor agonists for abuse due to unacceptable addiction liability. Thirty healthy adult volunteers aged from 29 to 45 years, free of psychiatric and substance abuse disorders, overweight, and non-smokers were enrolled in the study. Another Conclusion Advanced imaging capabilities have made it possible to visualize and study cerebral metabolism in new ways, allowing researchers to use imaging and functional approaches in similar ways adopted by molecular biology and genetics. The authors got better understanding of the problem in the third group of patients, the high content of anti-epileptic drugs appeared to be satisfactory for control of seizures and they coordinated well with other therapies. In study done by Minami Hui et al on Healthy adult males ampoule of fentanyl was administered at varying doses and maximum plasma concentrations were measured at 1 ng/ml and 6.5 ng/ml respectively. Maximum detectable effect of fentanyl was within 1. 0 ng/mL. Fentanyl induced hyperalgesia was observed in animals at 4 time point5 5 to 6. 5 hours. Therefore, it is agreed upon this time that one is hyperalgesic will be in group A accompanied by lowering the pressure pain threshold in group A as the population of sub-groups of interest comprising two sub-groups 7. 86 ng/mL were in group A.

In a study by Kawanaka et al15 after surgical procedures, both groups showed similar pressure pain threshold and numeric rating scale scores with no remarkable differences. Pain threshold in both groups decreased significantly at 3 hours postoperative in relation to pre-operative measures but restored at 24 hours. Also, the combination of both opioids seen in the trial led to hyperalgesia regardless of the fentanyl dose used.

Both retrospective cohort studies indicated reduced postoperative opioid consumption. According to Wang et al16, there was a 44 percent rate of reduction of opioid use for the modulo (MME) measurement on the day zero postoperative (15.8 vs 36, p=0.025) however there was no such decrease on day one postoperative. In the same vein, Eisenbraun et al17 also focused on postoperative day restrictions, showing reduction of opioid intake on postoperative days 0, 1, 2 and 3 relative to both standard of care and Ketamine multimodal regimen. For instance, on the first postoperative day, the opioid consumption was reduced by 82 percent as compared to the normal treatment and by 64 percent within the ketamine group.

None of the four randomized controlled trials commented on opioid requirements at discharge. However, an extended follow-up study by Murphy et al[18] originating from the initial randomized controlled trial, assessed opioid requirements at 1, 3, 6, and 12 months. A 2022 study by Song et al[19] examined chronic opioid use in noncancer pain patients. Between 2010 and 2019, the prevalence rose from 0.46% to 2.63%. Chronic opioid users had a higher 10-year all-cause mortality, with a hazard ratio of 1.21 (95% CI 1.13–1.31, p<0.01). Long-term opioid use was linked to significant morbidity, including hyperalgesia, tolerance, and withdrawal.

Lui et al20 reported that moderate-to-severe pain was found on the first postoperative day in 48.7% of patients,

and these patients were associated with poor recovery and reduced patient satisfaction. Systemic opioids were needed in 68% of patients on the same postoperative day, and intravenous patient-controlled analgesia was used in 89% of them. Nerve blocks in the postoperative period were rarely required.

5. CONCLUSIONS

High intraoperative opioid dose is an anaesthetic factor that can be modulated and varies with the practice of the individual anaesthetist and impacts postoperative outcomes. More conservative standards of intraoperative opioid dosing might reduce the occurrence of readmission after surgery, especially for ambulatory surgery.

6. REFERENCES

1. Williams, J.T.; Ingram, S.L.; Henderson, G.; Chavkin, C.; von Zastrow, M.; Schulz, S.; Koch, T.; Evans, C.J.; Christie, M.J. Regulation of mu-opioid receptors: Desensitization, phosphorylation, internalization, and tolerance. *Pharmacol. Rev.* **2013**, *65*, 223–254.
2. Bull, F.A.; Baptista-Hon, D.T.; Sneddon, C.; Wright, L.; Walwyn, W.; Hales, T.G. Src Kinase Inhibition Attenuates Morphine Tolerance without Affecting Reinforcement or Psychomotor Stimulation. *Anesthesiology* **2017**, *127*, 878–889.
3. Mauermann, E.; Filitz, J.; Dolder, P.; Rentsch, K.M.; Bandschapp, O.; Ruppen, W. Does Fentanyl Lead to Opioid-induced Hyperalgesia in Healthy Volunteers?: A Double-blind, Randomized, Crossover Trial. *Anesthesiology* **2016**, *124*, 453–463.
4. Kawanaka R, Sakuma S, Kokubun H, Tetsu S, Tagaito Y, Igarashi T, Liang SG, Aoe T. Effects of Intraoperative Opioid Administration on Postoperative Pain and Pain Threshold: A Randomized Controlled Study. J Clin Med. 2022 Sep 23;11(19):5587.
5. Wang DJ, Song P, Nault KM (2021) Impact of intraoperative methadone use on postoperative opioid requirements after cardiac surgery. Am J Health-Syst Pharm 79(8):636–42.
6. Eisenbraun A, Schroeder D, Schaff HV, Martin E, Wittwer ED (2023) Single-center retrospective comparison of opioid-based and multimodal analgesic regimens in adult cardiac surgery. J Cardiothorac Vasc Anesth 37(7):1179–87.
7. Murphy GS, Avram MJ, Greenberg SB, Shear TD, Deshur MA, Dickerson D et al (2020) Postoperative pain and analgesic requirements in the first year after intraoperative methadone for complex spine and cardiac surgery. Anesthesiol 132(2):330–42.
8. Song I-A, Choi H, Oh TK. Long-term opioid use and mortality in patients with chronic non-cancer pain: Ten-year follow-up study in South Korea from 2010 through 2019. Clin Med. 2022;51:101558.
9. Liu Y, Xiao S, Yang H, Lv X, Hou A, Ma Y, Jiang Y, Duan C, Mi W; CAPOPS Group. Postoperative pain-related outcomes and perioperative pain management in China: a population-based study. Lancet Reg Health West Pac. 2023 Jun 10;39:100822.