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Intraoperative Use of Dexmedetomidine to Reduce Postoperative Analgesic Requirement

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ABSTRACT

Objective: to assess the effect of Dexmedetomidine given intraoperatively compared to placebo on acute postoperative pain and requirement of analgesics after surgery.

Study Design: Quasi-experimental study.

Place and Duration of Study: Combined Military Hospital, Multan Pakistan from May to Dec 2023.

Methodology: One hundred and sixty patients aged 18-40 years with no known comorbidities were selected. Cases were divided into two Groups having 80 cases in a Group. Group A was given intraoperative Dexmedetomidine and Group B was given placebo in equal volumes. Postoperatively, pain was assessed using visual analogue score at different intervals of time. Pain values of both the Groups were compared.

Results: Mean Age and weight of the patients in Group A and B were comparable and the difference was not significant, *p*-value for age and weight difference at 0.37 and 0.24, respectively. Postoperative analgesia (Nalbuphine) requirement was lesser in Group A than B till 8th postoperative hour, mean value 3.9±1.01 mg and 5.04±4.38 mg, respectively (p 0.024). Median Visual analogue score were significantly lesser in Group A compared to Group B till 8th postoperative hour, median value 1 and 2 respectively whereas $p<0.01$.

Conclusion: Intraoperative use of Dexmedetomidine significantly reduces the pain intensity post operatively. Hence, the post-operative requirement of intravenous opioids is reduced.

Keywords: Acute pain, Anaesthesia, Dexmedetomidine, Perioperative medicine, Postoperative pain, Surgery.

How to Cite This Article: *Aslam K, Abdullah, Saeed M, Waseem SM, Saqib NU, Abbas A. Intraoperative Use of Dexmedetomidine to Reduce Postoperative Analgesic Requirement. Pak Armed Forces Med J 2026; 76(4): 472-475. DOI: https://doi.org/10.51253/pafmj.v76i4.12030*

INTRODUCTION

Pain is an unpleasant sensation having physical and psychological effects,[1] which is experienced by more than 370 million patients undergoing surgeries every year worldwide.[2] A considerable percentage of cases experience moderate to severe post-surgical pain and its treatment is usually graded is inadequate by the patients.[3] The continuation of acute pain may lead to chronic post-surgical pain thereby disrupting the quality of life and generating psychological issues at later stage.[4] The current practice to control this issue rely on the use of opioids, which have their own undesired side effect profile leading to delayed recovery and discharge of the patient from hospital.[5]

Dexmedetomidine is an agonist at the alpha - 2 adrenoreceptors, it induces analgesia by modulation at three distinct levels. Firstly, the alpha - 2 adrenoceptors in the locus coeruleus which is situated superiorly to the spinal column. This activation subsequently amplifying the inhibition of nerve conduction within the dorsal horn. This results in pain relief and analgesia. Secondly, at the level of spinal column, Dexmedetomidine binds to alpha-2 adrenergic receptors in the posterior horn, leading to cell membrane hyperpolarization. This process inhibits the transmission of pain stimulus. Lastly, at the outer level, Dexmedetomidine blocks A, D and C fibers, avoiding the transmission of painful stimuli to the spinal column.[6,7] A review article including studies from 1996 to 2021 comprising on 13 trials and 882 patients published by Syrous *et al*. summarized that, the intraoperative use of Dexmedetomidine during surgery has been linked to reduced postoperative pain and lower opioid requirements, while also contributing to stable hemodynamic conditions throughout the procedure.[8] Similarly, a randomized control trial on 91 women (aged 30-70 years) by Rekatsina *et al.* found that intraoperative use of Dexmedetomidine was associated with decreased requirement of postoperative Morphine compared to control Group (0.9% normal saline) in post anesthesia care unit, mean morphine values 9.02±2.78 and 8.41±1.45, respectively.[9] Contrary to these a study by Wang *et al*. finds no effect of Dexmedetomidine on pain after surgery.[10] Due to these different findings, we decided to evaluate the effectiveness of intraoperative Dexmedetomidine in reducing the need for postoperative analgesics. Therefore, this study

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Received: 05 Apr 2024; revision received: 31 May 2025; accepted: 03 Jun 2025

aims to assess the efficacy of intraoperative Dexmedetomidine in reducing postoperative analgesic requirements in patients undergoing abdominal surgeries with a focus on opioid consumption and pain scores.

METHODOLOGY

This was a Quasi experimental study conducted in Anesthesiology Department, Combined Military Hospital, Multan over a period of six months from June 2023 to December 2023. Permission was granted by hospital ethical committee for this study vide notification number ERC-87/Trg23 dated 1st Feb 2023. Sample size was calculated by OpenEpi calculator using mean difference parameter of postoperative morphine requirement for demedetomidine and placebo Group as 9.02±2.78 and 10.40±3.309, respectively. Calculated sample size turned out to be 154 but we increased to 160.

Inclusion Criteria: American society of Anesthesiology health status (ASA) I or II patients of either gender aged between 18 to 40 and undergoing any non-obstetrical, fully invasive intra-abdominal surgery under general anesthesia (GA) were included.

Exclusion Criteria: Patients having known allergies to Dexmedetomidine, addicted to any narcotic or alcohol (based on history), acute respiratory tract infection (based on clinical examination), any chronic kidney, hepatic or cardiac disease (based on medical record) were excluded from the study.

One hundred and sixty patients were included in the study after careful physical examination and detailed history taking in pre-anesthesia assessment clinic. Written informed consent was taken from every individual to include them in the research and data collection. Gender, age and weight of all were recorded in a preformed performa. Patients were divided in two Groups A and B. Patients were divided equally among two Groups, n=80 for each Group by non-probability consecutive sampling. Intraoperatively, Group A was infused Dexmedetomidine and Group B was given placebo (0.9% normal saline). Just prior to start of general anesthesia induction Group A received initial dose of Dexmedetomidine 0.5 ug/ kg mixed in 50 ml of 0.9% normal saline over time span of ten minutes and then infusion of Dexmedetomidine was given at rate of 0.2 ug/ kg/ hour throughout the duration of surgical procedure till the end of the procedure. In Group B just prior to the start of general anesthesia induction 50 ml of 0.9% normal saline (placebo) was infused over ten minutes and then the same saline continued to be infused at the rate of 0.2 ug/ kg/ hour throughout the duration of surgical procedure till the end of the procedure. These were given by a trainee anesthetist who was blind to the infusion nature (drug). Vitals (mean arterial blood pressure, pulse rate, oxygen saturation) were under persistent observation during anesthesia period for patient safety. All patients were anesthetized using Nalbuphine 0.1mg/kg, Propofol 2mg/ kg and Atracurium 0.5 mg / kg. Airway was secured with endotracheal tube and maintenance of anesthesia was done using Isoflurane 1-2% in oxygen in both Groups. Endotracheal intubation was done in both Groups. Atracurium 0.1mg/ kg was given intraoperatively as per requirement. Additionally, intravenous Paracetamol 1-gram infusion was given to all at 20 minutes starting from the time of surgery. At the completion of surgery muscle relaxation was reversed using neostigmine and glycopyrolate. Awake extubation was done and patients were transferred to post anesthesia care unit (PACU). After fully conscious and vitally stable they were shifted from PACU to indoor wards. All the patients were given intravenous paracetamol 1g at 8 hours. Patients were observed for Pain using visual analogue score (VAS) ranging from 0 to 10 which denotes no pain to worst pain from lowest to highest at 4th, 8th and 12th postoperative hours and recorded on the preformed performa, by a trainee anesthetist having 2 years of fellowship experience. Intravenous Nalbuphine in 0.05mg / kg was given whenever visual analogue scale score exceeded three and recorded in performa.

Data analysis was done by using statistical software package for social sciences (SPSS) 25. Quantitative variables such as age, weight and time duration were summarized using Mean±SD. Categorical variables including gender and pain scores were expressed as frequencies and percentages. Since Visual Analogue Scale (VAS) scores and Nalbuphine bolus requirement were not normally distributed, they were presented as median and interquartile range (IQR) and Group comparisons were made using the Mann–Whitney U test. The p-value of ≤0.05 was considered statistically significant.

RESULTS

One hundred and sixty patients, eighty in each completed the study. The mean ages patients in Group A and B were 33.13±5.94 years and 33.95±5.67 years which were comparable and the difference was

statistically non-significant (*p* 0.37) and so was the case with weight of the patients, details as per Table-I. The use of rescue analgesia, namely Nalbuphine, was notably greater in the Group B over the 12-hour post-operative period compared to the Group A, with this difference reaching statistical significance. A summary of the total Nalbuphine consumption by the 4th, 8th, and 12th hours after surgery is provided in Table-II. Analgesic requirements rose steadily across each time point.

Table-I: Characteristics of Groups (n=180)

Variables		Dexmedetomidine Group (n=80)	Placebo, 0.9% saline Group (n=80)	*p*-value
Gender	Male	39(48.75%)	45(56.25%)	-
	Female	41(51.25%)	35(43.75%)	-
Age (Years)		33.13±5.94	33.95±5.67	0.37
Weight (Kg)		70.81±8.34	69.06±10.48	0.24

Table-II: Postoperative Nalbuphine Usage (n=180)

Parameters	Study Groups		*p*-value
	Dexmedetomidine Group (n=80) Median (IQR)	Placebo, 0.9% saline Group (n=80) Median (IQR)	
Nalbuphine usage mg (1-4 hours)	1.85(1.0-2.1)	2(1.5-2.7)	0.01
Nalbuphine usage mg (4-8 hours)	4(3.0-5.0)	5(4.0-5.0)	< 0.001
Nalbuphine usage mg (8-12 hours)	6.35(4.8-8.0)	6.8(4.8-8.2)	0.41

Group A demonstrated significantly lower VAS scores at both the 4th and 8th hours after surgery (*p*-values of 0.001 and <0.001, respectively). Although the VAS scores in Group A continued to stay relatively low throughout the monitoring period, the difference between Groups was no longer statistically significant by the 12th hour post-operation. Details given in Table III.

Table-III: Post-Operative Visual Analogue Score (VAS) (n=180)

Parameters	Study Groups		*p*-value
	Dexmedetomidine Group (n=80) Median (IQR)	Placebo, 0.9% saline Group (n=80) Median (IQR)	
Visual Analogue Score at 4th hour	0 (0-1)	1 (0-2)	<0.01
Visual Analogue Score at 8th hour	1 (0-2)	2 (1-3)	<0.03
Visual Analogue Score at 12th hour	2 (1-3)	2 (1-4)	0.76

DISCUSSION

We focused on the efficacy of intraoperative use of Dexmedetomidine in term of intensity of post-operative pain. The reduction in the pain intensity not only improves the patient's satisfaction but the consumption of analgesics including opioids also reduced. In that way we avoided the side effects of opioid consumption. As an essential part of multimodal analgesia strategy, Dexmedetomidine has been extensively used in perioperative setting to enhance the sedation and pain relief as an adjuvant measure in clinical practice.[11,12]

Pain intensity within first eight hours after surgery was significantly reduced in our observation by intraoperative administration of Dexmedetomidine. This conclusion has resemblance with the results obtained by Ly X *et al*.[13] Which states that the intensity and time in pain of Group of individuals who were given intraoperative Dexmedetomidine was reduced as compare to the individuals who were given placebo. Bielka *et al*. used Dexmedetomidine infusion intraoperatively and compared the analgesic (morphine) requirement to a placebo Group, this randomized control trial found out 5mg versus (vs) 15mg morphine requirement in postoperative period in Dexmedetomidine and placebo Groups respectively which are consistent with our results postoperative Nalbuphine requirement in Dexmedetomidine vs placebo Groups having similar *p*-value of 0.01 at 4th and 8th postoperative hours.[14] Results of our study are also consistent with another randomized control trial by Qin Ye *et al*. in terms of VAS and opioid requirement in post-operative period.[15]

Similarly, Wei Tseng *et al*. conducted a randomized control trial with use of intraoperative Dexmedetomidine and placebo and found out that Dexmedetomidine Group required lesser post-operative fentanyl as compared to placebo, this difference remained significant for 24 hours' in postoperative period. The same significance was maintained in our study till 8th postoperative hour but diminished at 12th hr. This difference can be related to difference of opioid agent used (fentanyl/ Nalbuphine) and dose of intraoperative Dexmedetomidine (0.6/ 0.8 mcg/ kg).[16] Mao Yu *et al*. conducted a similar trial by using intraoperative Dexmedetomidine and normal saline and the results were contrary to our study and commonly found literature on the article, they concluded Dexmedetomidine have no added effect on postoperative pain relief.[17] The difference may be subject to lesser intraoperative Dexmedetomidine dose (0.2 to 0.4 mcg/ kg) used in their study and the nature of under trial surgery (lateral thoracotomy for

esophageal cancer patients) as thoracotomy is graded as one of the highest pain causing procedures.[18] Recent advances in Enhanced Recovery After Surgery (ERAS) advocates the control of postoperative pain as corner stone element,[19] and comprehensive review published by Liu Zhe *et al*. strongly advocates the use of intraoperative Dexmedetomidine as part of ERAS to control postoperative pain,[20] and same is the recommendation of our study based on our results.

LIMITATION OF STUDY

Data of pain intensity was collected in the first 12 hours after surgery. Long term effects of Dexmedetomidine were not studied.

CONCLUSION

Intraoperative use of Dexmedetomidine significantly reduces the pain intensity post operatively. Hence, the post-operative requirement of intravenous opioids is reduced.

Conflict of Interest: None.

Funding Source: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

KA & A: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MS & SMW: Conception, data analysis, drafting the manuscript, approval of the final version to be published.

NUS & AA: Data acquisition, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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