ORIGINAL ARTICLES

DEXMEDETOMIDINE FOR ACUTE POSTOPERATIVE ANALGESIA IN PATIENTS UNDERGOING LAPAROTOMY

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ABSTRACT

Objective: To find the effect of dexmedetomidine on acute post-operative analgesia and on postoperative opioid requirement.

Study Design: Quasi experimental study.

Place and Duration of Study: The study was conducted at department of Anaesthesia and Intensive care, CMH Rawalpindi, from Jan 2015 to Oct 2015.

Methodology: In this study 80 patients were divided in two equal groups. Group A was controlled group in which saline infusion was used and Group B was study group in which dexmedetomidine infusion was used. Both groups were anesthetized with similar technique and were given nalbuphine 0.1mg/kg in the beginning. Group B was started dexmedetomidine almost half hour before end of procedure and group A was given normal saline. Infusion of dexmedetomidine continued for 8 hours postoperatively. Rescue nalbuphine of 0.05mg/kg was given in both groups when visual analogue scale score was 3 or more.

Results: Eighty patients including 48 (60%) males and 32 (40%) females were enrolled in study. In group A loading dose of nalbuphine was 7.02 ± 0.76 mg and in group B it was 6.93 ± 1.00 mg. Mean loading dose of dexmedetomidine was 32.98 ± 9.11µg. Mean Dexmedetomidine given in infusion was 105.56 ± 29.16 µg. There was significant decrease in VAS score in group B. In group A total postoperative nalbuphine used was 8.13 ± 2.86 mg and in dexmedetomidine group total nalbuphine used was 5.01 ± 1.93 mg. The *p*-value was 0.001 which was significant.

Conclusion: Use of dexmedetomidine resulted in reduced acute postoperative pain as shown by better visual analogue scale profile. It also resulted in reduced opioid requirement in postoperative period. We suggest that studies should be done which also include these factors and have large sample size so results can be generalized on population.

Keywords: Acute postoperative pain, Dexmedetomidine, Nalbuphine, Postoperative analgesia.

INTRODUCTION

Severe acute postoperative pain is associated with delayed recovery and higher incidence of complications and if not treated properly it can progress to chronic pain[1]. Hence satisfactory analgesia is of prime importance in post-operative period. It results in reduced stress response, lesser delirium, early recovery and early discharge from hospital. Traditionally intravenous opioids are given to provide analgesia in post-operative period but these have side effects such as respiratory depression, nausea and vomiting. But now a days multimodal analgesia is recommended in which one or more adjunct drugs have been used to supplement analgesia and to reduce the dose of opioids.

Alpha2-adrenergic receptor (α2-AR) agonists are being used as analgesic adjuvants. These drugs result in sedation, anxiolysis, sympatholysis and analgesia but without respiratory depression[2]. Combination of α2-AR agonist with opioids produces a synergistic analgesic effect without increasing the opioid related adverse effects. A well-known α2-AR agonist, clonidine has been used to supplement analgesia and anasthesia[3]. Dexmedetomidine is a newer agent of same class and has 8 times more affinity for alpha 2 receptors than clonidine. As compared to

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clonidine it has shorter half-life, more protein binding and more lipophilic action. Dexme-detomidine has been used as a short sedative agent in ICUs due to its short plasma half-life of 2 to 2.5 hours[4,5]. But now it is being used as adjunct for anaesthesia by using it through intravenous infusions and mixing it in epidural and local anaesthetics for nerve blocks[6,7]. Its analgesic properties are being recognised and no it is being studied as part of multimodal analgesia through intravenous and neuraxial routes[8,9].

The mechanism of the analgesic action of dexmedetomidine is not fully understood. It is proposed that it may have action on supraspinal, spinal and peripheral α2 adrenoceptors which result in antinociception[10]. Studies have reported that dexmedetomidine not only supplements analgesia but also reduces the dose of morphine required in postoperative period[11,12]. Similar reduction in opioid requirement and lesser side effects have been described in children[13].

After abdominal surgery, patients experience severe pain and if it is not treated properly it results in variable hemodynamics, delayed recovery, respiratory complications and it can be converted into chronic pain. In our setups nalbuphine is widely used for acute postoperative pain management. We used dexmedetomidine in patients undergoing laprotomy with the hypothesis that it will reduce the dose of nalbuphine required for postoperative analgesia. Furthermore dexmedetomidine is not widely available and routinely used in our country, so it will be one of the initial studies with this drug in our literature.

METHODOLOGY

This quasi experimental study was conducted in Anesthesia and Intensive care department of Combined Military Hospital Rawalpindi from January 2015 to October 2015. It was approved by the institutional medical ethics committee. Written informed consent for participation in this study and use of unknown anesthetic agent was obtained from all the participants before the start of the study.

Sample size was calculated from cumulative 24 hours opioid use in a study where 29% less opioid was required in dexmedetomidine group[14]. G*Power 3.1.9.2 calculator was used and significance level was kept 0.05 with confidence interval 0.95. Total sample size was calculated 76 however we included 80 patients in this study by consecutive type of non-probability sampling technique. Patients were divided in two equal groups.

Patients undergoing abdominal surgery (laparotomy) from both genders, age between 30 and 75 and American Society of Anaesthesiologists grade I and II were included in study. Patients who had ischemic heart diseases, hypertension, COPD, opioid or sedative–hypnotic drugs addiction, use of beta blockers, obesity (BMI >30), postoperative nausea and vomiting history; or neuropsychiatric diseases were excluded from study. Patients were instructed regarding the use of visual analogue scale from 0 to 10 (0=no pain, 10=worst possible pain).

Patients were divided randomly in two equal groups by computer generated randomization tables by an independent nurse before taking the patient to the operation theatre. Patients who were placed in control group were named group A and those receiving dexmedetomidine were named group B. 0.9% sodium chlo-ride 50 mL for group A and Dexmedetomidine 200 µg diluted in 50 mL (4ug/ml) for group B were prepared. Loading dose of dexmedetomidine is 0.5ug/kg over ten minutes and then infusion of dexmedetomidineis given at rate of 0.2ug/kg/hr. Volumes of loading dose and infusion rate were calculated by same formula for infusions in both groups.

In both groups anesthetic technique was same. Peripheral line was inserted in upper arm and standard anesthesia monitoring including ECG, SpO2, non-invasive blood pressure and end tidal carbon dioxide were used. Induction was done with propofol 2mg/kg, relaxation with atracurium 0.5mg/kg; Airway was secured with ETT and maintenance of anesthesiawas done with isoflurane in 40% O_2. Analgesia was given

with nalbuphine 0.1mg/kg at beginning in both groups. Atracurium 0.1mg/kg was given in boluses as required. Almost half hour before end of surgeryinfusion pumps were attached to patients according to their groups and infusions started according to calculated volumes and rate. At the end of surgery 0.05mg/kg of nalbuphine and 1g paracetamol infusion was given in both groups as part of multimodal analgesia. When patient started breathing spontaneously, reversal with neostigmine and glycopyrrolate was given and extubation done. Infusion continued post-operatively and patients were shifted to post anaesthesia care unit. When they fulfilled the modified Aldrete score criteria, they were shifted to intensive care unit. Infusion continued for the total duration of 8 hours. Rescue bolus of nalbuphine (0.05mg/kg) was given whenever visual analogue scale score was 3 or more in both groups. Bradycardia was treated withbolus of atropine (0.5mg) and hypotension was treated with intravenous fluids and bolus of phenylephrine (50ug).

An independent nurse who was unaware of the infusion and group of patient filled the performa for each patient for 8 hours postoperatively. It included patient profile, visual analogue scale score (0=no pain and 10=worst possible pain), dose of dexmedetomidine, dose of nalbuphine given, episodes of bradycardia(heart rate less than 60) and hypotension(systolic blood pressure less than 100 or 20% decrease from baseline value).

Quantitative data were expressed as mean and standard deviation and were analysed with an independent sample t-test. Categorical data were expressed as frequency and percentages, and analysed by using chi square test. The *p*-values ≤0.05 were considered statistically significant. Statistical analysis was performed with SPSS-16.

RESULTS

Total 80 patients undergoing laparotomy, who fulfilled inclusion and exclusion criteria, were included in the study. They were randomized in group A (controlled group) and group B (Dexmedetomidine group). All the patients were followed up and their data was collected and analysed.

There were 48 (60%) males and 32 (40%) females in total. Demographic data of both groups was compared (table-I).

In group A loading dose of nalbuphine was 7.02 ± 0.76 mg and in group B it was 6.93 ± 1.00 mg. A *p*-value was 0.671 which was non-significant. Loading dose of nalbuphine was comparable between two groups. Mean loading

Table-I: Demographic data.

Variable		Group		*p*-value*
		Control (n=40)	Dexmedtomidine (n=40)	
Gender	Male	25 (62.5 %)	23 (57.5%)	0.653
	Female	15 (37.5 %)	17 (42.5%)	
Age (years)		38.7 ± 12.32	43.15 ± 10.53	0.087
Weight (kg)		70.22 ± 7.65	69.45 ± 10.09	0.5946

*p-value less than 0.05 is considered significant.

Table-II: Visual analogue scale score.

VAS	Control Group (n=40)	Dexmedtomidine Group (n=40)	*p*-value*
At 2 hrs	3.75 ± 0.83	2.95 ± 0.71	$p < 0.01$
At 4 hrs	2.70 ± 0.75	2.12 ± 0.68	$p < 0.01$
At 8 hrs	2.42 ± 0.71	2.07 ± 0.57	0.018

*p-value less than 0.05 is considered significant.

dose of dexmedetomidine was 32.98 ± 9.11µg. Mean Dexmedetomidine given in infusion was 105.56 ± 29.16 µg. While mean of total dexmedetomidine used was 138.67 ± 38.31 µg. Comparison of Visual analogue scale score and *p*-values (table-II).

Postoperatively patients were given boluses of nalbuphine for pain relief whenever VAS score was 3 or more. In group A total postoperative nalbuphine used was 8.13 ± 2.86 mg. While in dexmedetomidine group (group B) total postoperative nalbuphine used was 5.01 ± 1.93 mg. The *p*-value was 0.001 which was significant. It means that there was significant reduction in the postoperative requirement of nalbuphine after the use of dexmedetomidine.

Bradycardia occurred in 3 (7.5%) patients in group A and in 4 (10%) patients in group B. A *p*-value was 0.697 which was nonsignificant. Hypotension occurred in 3 (7.5%) patients in group A and in 6 (15%) patients in group B. A *p*-value was 0.294 which was also nonsignificant.

DISCUSSION

In our study we started dexmedetomidine intraoperatively and continued it for 8 hours post operatively to study its analgesic and opioid sparing effects. Resultsshowed a significant reduction in opioid requirement in post op period. Similar results were shown by other studies. In a study conducted in patients undergoing gynaecological procedures, it was shown that patients who received intraoperative dexmedetomidine required less opioids both in intra and postoperative periods[12]. In another study, authors showed that use of dexmedetomidine resulted in opioid sparing, less pain and coughing in patients after partial laryngectomy. They used sufentanil in their study and its consumption was 47.8 ± 4.7µg in controlled group as compared to dexmedetomidine group in which it was 38.0 ± 1.8µg and *p*-value was 0.001 which was comparable to our study[15].

Lin *et al*. suggested in their study that dexmedetomidine improves analgesia by synergistic analgesic interaction with opioids, reducing stress, and attenuation of motivational component of pain. They showed that in 24 hour postoperative period cumulative morphine use was 29% less in dexmedetomidine group than in morphine only group (23.3 ± 10 mg vs 32.8 ± 12.4 mg, $p<0.01$)[14]. VAS scores at rest and with movement were also significantly reduced in dexmedetomidine group in their study.

In our study visual analogue scores at 2 hours (*p*-0.000), 4 hours (*p*-0.001) and 8 hours (*p*-0.018) were also significantly reduced in Dexmedetomidine group as compared to controlled group. These results are similar to study conducted by Ge *et al* in patients undergoing abdominal colectomy[9]. They showed that use of dexmedetomidine results in significant decrease in VAS score postoperatively for 24 hours ($p<0.05$). Another study showed reduced VAS in first 24 hours by use of dexmedetomidine[16]. Similar reduction in VAS was shown by Ren *et al*. They continued dexmedetomidine for 72 hours postoperatively and showed that it resulted in better pain control, less opioid requirement and better patient satisfaction[17].

Loading dose of dexmedetomidine causes hemodynamic changes like hypertension, hypotension and bradycardia. So we used intraoperatively half (0.5µg/kg) the prescribed loading dose and lowest (0.2µg/kg/hr) dose for infusion[18]. In our study dexmedetomidine group showed greater variation in HR and MAP from pre-surgery baseline values after surgery. But decrease in HR and MAP was not clinically significant. When patient is not hypovolemic and not on beta blockers or antihypertensive agents, his hemodynamics usually remain stable with the use of dexmedetomidine. It was suggested in a study that good sleep quality and the sympathoinhibitory effect of dexmedetomidine result in hemodynamic stability[19].

Our study had some limitations. First, we studied effects of dexmedetomidine only for 8 hours. These should be studied for at least 24 hours in postoperative period because it is the time during which maximum pain occurs.

Secondly we did not study patient satisfaction and sedation effects. Dexmedetomidine can also be used along with opioids in patient controlled analgesia regimes. Reduction in opioid associated adverse effects should also be studied. We recommend that this study should be conducted in diverse population from different hospitals and undergoing different surgical procedures so that these results can be generalized on larger population.

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CONCLUSION

Use of dexmedetomidine resulted in reduced acute postoperative pain as shown bybetter visual analogue scale profile. It also resulted in reduced opioid requirement in postoperative period.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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