Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com/sjams/

OPEN ACCESS

Anesthesiology

Role of Dexmedetomidine as Preemptive Analgesic on Postoperative Pain Following Open Abdominal Hysterectomy under General Anaesthesia: A Placebo Controlled Study

Dr. Syed Ariful Islam[1*], Dr. Md. Saydur Rahman[2], Dr. MD. Imrul Islam[3], Dr. A. K. M. Faizul Hoque [4], Dr. Mohammad Shamsul Arefin[5], Dr. Md. Jobayer Hossain[6], Dr. Mohinee Begum[7], Prof. AKM Akhtaruzzaman[8], Prof. Moinul Hossain[9]

[1]MBBS, MD, EMO, Brahmanbaria General Hospital, Brahmanbaria, Bangladesh
[2]MBBS, MD, Specialist, Dept. of Anesthesiology, Asgor Ali Hospital, Dhaka, Bangladesh
[3]MBBS, MD (Anaesthesiology), Medical Officer, Dept. of Anaesthesiology & ICU Rajshahi Medical College Hospital, Rajshahi, Bangladesh
[4]Associate Professor, Department of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU, Dhaka, Bangladesh
[5]MD, Junior Consultant, Department of Anaesthesia, National Institute of Neurosciences, Dhaka, Bangladesh
[6]MD, Consultant, Dhaka Pain & Spine Center, Dhaka, Bangladesh
[7]FCPS (Obstetrics and Gynaecology), Medical Officer, Brahmanbaria (sadar) Upazila Health Office, Brahmanbaria, Bangladesh
[8]Chairman, Department of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU, Dhaka, Bangladesh
[9]Professor, Department of Anaesthesia, Analgesia and Intensive Care Medicine,BSMMU, Shahbagh, Dhaka, Bangladesh

DOI: 10.36347/sjams.2020.v08i07.021 | **Received:** 08.07.2020 | **Accepted:** 15.07.2020 | **Published:** 21.07.2020

***Corresponding author:** Dr. Syed Ariful Islam

Abstract **Original Research Article**

Background: Abdominal hysterectomy is a common and major surgery associated with moderate to severe pain. Various short and long term complications may occur if the pain is treated inadequately. Different drugs and interventions are currently being practiced for adequate pain management. Among them, preemptive analgesia was adopted with the aim to reduce the dose of opioid by preventing central sensitization. Thereby, avoiding dose related side effects despite providing adequate analgesia. The dexmedetomidine, a highly potent α2 agonist with several perioperative beneficial properties, was investigated for its status as preemptive analgesic. ***Objective:*** The present study was designed to evaluate the role of preemptive dexmedetomidine on postoperative analgesia following open abdominal hysterectomy under general anaesthesia. ***Methods:*** Forty ASA I and II, aged more than 18 years patients, undergoing open abdominal hysterectomy were allocated into 2 equal groups (n=20 in each group) by a computer-generated randomization table. Group A and B received equal volumetric (0.25ml/kg) dexmedetomidine and normal saline respectively, 20 minutes prior to induction of general anaesthesia. VAS and PCA morphine consumption, heart rate, mean arterial pressure and capillary oxygen saturation was recorded at defined postoperative time points and adverse effects were noted. ***Results:*** The total amount of postoperative morphine requirement after 24 hours was 30.98±1.15 mg in group A and 32.15±2.16 mg in Group B (p value=0.039) which is significantly higher in group B. The group A had significantly lower VAS score in both the resting (P= 0.001, 0.001, 0.019, 0.010and 0.042) and movement state (P = 0.001, 0.006, 0.007, 0.029 and 0.035) for time points of 1st, 2nd, 6th, 12th and 24th hours post-operatively, compared to the group A. Furthermore, we observed, there was significant obtundation of HR and MAP, evoked by intubation and extubation in group A. Similar response was seen just after extubation. HR was significantly (P<0.05) lower in group A at all postoperative follow up. Additionally, group A had lower MAP compared to group B. The opioid related adverse events were slightly lower in dexmedetomidine group. ***Conclusion:*** Preemptive use of intravenous dexmedetomidine reduced postoperative pain intensity, opioid requirement and rendered better haemodynamic stability.

Keywords: Preemptive, dexmedetomidine, abdominal hysterectomy, anaesthesia, postoperative anaesthesia.

Copyright @ 2020: 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 for non-commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

INTRODUCTION

Pain is the prime concern for most the patients undergoing surgeries despite development of newer generations of analgesic drugs, different strategies and interventions during perioperative period. Preemptive analgesia is a pharmacologic strategy based on administration of analgesic drug prior to surgical stimulation in order to prevent postoperative pain [1]. It prevents the central sensitization by reducing nociceptive input, preventing central transmission of the impulse (central sensitization), increasing the nociception threshold and eventually, pain memory

after surgery is also reduced [2, 3]. It provides some short-term (reduction in perioperative pain and acceleration of recovery) and long-term (prevention of chronic pain syndrome) benefits.

The opioids are the most commonly used analgesic agents for postoperative analgesia, but it is associated with the dose related with short-term adverse effects like nausea, vomiting, pruritus, urinary retention, constipation and respiratory depression and long-term effects like addiction, tolerance and dependence, opioid induced hyperalgesia (OIH). Preemptive analgesia reduces analgesic requirement and its side effects. Abdominal hysterectomy (AH) is considered a major and common gynaecological surgery, causing moderate to severe pain [4, 5]. Postoperative pain is associated with adverse effects involving every systems of the body. Additionally, it minimizes the quality of life, functional status, recovery and maximizes the risk of related complications, hospital stay, readmission and patient dissatisfaction [6].

The dexmedetomidine is a potent and highly selective α-2 adrenoceptor agonist with some special characteristics. It has sedative, amnestic, anxiolytic, sympatholytic, analgesic, anti-shivering and antisialogogue activities [7, 8]. It has the ability to potentiate the effects of all intraoperative anesthetics [9-12]. Moreover, it attenuates stress-induced sympathoadrenal responses and maintain hemodynamic stability during intubation, surgery and also emergence from anesthesia [13]. It prevents postoperative nausea, vomiting, shivering and at the same time it offers potential benefit towards neuroprotection, cardioprotection and renoprotection [14]. It may be an attractive agent for use in perioperative period because of these properties even as analgesic adjunct [15]. It offers a superior analgesic effect compared to clonidine by both spinal and supraspinal mechanisms [16]. Regarding the spinal mechanism, α-2C and α2A receptors situated in the neurons of dorsal horn especially lamina II (substantia gelatinosa) of the spinal cord. It act on both pre and postsynaptic mechanisms to produce antinociception by (1) reducing the excitability of the central terminal of the primary afferent fibers, (2) directly reduces pain transmission by reducing the release of pronociceptive neurotransmitter- substance P and glutamate from primary afferent terminal and (3) by hyperpolarizing spinal interneurons via G-protein-mediated activation of potassium channels [17, 18]. This hyperpolarized state makes the generation of new action potentials virtually refractory and impossible to further stimulation [19]. Suggested supraspinal mechanism is activation of α-2A receptors at the locus coeruleus in the brain stem causing decrease in norepinephrine release from pre-synaptic neurons with inhibition of postsynaptic activation [20]. Therefore, the exploration of better preemptive analgesic from the current and newer analgesics (including dexmedetomidine) for postoperative pain control and uncovering the possibilities for new combinations of multimodal analgesia is unrelenting.

MATERIALS AND METHODS

This randomized, single-blind, placebo controlled study, took place at BSMMU after permission from the Institutional Review Board. Written informed consent was taken from each patient. The patients aged more than 18 years, ASA physical status I or II posted for abdominal hysterectomy under general anesthesia were enrolled in this study. The patients were excluded from the study having cardiac instability (SBP>140 mm of Hg, SBP <90 mm of Hg, HR<60 bpm, EF<40%), acute or severe bronchial asthma or other obstructive airways disease (SpO_2<90%), chronic kidney disease [S. Creatinine >1.3 mg/ml, hepatic dysfunction (Serum albumin <2.8 g/dl, prothrombin time > 6.0 and SGPT> 100U/L) or allergic to the study drugs [21]. Sample size was calculated assuming error=0.05, power =0.80 [22]. A computer-generated randomization table was used to allocate the patients into 2 equal groups (n=20).

The group A received dexmedetomidine and group B was infused normal saline as placebo. The dexmedetomidine vial contains 200 µg/2ml. In group A (dexmedetomidine), one vial was diluted in 0.9% normal saline to make 50 ml solution containing dexmedetomidine 4µg/ml. On the other hand, group B received only 0.9% normal saline. The total volume infused in both groups was 0.25 ml/kg (1µg/kg) of solution (In case of Group A, 0.25 ml is 1 mcg of dexmedetomidine) which was started 20minutes before initiation of anaesthesia at the rate of 1 ml (15 drops) per minute. For induction, patients from the both groups received fentanyl (1.5 mcg/kg), propofol (1.5mg/kg) intravenously. For muscle relaxation and intubation suxamethonium (2mg/kg) was given intravenously. Immediately after intubation, the patients were mechanically ventilated using semi-closed system with an oxygen and nitrous oxide (33:66) to keep $EtCO_2$ within 30–35 mmHg. For maintenance of anaesthesia and muscle relaxation, vecuronium bolus 0.1 mg/kg was given followed by intermittent dose of 0.03 mg/kg 15-20 minutes intervals, Halothane 0.4-0.8 MAC, along with nitrous oxide and oxygen 66/33 ratio, were administered. All the patients were monitored and recorded for vital parameters like HR, MAP and SpO_2 at regular intervals. But above parameters were recorded at the baseline, after intubation, and after extubation. At the end of the surgery, neuromuscular blocking effects of vecuronium was reversed, by administrating atropine 0.02 mg/kg and neostigmine 0.04 mg/kg, the tracheal tube was removed and patients were transferred to the post-anesthesia care unit (PACU).

At the post anaesthetic care unit (PACU), they were reminded about the method of operating the PCA. Patients were observed for 24 hours after operation in the post-anaesthesia care unit (PACU). Postoperative

analgesia was managed by PCA, which was programmed to deliver morphine in the following order- Mode- PCA only, PCA dose- 1mg on demand with lockout interval- 10 minute and 4 hour limit: 10 mg. Total dose of morphine and pain score by visual analogue score (VAS), were recorded at the time intervals of 1 (T1), 2 (T2), 6 (T3), 12 (T4), 24 (T5) hours. Heart rate (HR), mean arterial pressure (MAP) and oxygen saturation (SpO_2) were also recorded at the time intervals of 1 (T1), 4 (T2), 8 (T3), 12 (T4), 16 (T5), 20 (T6) and 24 (T7) hours. Sedation score was also recorded at the interval of 1 (T1), 2 (T2), 6 (T3), 12 (T4), 24 (T5) hours.

STATISTICAL ANALYSIS

All the relevant collected data was compiled on a master chart first. Then organized by using scientific calculator and standard statistical formula. Percentages were calculated to find out the proportion of the findings. Further statistical analysis of the results was done by computer software devised as the statistical package for social scientist (SPSS) version 21.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Qualitative variables of this study had been expressed as percentage. Quantitative variables were expressed as mean ± standard deviation. Student unpaired t-test was used for quantitative variables like mean arterial pressure (MAP), heart rate (HR) and capillary oxygen saturation (SpO_2) at different intervals. P value of qualitative variables were derived from chi square test. The results were presented in tables, charts etc. A "p" value <0.05 was considered as significant.

OBSERVATIONS AND RESULTS

Patients from both groups had comparable demographic parameters including age, weight, height, ASA physical status (Table-1). There is no significant difference regarding the baseline heart rate (HR) and mean arterial pressure (MAP) between the two groups.

Postoperative pain was assessed by VAS score in both groups during resting and movement. Patients from the group A had a lower VAS score compared to the group B in both the resting (Table-2, P= 0.001, 0.001, 0.019, 0.010 and 0.042) and movement state (Table-2, P = 0.001, 0.006, 0.007, 0.029 and 0.035) for time points of 1st, 2nd, 6th, 12th and 24th hours post-operative period respectively.

Table-1: Demographic data (n=40)

Particulars of the patient	Group-A (n=20)	Group-B (n=20)	p value
Age (in years)	42.8±5.2	44.8±5.4	[a]0.25[ns]
Range (min, max)	37,54	36, 54	
Height (in cm)	155.1±6.42	153.8±7.11	[a]0.53[ns]
Range (min, max)	144, 165	140, 167	
Weight (in kg)	59.6±7.69	61.1±9.04	[a]0.59[ns]
Range (min, max)	43, 75	48, 82	
ASA Grade			
Grade I	14 (70.0%)	15 (75.0%)	[b]0.72[ns]
Grade II	6 (30.0%)	5 (25.0%)	

ns= not significant

Values were expressed as mean±SD or in frequency. Written percentages were calculated on column total. [a]P values were attained by unpaired t-test and [b]P was derived from chi square test.

Table-2: Comparison of post-operative morphine requirement and VAS score at rest and movement (n=40)

PCA and VAS each group	Group-A	Group-B	p value
PCA Morphine (in mg)	**(n=20)**	**(n=20)**	
After 1 hour	1.85±0.75	3.65±1.04	0.001[s]
After 2 hours	3.85±0.81	6.95±1.36	0.001[s]
After 6 hours	10.15±1.79	12.7±2.56	0.006[s]
After 12 hours	17.55±1.85	18.75±1.31	0.023[s]
After 24 hours	30.98±1.15	32.15±2.16	0.039[s]
VAS at rest			
After 1 hour	3.40±0.88	5.9±0.72	0.001[s]
After 2 hours	3.45±0.69	5.8±0.70	0.001[s]
After 6 hours	3.60±0.73	4.1±0.56	0.019[s]
After 12 hours	3.30±0.66	3.8±0.50	0.010[s]
After 24 hours	2.98±0.69	3.4±0.57	0.042[s]
VAS at movement			
After 1 hour	4.95±0.69	6.85±0.75	0.001[s]
After 2 hours	4.85±0.72	5.35±0.67	0.006[s]
After 6 hours	4.55±0.51	5.01±0.85	0.007[s]
After 12 hours	4.70±0.86	5.25±0.66	0.029[s]
After 24 hours	4.25±1.34	4.95±0.51	0.035[s]

s= significant

Values were expressed as Mean±SD or in frequency. P values were attained by unpaired t-test.

PCA Morphine requirement was recorded at 1st, 2nd, 6th, 12th and 24th hours. Total morphine consumption were noted. Patients from the group A (30.98±1.15 mg) required significantly reduced (P=0.039) morphine than the group B (32.15±2.16 mg). The difference of morphine requirement within the group at postoperative period between 2 to 6 hours was statistically significant in in group A (P=0.001) and in between 1 to 2 hours in group B (P=0.001). But, the total consumption at 6th hour was still significantly less in group A (P=0.006). Group A patients had more sedation score than Group B in all postoperative follow up. But both group were more sedated after 12th hour (Group A-2.00±0.73 and Group B-1.85±0.67, P=0.502). However, after 24 hours, sedation score was reduced (Group A-1.50±0.61and Group B-1.40±0.50, P=0.574). However, no patient had sedation score more than 3 at any follow up. Intraoperative fentanyl requirement was also significantly reduced (P=0.001) in dexmedetomidine group (Table-3).

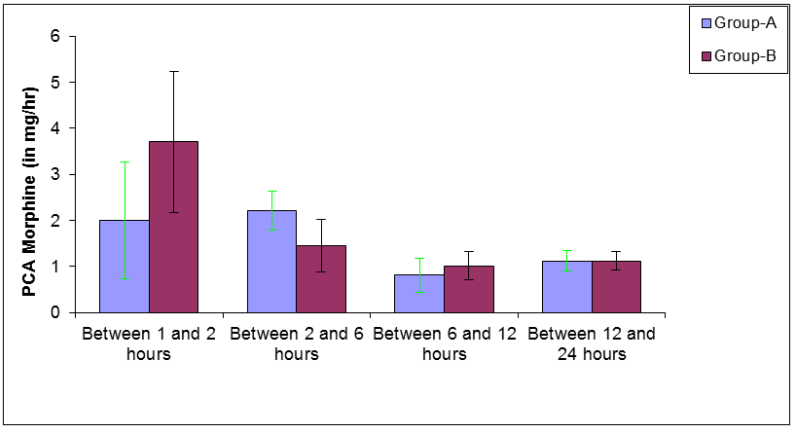

Fig-1: Bar chart shows difference of morphine requirement within the group between the follow up at postoperative period

Table-3: Comparison of total fentanyl requirement during surgery

Intraoperative fentanyl requirement	Group-A (n=20)	Group-B (n=20)	p value
Total (in µg)	88.0±11.96	124.0±16.67	0.001[s]

s= significant, ns= not significant

Values were expressed as Mean±SD or in frequency. P values were attained by unpaired t-test.

It was observed that, there was increases in HR and MAP above baseline evoked by intubation reflex in both groups during induction of general anaesthesia. However, this response was significantly obtunded in group A (P=0.001). Similar observation was seen after extubation where MAP (P=0.004) and HR (P=0.001) was significantly attenuated (Figure 1 & 2). Moreover, HR and MAP returned to the baseline levels after 24 hours surgery. Group A had lower and stable HR and MAP compared to group B (Figure 4 & 5) in different follow up during postoperative period. However, the difference of MAP was not significant at 12th, 16th, 20th and 24th hours. Both group had comparable SpO_2 in all perioperative period.

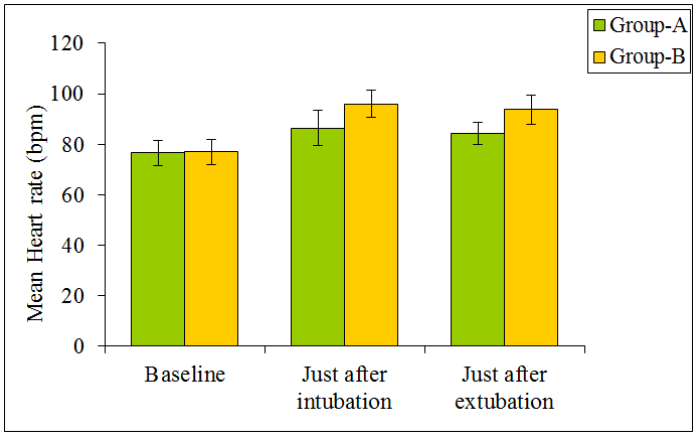

Fig-2: Bar chart showing heart rate (beats/minute) variations between two groups during surgery (Data are mean with error bars showing SD)

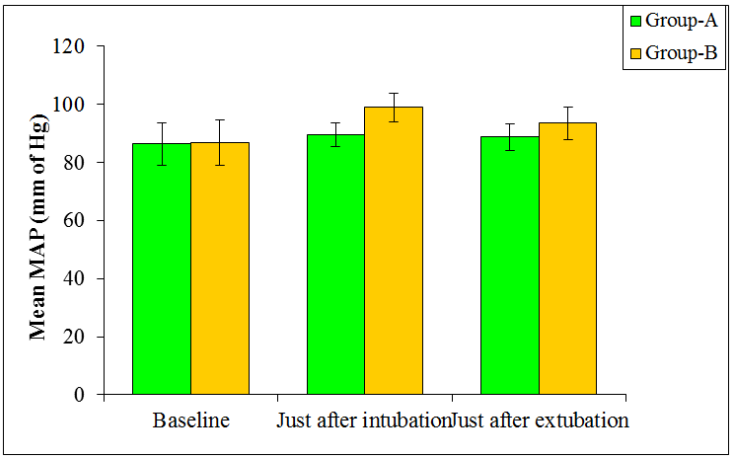

Fig-3: Bar chart comparing MAP variations during surgery (mm of Hg) between the two groups (Data are mean with error bars showing SD)

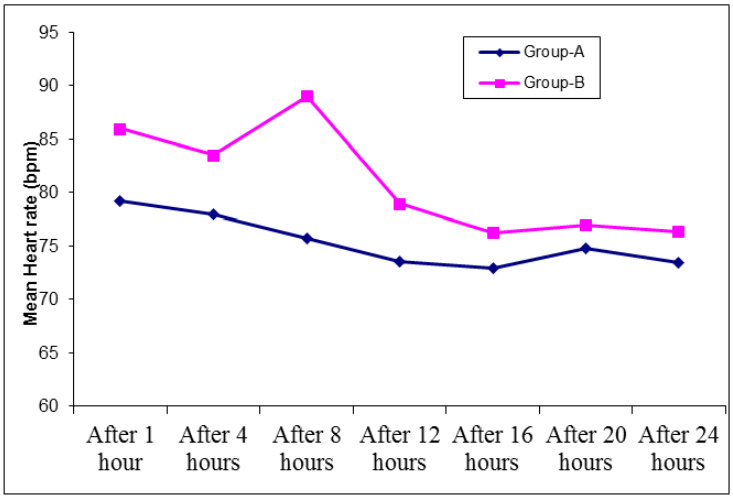

Fig-4: Line chart showing HR in different follow up at postoperative period

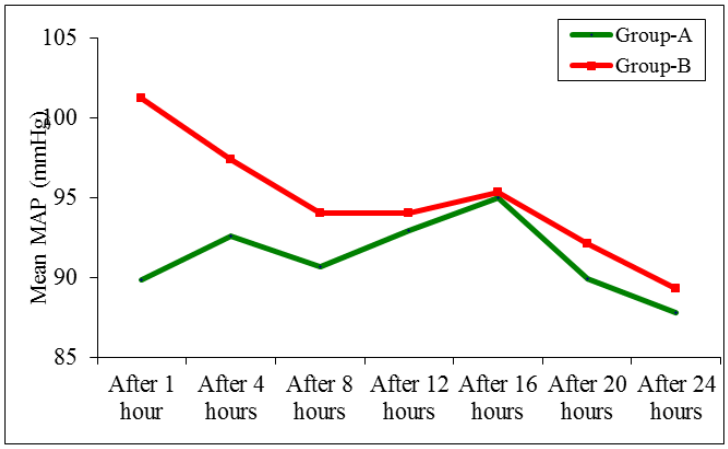

Fig-5: Line chart showing MAP in different follow ups at postoperative period

Postoperative adverse effects were also observed regarding the between the two groups during the first 24 hours. In general, the group A patients trended towards suffering from less adverse effects, such as nausea, vomiting, than those in the group B (Table-4) but the findings were insignificant.

Table-4: Comparison of postoperative side-effects in patients between the two groups. Values are number (proportion)

Adverse effects	Group-A	Group-B	p value
Nausea	4 (20%)	5 (25%)	0.70^{ns}
Vomiting	2 (10%)	4 (20%)	0.38^{ns}
Dizziness	6(30%)	7 (36%)	0.74^{ns}
Bradycardia	2(10%)	2 (10%)	1.00^{ns}
Tachycardia	1(5%)	3 (15%)	0.29^{ns}
Pruritus	3 (15%)	4 (20%)	0.68^{ns}
Respiratory depression	0	0	

ns= not significant

Values were expressed as Mean±SD or in frequency. P values were attained by chi square test.

DISCUSSION

The open abdominal hysterectomy is considered as a major surgery and is associated with a moderate to severe pain [4]. The opioids, commonly morphine is used for pain control following abdominal hysterectomy [23]. Previously, numerous studies had been done to explore a perfect drug, technique or combination to minimize the adverse effects of opioid by reducing its consumption. In this constant endeavor, dexmedetomidine, a highly selective α2 agonist various beneficial characteristics, including perioperative analgesia. Recently, it was investigated in different doses, routes and period of surgery [16]. It is about eight times more specific for α2 adrenoreceptors with an α2:α1 selectivity ratio of 1600:1 compared to clonidine. In this study, our preservance was to explore the role of dexmedetomidine as preemptive analgesic.

In this study, the demographic profile of our patients was comparable with respect to mean age, height, weight, ASA grade, mean duration of surgery and anaesthesia.

At baseline, the HR (P=0.847) and MAP (P=0.891) were almost same between the two groups. However, it was found that, group A (dexmedetomidine) had a significantly lower HR and MAP just after intubation (P=0.001) and extubation MAP (P=0.004 and 0.001 respectively). Dexmedetomidine attenuates sypathatoadrenal response by activation of presynaptic α2 receptors in sympathetic nerve endings resulting in decreased release of noradrenaline. Moreover, stimulation of postsynaptic α2 receptors of locus coeruleus causes inhibition of norepinephrine release [25]. Patel *et al*., administered dexmedetomidine intravenously as loading dose of 1 μg/kg over 10 min prior to induction in group B and observed, dexmedetomidine significantly attenuated stress response to intubation with lesser increase in heart rate (10% vs. 17%), systolic (6% vs. 23%) and diastolic (7% vs. 20%) blood pressure as compared to the control group (P <0.05) [26].

In the current study, MAP and HR were significantly higher in group B in the postoperative period compared to group A where MAP and HR were towards the baseline. Recordings at 12^{th}, 16^{th}, 20^{th} and 24^{th} hours revealed lower MAP in group A, but not statistically significant (P=0.52, 0.77, 0.06, 0.12 respectively) may be due to decreased plasma level of dexmedetomidine. Similarly, Beegum *et al.*, observed that the mean diastolic blood pressure was reduced significantly at 0, 15, 30 min and 1^{st}, 2^{nd}, 3^{rd}, 6^{th} $12^{th}$and 24 hours in the Dexmedetomidine group compared to the control group postoperatively. But, the mean systolic blood pressure was not significantly lower in Dexmedetomidine group after 12^{th} hour [25]. Similarly, Ren *et al*., showed that the groups received dexmedetomidine had significantly lower (P <0.05) HR and MAP than control group [27].

Regarding the pain intensity, it was observed that, patients from the group A had a lower VAS score in both the resting (P= 0.001, 0.001, 0.019, 0.010 and 0.042 for time points of 1, 2, 6, 12 and 24 hours) and movement state (P = 0.001, 0.006, 0.007, 0.029 and 0.035 for time points of 1, 2,6,12 and 24 hours) postoperatively, compared to the group B. However, VAS score almost consistently declined over time in both groups. Ren *et al*., and Ge *et al*., studies showed a similar trend where DEX reduced postoperative pain whether used intraoperatively or postoperatively [27, 28]. In another study, Wang *et al*., demonstrated a similar pain perception within the first postoperative 48 hours in the DEX and fentanyl groups. DEX alone for intravenous patient-controlled analgesia reduced postoperative pain in that study [29]. A previous study, Li *et al*., demonstrated that the postoperative pain of propofol-based anesthesia decreased significantly at 0.5 and 1 hour in DEX patients following gynecological laparoscopies [30]. Hence, Wang *et al*., thought that the analgesic effect of postoperative DEX was due to the direct action of DEX. Hwang *et al*., indicated that DEX showed superior efficacy for analgesia after spinal surgery, and the authors concluded that DEX might be a substitute for remifentanil as an adjuvant in total intravenous anesthesia [31].

Total postoperative morphine requirement after 24 hours was significantly lower in group A compared to group B (P=0.039) in this study. Recently, Fan *et al*., observed that, the total morphine consumption 24 hours after radical mastectomy was significantly less (P<0.05) in dexmedetomidine group than placebo who received 1 µg/kg as a loading dose before induction and intraoperative infusion of 0.4 µg/kg/h [32]. Gurbet *et al.*, assigned two group where Group D patients received an initial loading dose of dexmedetomidine 1µg/kg over 30 min prior to induction, followed by an intraoperative infusion 0.5 µg/kg/hr. After 48 hour postoperatively, placebo group had significantly higher mean cumulative morphine consumption than dexmedetomidine group (P<0.01) [33]. In another study, Ge *et al*., intraoperative infusion of DEX (0.4mg/kg/h) during abdominal colectomy versus saline revealed, DEX group required significantly less morphine than saline group. According to them, though DEX has a short plasmatic half-time of 2 to 2.5 hours, the underlying mechanisms of the prolonged analgesic effect of DEX are not well explained [34]. It is speculated that, sedative effect, α2a receptor dependent downstream mechanism and the potentiation of the effect of the other analgesics might be the reason behind. On the contrary, Nithipanich *et al.*, found less 24 hours total morphine requirement delivered by PCA, but the difference was insignificant (p=0.39) in dexmedetomidine premedicated group following AH may be due to race, ethnic issues, level of education, so not feared to press button of PCA and lower pain threshold [35].

Central inhibition of sympathetic outflow and stimulation of parasympathetic outflow due to stimulation of α2 receptors at the locus coeruleus in the brainstem plays a prominent role in the sedation and anxiolysis produced by dexmedetomidine [36]. Group A patients had slightly more sedation score than Group B in all postoperative follow up. But both group were more sedated after 12th hour (Group A-2.00±0.73 and Group B-1.85±0.67, P=0.502), may be due to better analgesia and circadian rhythm. However, after 24 hours, sedation score was reduced (Group A-1.50±0.61and Group B-1.40±0.50, P=0.574). However, no patient had sedation score more than 3 at any follow up. Sedation induced by dexmedetomidine is unique, as it does not depend primarily on activation of the GABA receptors. Moreover, the primary site of action of α2 agonist is the locus coeruleus and not the cerebral cortex [37].

The study showed that, the Group-A patients trended towards suffering from less adverse effects but the difference was not statistically significant. Dizziness and nausea were more common adverse effects in both groups. Similarly, Wang *et al*., found nausea 5.0% in group A and 31.3% in group B [29]. Comparably, Choi *et al*., demonstrated that intravenous PCA with fentanyl, with a lower background dose, resulted in a 23.2% incidence of PONV following colorectal cancer laparoscopic surgery [38]. Other studies, Ren *et al*., and Liang *et al*., also showed that DEX reduced the incidence of PONV [27, 39]. No patient developed bradycardia or hypotension in the DEX group.

CONCLUSION

The results of the study indicate that, preemptive administration of dexmedetomidine provided better postoperative analgesia, reduced morphine consumption, rendered better haemodynamic stability and less side effects than placebo group following abdominal hysterectomy under general anaesthesia.

REFERANCES

1. Beyaz SG, Bayar F, Erdem AF. Acute Postoperative Pain. Anesthesia and Clinical. Research, 2011;4:286.
2. Azari L, Santoso JT, Osborne SE. Optimal pain management in total abdominal hysterectomy. Obstetrical & Gynecological Survey, 2013;68(3):215-27.
3. Kelly DJ, Ahmad M, Brull SJ. Preemptive analgesia II: recent advances and current trends. Canadian Journal of Anesthesia, 2001;48(11), p.1091.
4. Sutton C. Past, present, and future of hysterectomy. Journal of Minimally Invasive Gynecology, 2010;17(4):421-35.
5. Perniola A, Gupta A, Crafoord K, Darvish B, Magnuson A, Axelsson K. Intraabdominal local anaesthetics for postoperative pain relief following abdominal hysterectomy: a randomized, double-blind, dose-finding study. European Journal of Anaesthesiology, 2009;26(5):421-429.
6. Kehlet H. Glucocorticoids for peri- operative analgesia: how far are we from general recommendations?. Acta Anaesthesiologica Scandinavica, 2007;51(9):1133-5.
7. Carollo DS, Nossaman BD and Ramadhyani U. Dexmedetomidine: a review of clinical applications. Current Opinion in Anesthesiology, 2008;21(4):457-61.
8. Venn RM, Bradshaw CJ, Spencer R, Brealey D, Caudwell, E, Naughton C, Vedio A, Singer M, Feneck R, Treacher D, Willatts SM. Preliminary UK experience of dexmedetomidine, a novel agent for postoperative sedation in the intensive care unit. Anaesthesia, 1999;54(12):1136-42.
9. Aantaa R, Kanto J, Scheinin M. Intramuscular dexmedetomidine, a novel alpha2 adrenoceptor agonist, as premedication for minor gynaecological surgery. Acta Anaesthesiologica Scandinavica, 1991;35(4):283-8.
10. Aantaa R, Kanto J, Scheinin M, Kallio A and Scheinin H. Dexmedetomidine, an alpha2-adrenoceptor agonist, reduces anesthetic requirements for patients undergoing minor

gynecologic surgery. Anesthesiology, 1990;73(2):230-5.
11. Buhrer M, Mappes A, Lauber R, Stanski DR and Maitre PO. Dexmedetomidine decreases thiopental dose requirement and alters distribution pharmacokinetics. Anesthesiology, 1994;80(6):1216-27.
12. Aho MS, Erkola, OA, Scheinin H, Lehtinen AM and Korttila KT. Effect of intravenously administered dexmedetomidine on pain after laparoscopic tubal ligation. Anesthesia & Analgesia, 1991;73(2):112-8.
13. Scheinin B, Lindgren L, Randell T, Scheinin H and Scheinin M. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and peroperative fentanyl. BJA: British Journal of Anaesthesia, 1992;68(2):126-31.
14. Panzer O, Moitra V, Sladen R. Pharmacology of Sedative-Analgesic Agents: Dexmedetomidine, Remifentanil, Ketamine, Volatile Anesthetics, and the Role of Peripheral Mu Antagonists. Anesthesiology Clinics, 2011;29(4):587-605.
15. Carli F and Baldini G. 'Perioperative Pain Management & Enhanced Outcome', Butterworth F, Mackey C, Wasnick D (5), Morgan & Mikhail's Clinical Anesthesiology, McGraw-Hill Education, New York, 2013:1100-1.
16. Grosu I, Lavand'homme P. Use of dexmedetomidine for pain control. F1000 Medicine Reports.
17. Calvillo O, Ghignone M. Presynaptic effect of clonidine on unmyelinated afferent fibers in the spinal cord of the cat. Neuroscience Letters, 1986;64(3):335-9.
18. Ono H, Mishima A, Ono S, Fukuda H and Vasko MR. Inhibitory effects of clonidine and tizanidine on release of substance P from slices of rat spinal cord and antagonism by α-adrenergic receptor antagonists. Neuropharmacology, 1991;30(6):585-9.
19. Kuraishi Y, Hirota N, Sato Y, Kaneko S, Satoh M, Takagi H. Noradrenergic inhibition of the release of substance P from the primary afferents in the rabbit spinal dorsal horn. Brain research, 1985;359(1):177-82.
20. Yoshitomi T, Kohjitani A, Maeda S, Higuchi H, Shimada M, Miyawaki T. Dexmedetomidine enhances the local anesthetic action of lidocaine via an α-2A adrenoceptor. Anesthesia & Analgesia, 2008;107(1):96-101.
21. Alam M, Chowdhury F, Chowdhury F, Saha A, Hoque A and Rahman M. Creatinine clearnce Rate (CCR) in Dignosing Different stages of chronic kidney Disease (CKD) - An update and review. Journal of Medicine, 2006;7(2):64-69.
22. Schulz K, Grimes D. Sample size calculations in randomised trials: mandatory and mystical. The Lancet, 2005; 365(9467):1348-53.
23. Movafegh A, Shoeibi G, Ansari M, Sadeghi M, Azimaraghi O, Aghajani Y. Naloxone infusion and post- hysterectomy morphine consumption: a double- blind, placebo- controlled study. Acta Anaesthesiologica Scandinavica, 2012; 56(10):1241-9.
24. Vadivelu N, Mitra S, Narayan D. Recent Advances in Postoperative Pain Management. The Yale Journal of Biology and Medicine, 2010;83(1):11–25.
25. Beegum TS, Bindu M, Lesna MP, Suresh V. Postoperative Analgesic Requirements in Patients Receiving Intraoperative Dexmedetomidine Infusion. International Journal of Health Sciences and Research, 2015;5(8):145-54.
26. Patel C, Engineer S, Shah B and Madhu S. Effect of intravenous infusion of dexmedetomidine on perioperative haemodynamic changes and postoperative recovery: A study with entropy analysis. Indian Journal of Anaesthesia, 2012; 56(6):542.
27. Ren C, Chi M, Zhang, Y, Zhang Z, Qi F, Liu Z. Dexmedetomidine in postoperative analgesia in patients undergoing hysterectomy: a consort-prospective, randomized controlled trial, 2015. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4616704/ pdf/medi-94-e1348.pdf
28. Ge DJ, Qi B, Tang G, Li JY. Intraoperative dexmedetomidine promotes postoperative analgesia in patients after abdominal colectomy: a consort-prospective, randomized, controlled clinical trial. Medicine, 2015;94(37):1-5.
29. Wang X, Liu W, Xu Z, Wang F, Zhang C, Wang B, Wang K, Yu J. Effect of dexmedetomidine alone for intravenous patient-controlled analgesia after gynecological laparoscopic surgery: a consort-prospective, randomized, controlled trial. Medicine, 2016;95(19):1-7.
30. Li M, Mei W, Wang P, Yu Y, Qian W, Zhang ZG, Tian YK. Propofol reduces early post- operative pain after gynecological laparoscopy. Acta Anaesthesiologica Scandinavica, 2012;56(3):368-75.
31. Hwang W, Lee J, Park J, Joo J. Dexmedetomidine versus remifentanil in postoperative pain control after spinal surgery: a randomized controlled study. Bio Med Central Anesthesiology, 2015;15(1):21.
32. Fan W, Xue H, Sun Y, Yang H, Zhang J, Li G, Zheng Y, Liu Y. Dexmedetomidine Improves Postoperative Patient-Controlled Analgesia following Radical Mastectomy. Frontiers in Pharmacology, 2017:1-5.
33. Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN and Ozcan B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Canadian Journal of Anesthesia, 2006;53(7):646.
34. Ge DJ, Qi B, Tang G, Li JY. Intraoperative dexmedetomidine promotes postoperative

analgesia and recovery in patients after abdominal hysterectomy: a double-blind, randomized clinical trial. Scientific Reports, 2016;6:1-7.

35. Nithipanich P, Mingsaun A and Marom S. The effect of pre-anesthetic administration of dexmedetomidine on postoperative pain and morphine consumption in patient receiving abdominal hysterectomy. Thai Journal of Anesthesiology, 2016;42(2):96-105.
36. Bindu B, Pasupuleti S, Gowd U P, Gorre V, Murthy RR, Laxmi MB. A double blind, randomized, controlled trial to study the effect of dexmedetomidine on hemodynamic and recovery responses during tracheal extubation. Journal of Anaesthesiology, Clinical Pharmacology, 2013;29(2):162–167.
37. Callado LF, Stamford JA. Alpha2A- but not alpha2B/C- adrenoceptors modulate noradrenaline release in rat locus coeruleus: voltammetric data. European Journal of Pharmacology, 1999;366:35-9.
38. Choi YY, Park JS, Park SY, Kim HJ, Yeo J, Kim JC, Park S, Choi GS. Can intravenous patient-controlled analgesia be omitted in patients undergoing laparoscopic surgery for colorectal cancer? Annals of Surgical Treatment and Research, 2015;88(2):86-91.
39. Liang X, Zhou M, Feng JJ, Wu L, Fang SP, Ge XY, Sun HJ, Ren PC, Lv X. Efficacy of dexmedetomidine on postoperative nausea and vomiting: a meta-analysis of randomized controlled trials. International Journal of Clinical and Experimental Medicine, 2015;8(6):8450.