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THE EFFECT OF SINGLE PREOPERATIVE DOSE OF DEXMEDETODINE VERSUS FENTANYL AS A ANAESTHETIC REQUIREMENT AND PERIOPERATIVE HEMODYNAMIC

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Abstract

Background: Unrelieved post-operative pain may bring about physical suffering as well as a couple of physiological and mental effects, which may adversely affect the peri-operative outcome and make contributions to growth during the period of stay in the health center. **Aim:** To study the difference in haemodynamic responses of dexmedetomidine and fentanyl in patients undergoing laparoscopic surgery. **Material and methods: 50** patients were divided into two groups of 25 each randomly. In Group F, fentanyl 0.5 μg/kg as loading dose over 10 minutes prior to induction followed by 0.2-0.7 μg/kg/hr as maintenance dose and in Group D, Dexmedetomidine 0.5 μg/kg as loading dose over 10 minutes prior to induction followed by 0.2 μg/kg/hr-0.7 μg/kg/hr as maintenance dose till surgery was over. Haemodynamic variables and Visual Analogue Scale (VAS) scores were recorded continuously. **Results** : Profiles of intra-operative hemodynamic changes had been similar in each group regarding heart rate (HR), diastolic blood pressure, and mean arterial pressure except within the systolic blood pressure where Dexmedetomidine significantly decreased it compared to Paracetamol ($P = 0.014$). Postoperatively 4th h and 24th h changes in mean HR between the two groups changed into a statistically significant ($P < 0.05$). visual analog scale scores have been significantly lower inside group P than in group D at 8th, 16th, and 24th h ($P < 0.001$). Sedation scores have been statistically better inside group D compared with group P at postoperative 4th, 8th, 16th, and 24th h ($P < 0.006$). **Conclusion:** Dexmedetomidine is better drug as compared to fentanyl for maintaining the haemodynamic response during intubation and intraoperative period.

Key words: Dexmedetomidine, laparoscopic c , multimodal analgesia, fentanyl

Introduction

Dexmedetomidine is the active d-isomer of medetomidine, that is a selective and specific α2- adrenoceptor agonist. [1] It acts by the central sympatholytic action. So it provides haemodynamic stability. It has both analgesic as well as anaesthetic sparing property.[2]The International Association for the Study of Pain (IASP) is the global professional forum for science, practice, and education in the field of pain. IASP brings together scientists, clinicians, health-care providers, and policymakers to stimulate and support the study of pain and to translate that knowledge into improved

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pain relief worldwide.Acute pain inside the perioperative setting is defined as pain that is present in the surgical patient due to pre-current disease, surgical procedure or a the aggregate of those which is detrimental to post operative final results. It will increase the sympathetic response of the body with a subsequent rise in oxygen consumption of body, the chance of deep vein thrombosis due to immobility and consequent pulmonary embolism. similarly, there may be sizable effects on the gut and urinary tract motility, which may lead, in turn to postoperative ileus, nausea, vomiting, and urinary retention.[3] As an end result,adequate pain comfort receives translated to better the perioperative outcome, early recovery, and reduced period of living in the health center.routine use of strong opioids is unwanted due to adverse consequences including nausea, vomiting, pruritus, and sedation. studies have shown that under-treatment of acute postoperative pain occurs due to the fact there may be an overestimation of the duration of action,strength of the opioid used and worry approximately respiratory depression, vomiting, sedation, and dependence. [4,5]

Dexmedetomidine is an incredibly selective α2 adrenoceptor agonist that provides sedation, analgesia, and sympatholytic without causing respiratory depression. previous studies document that intravenous dexmedetomidine has a definitive role in postoperative analgesia through the reduction of opioid consumption.[6] At the time of laparoscopy, endotracheal intubation and time of extubation are most critical events which provoke transient, but marked sympatho-adrenal response such as tachycardia and hypertension. Also, Carbon dioxide (CO_2) used for creating pneumoperitoneum at the time of surgery, causes spikes in plasma levels of catecholamine and vasopressin. This leads to rise in intra-abdominal pressure due to raised diaphragm which leads to side effects on the CVS such as low cardiac output, rise in arterial pressure and increase systemic and pulmonary vascular resistance, leading to hypertension and tachycardia [7].

Several pharmacological agents such as opioids, beta blockers, calcium channel blockers, combined alpha and beta blockers, lignocaine, and alpha-2 receptor agonists have been used to maintain stable hemodynamics in the perioperative period. Fentanyl is a common choice for control of hemodynamics in the perioperative period. Though, it has some side effects like respiratory depression and increased incidence of postoperative nausea and vomiting (PONV). [8-9] Dexmedetomidine has sympatholytic, ant nociceptive, sedative, and anti-sialagogue properties without causing respiratory depression.[10-13] This study aimed at assessing the effect of intravenous dexmedetomidine and fentanyl on perioperative haemodynamics and recovery during postoperative period following elective laparoscopic surgical procedures.

Materials and Methods

The study was conducted in Prasad medical college, Junab Ganj, UP, Department of Anesthesiology and Critical Care. Ethical clearances was obtained from the Institutional Ethical Committee and written informed consent was taken, before carrying out the study, 50 patients aged 20-60 years, ASA-ps-I scheduled for laparoscopic cholecystectomy had been taken for those randomizedstudy. patients with body weight >80 kg, cardiovascular disorder, broncho-pulmonary disorder, renal, neurologic, gastrointestinal, and hepatic dysfunction, records of allergy, long-time period use of medicinal drugs which includes beta-blocker and different anti-hypertensives, antipsychotics, analgesics,alcohol, sedative, TCA, etc., patients with

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psychiatricillness, patient refusal had been excluded from this study patients have been randomly assigned to one of thefollowing groups: group F (n = 30) obtained IV 1gm Paracetamol infusion over 10 min pre-operatively and 6 hourly thereafter and group D (n = 30) received IV Dexmedetomidine 1 μg/kg bolus over 10 min pre-operatively and 0.2-0.4 μg/kg/h thereafter for 24 h using a computer-generated random-number table. within the pre-operative holding area, the patients found out and familiarized about 10 points visible analog scale (VAS)to assess their baseline pain with 0 = none to 10 = maximum. without delay earlier than entering the operating room patients were pre-medicated with the Midazolam2 mg, Ondansetron 4 mg, and Glycopyrrolate 0.2 mg IV.Intra-operative monitoring devices included pulse-oximetry, non invasive blood pressure, ECG, and capnography.

In both the Groups general anesthesia was administered after preoxygenation for 3 minutes with Inj. Sodium Thiopentone (2.5%) 4- 6 mg/kg to produce loss of eyelash reflex followed by Inj. Succinylcholine 1.5-2 mg/kg. Patients were ventilated with 100% O 2 and on achieving complete relaxation intubation was done with appropriate sized cuff portex endotracheal tube. Anesthesia was maintained in both the Groups with O (66%), N O (33%), Isoflurane, 2 2 Inj. Vecuronium 0.1 mg/kg as initial dose and 0.02 mg/kg as maintenance dose, and ventilation was continued with IPPV (intermittent positive pressure ventilation). Pulse, blood pressure Spo and BIS value were recorded before 2 induction, during laryngoscopy, every 1 minute upto 5 minutes after intubation and then every 10 minutes till extubation.Volatile anesthetics were titrated to maintain BIS value between 40-60, ideal for surgical plane of anesthesia. Patients were reversed with injection Glycopyrrolate (0.008mg/kg) and injection Neostigmine (0.05mg/kg) intravenously at the end of the surgery. Duration of surgery, duration of anesthesia, total dosage of Vecuronium (mg) was recorded. Total dosage of Isoflurane (ml/hr) was measured by using EHRENWORTH AND EISENKRAFT formula. (3x FGF x Volume %) Post-operative vitals, Ramsay sedation score and Visual Aaxnalouge Score for pain were recorded. Patients were observed for adverse effects like nausea, vomiting, bradycardia, and hypotension

Statistics Analysis

Mean ± SD were calculated for all the parameters to examine and were differentiated by (ANOVA) and repeated measures of ANOVA were used to evaluate the changes among the groups using SPSS 16. Wilks' Lambda test was used to analyze the parametric data. *P*-values considered significant were as follows: – $P < 0.05$– a Significant and $P > 0.001$ –a highly Significant.

Results

A total of 50 patients were enrolled and divided into two groups ($n = 25$). Two patients were excluded from final analysis due to repeated hypotension and bradycardia.

Table 1 shows there were no significant differences among the two groups with respect to age, weight, and height ($P > 0.05$).

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Table 1: Baseline demographic data

	Group D (N=25)	Group F (N=25)	P-value
Age (year)	41.6 ± 9.99	43.56 ± 8.24	
Hight (cm)	151.84 ± 8.38	154.44 ± 7.134	
Weight (kg)	54.68 ± 5.99	55.64 ± 6.50	

Intra-operative hemodynamic parameters were recorded at 5, 15, 30, 45, and 60 min after the completion of bolus dose infusion of study medication. Table 2 shows profiles of hemodynamic changes, which were similar in both groups in respect to HR, DBP, MAP except in SBP where Dexmedetomidine significantly reduced it in compare to Paracetamol ($P = 0.015$).

Table 2: Intra-operative hemodynamic parameters

Time (min)	**HR (min)**		**SBP (mmHg)**		**DBP (mmHg)**		**MAP (mmHg)**	
	Group D	**Group F**	**Group D**	**Group F**	**Group D**	**Group F**	**Group D**	**Group F**
5	101.28±8.48	92.4±8.49	116.96±10.41	129±7.86	82.84±5.80	83.24±5.10	86.8±5.83	94.44±6.60
15	100.32±7.44	96.88±22.49	120.72±18.34	116.96±8.31	79.48±4.0	77.6±3.21	87.32±5.80	87.68±6.06
30	102.44±6.86	90.72±6.90	125.08±8.95	124.84±7.49	84.48±5.12	84.44±4.68	91.96±5.85	94.72±6.14
45	102±4.76	87.2±5.67	123.36±8.64	121.68±8.38	81.44±5.24	81.44±5.24	93.2±6.30	88.64±5.0
60	99.12±4.17	88.32±6.04	123.56±8.83	119.28±6.66	79.44±6.26	82.52±5.88	93.84±5.57	88.48±6.10

Note:HR = Heart rate, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, MAP = Mean arterial pressure

Post-operative hemodynamic parameters were recorded at 4th, 8th, 16th, and 24th h. No significant differences in the post-operative hemodynamic parameters were seen in MAP, as shown in Table 3. Mean HR ranges from (84.48±5.12) to (85.24±4.94) for the Group D whereas, it ranges between (82.44±5.78) to (85.76±3.90) in Group F. Post-operatively 4th h and 24th h changes in mean HR between two groups was statistically significant ($P < 0.05$).

Table 3: Post-operative hemodynamic parameters

Time (h)	HR		MAP	
	Group F	Group D	Group F	Group D
4	84.48±5.12	78.36±4.72	88.56±6.31	83.12±4.40
8	85.24±4.94	78.44±4.59	93.04±5.15	93.04±5.15
16	86.52±3.90	85.76±3.90	90.04±5.74	90.04±5.74
24	89.12±4.94	82.44±5.78	88.04±4.42	88.04±4.42

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Note:HR = Heart rate, MAP = Mean arterial pressure

VAS score for post-operative pain were measured in a scale of 10 where 0 = no pain and 10 = maximum pain at 4th, 8th, 16th, and 24th h. Sedation was measured according to Ramsay sedation scale. VAS Scores were significantly lower in the Group D compared with Group F at 8th, 16th, and 24th h ($P < 0.001$). Sedation score were statistically higher in the Group F compared with Group D at 4th, 8th, 16th, 24th h ($P < 0.005$) as shown in Table 4.

Table 4: Post-operative analgesia and sedation score

Pain scale	**Group D**	**Group F**	**Sedation scale**	**Group D**	**Group F**
VAS 4	2.56±0.40	2.26±0.42	SS 4	1.96±0.39	2.51±0.34
VAS 8	1.71±0.46	2.33±0.35	SS 8	2.21±0.40	2.33±0.35
VAS 16	1.75±0.42	2.17±0.39	SS 16	2.03±0.44	2.3±0.33
VAS 24	1.89±0.36	2.17±0.39	SS 24	1.91±0.38	2.21±0.33

Note:VAS = Visual analog scale

Table 5: Distribution of cases according to duration of surgery

Duration of surgery	**Group D** Mean±SD	**Group F** Mean±SD	**P -value**
Duration (minute)	110.2±6.19	99.36±6.35	
Isoflurane (ml/hr)	7.35±0.77	13.93±3.13	

Table 6: Distribution of cases according to adverse effect

Adverse effect	**Group D**	**Group F**
Nausea/Vomiting	**0**	**0**
Shivering	**0**	**0**
Hypotension	**0**	**0**
Bradycardia	**1**	**0**

Discussion

This study has demonstrated that use of dexmedetomidine for intraoperative infusion helps attenuates stress responses to different noxious stimuli during surgery and helps maintain haemodynamic stability and early recovery [14]. Dexmedetomidine, and α-2 adrenoreceptor agonist is approved for sedation to start with intubated and mechanically ventilated patients by means of non-stop infusion for most effective in less than 24 h in an intensive care setting. α-2 adrenoceptor agonists are being increasingly used in anesthesia and critical care as they are not the most effective decrease sympathetic tone and attenuate the strain responses to anesthesia and surgery; however also cause sedation, analgesia, and anxiolysis. The bolus of 1 μg/kg Dexmedetomidine initially results in a transient increase

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in the blood strain and a reflex fall in HR, mainly in younger, healthful patients.[15] Given the propensity of the drug to produce hypotension and or bradycardia while it is administered to volunteers or patients, it becomes important to determine an infusion rate that would maximize the anesthetic and analgesic sparing impact even though, minimizing the occurrence of unfavorable cardiovascular side effects requiring therapeutic intervention. Jung et al. in their comparative study showed a significant gain of Dexmedetomidine at a dose of 1 μg/kg bolus followed by 0.2-0.7 μg/kg/h infusion for 24 h.[16] it is a safe sedative opportunity to benzodiazepine/opioid aggregate in patients undergoing monitored anesthesia take care of a large number of procedures due to its analgesic, "co-operative sedation" and shortage of respiration depression properties.[17] numerous findings lead to the conclusion that the principal sedative and antinociceptive effects of Dexmedetomidine is due to its stimulation of the α-2 adrenoceptors in the locus coeruleus.

In modern anesthesia practice, it is very essential to know the series of physiological changes (stress response), that occur during and after laryngoscopy. Under anesthesia stress response has been universally recognized phenomenon (J. Zargar et al, 2002). Stress response is accompanied by an increased stimulation of sympathetic efferent tracks, resulting in adrenergic response. It leads to release of catecholamines in the circulation, that can cause severe hypertension, tachycardia, cardiac arrhythmias, myocardial ischemia, left ventricular dysfunction and rupture of cerebral aneurysm in susceptible individuals.[1] Direct laryngoscopy and intubation are toxic stimuli. It can provoke stress response in the cardiovascular, respiratory and other physiological system. The magnitude of the response is greater with increasing force and duration of laryngoscopy. After intubation, the response reaches its maximum level within 1 min and ends in 5-10 min.[18] To prevent rise in blood pressure, it is important to limit the time for laryngoscopy. The present study was undertaken to assess and compare the effects of Dexmedetomidine and Fentanyl on laryngoscopic stress response and hemodynamic stability during general anesthesia. In 1997, C.J. Lawrence et al did a double-blind placebo controlled study to investigate the effect of a single pre-induction intravenous dose of Dexmedetomidine 2 μg/kg on anesthetic requirement and peri-operative hemodynamic stability. They found that laryngoscopy and tracheal intubation caused 0 and 31 mm of Hg increase in the mean systolic blood pressure, 1 and 26 mm of Hg increase in the mean diastolic blood pressure and 13 and 29 beats/minutes increase in the mean heart rate in Dexmedetomidine and Placebo Groups, respectively. These two Groups were compared during first 51 minutes after tracheal intubation. During this period, mean systolic blood pressure, diastolic blood pressure and heart rate were significantly lower in the Dexmedetomidine Group in comparison to placebo Group ($P<0.001$). One minute after postextubation the mean systolic blood pressure and heart rate were significantly lower in the Dexmedetomidine Group as compared to its counterpart.($P<0.001$). In the post anesthesia care unit, over a three hour period, the mean systolic blood pressure, diastolic blood pressure and heart rate were significantly low in Dexmedetomidine Group.($P<0.001$) Dexmedetomidine has sedative and analgesic property via central actions in the locus coeruleus and in the dorsal horn of the spinal cord.[5] Dexmedetomidine has also been used in normal adult as well as in patients having coronary heart disease. It provides hemodynamic stability perioperatively.

Fentanyl produces analgesia, sedation and in large doses unconsciousness and anesthesia by virtue of its agonist effect on opioid receptor. These receptors are located in thalamus, hypothalamus, reticular system and gamma neurons. It prevents

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release of substance-P along with pain pathway and release dopamine and acetylcholine in central nervous system. High dose of opioids dull the neuroendocrine stress response to surgery.[19-20] It was inferred that, Dexmedetomidine an α agonist agent, when used 2 as a pre-induction drug, reduces stress response to laryngoscopy and tracheal intubation, therefore reduces heart rate and blood pressure perioperatively. Fentanyl, an opioid agonist agent, however increases the heart rate & blood pressure during laryngoscopy and tracheal intubation nonetheless it was significant when compared with the baseline value of that Group.

During the postoperative period, recovery and longer discharge time of patients from post anaesthesia recovery room receiving perioperative dexmedetomidine infusion. In their study, Massad IM et al., found that combining dexmedetomidine to other anaesthetic agents, leads to a balanced anaesthesia and a significant drop in the incidence of PONV postoperatively [21].Therefore, it was inferred that Fentanyl can also help to reduce laryngoscopic stress response, as the rise in hemodynamics after laryngoscopy and intubation was within the normal limits of heart rate and blood pressure. Thus it may be recommended in patients' with cardiovascular instability, ischemic heart disease and hypertension.

Strength and Limitations of the Present Study

There are a few drawbacks to the study. In the present study, only 20–60 years ages subjects participated in the research as well a reduced sample size. Hence, in the feature, we would like to include an increase in the number of participants to reach a concrete conclusion, Our results cannot be applied to major extensive surgeries in which effect of Dexmedetomidine need to be studied. Further use of intraoperative fentanyl may have also contributed better VAS score in immediate post operative period.

Conclusion

Dexmedetomidine, during intraoperative infusion, controls stress response to various noxious stimuli and maintains haemodynamic stability. Dexmedetomidineis superior to fentanyl for analgesia in short surgical procedures and should form a part of multi-modal analgesia. The use of Dexmedetomidine provides multimodal analgesia with minimum sedation in short surgical procedures and fentanyl provides analgesia and cooperative sedation

Reference

1. Savola JM, Ruskoaho H, Puurunen J, Salonen JS, Kärki NT. Evidence for medetomidine as a selective and potent agonist at alpha 2-adrenoreceptors. J Auton Pharmacol. 1986;6:275–84.
2. Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, Ozcan B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Can J Anaesth. 2006;53:646–52.
3. American Society of Anesthesiologists: Practice guidelines for acute pain management in the perioperative setting: A report by the American Society of Anesthesiologists Task Force on Pain Management, Acute Pain Section. Anesthesiology 1995; 82:1071.
4. Pre-emptive analgesia- why its effect is not always obvious. Anaesthesiology 1996; 84:1015.

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5. Woolf CJ, Chong M: Pre-emptive analgesia- treating postoperative pain by preventing the establishment of central sensitization. Anaesth Analg 1993;77:362.
6. Tufanogullari B, White PF, Peixoto MP, Kianpour D, Lacour T, Griffin J, et al. Dexmedetomidine infusion during laparoscopic bariatric surgery: the effect on recovery outcome variables. Anesth Analg 2008; 106: 1741-8.
7. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anaesth Analg. 2000;90:699–705.
8. Apfel CC, Heidrich FM, Jukar-Rao S, Jalota L, Hornuss C, Whelan RP, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. Br J Anaesth 2012;109:742-53.
9. Gan TJ. Mechanisms underlying postoperative nausea and vomiting and neurotransmitter receptor antagonist-based pharmacotherapy. CNS Drugs 2007;21:813-33.
10. Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M. The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. Anesthesiology 2003;98:428-36.
11. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs 2000;59:263-8.
12. Hsu YW, Cortinez LI, Robertson KM, Keifer JC, Sum-Ping ST, Moretti EW, et al. Dexmedetomidine pharmacodynamics: Part I: Crossover comparison of the respiratory effects of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology 2004;101:1066-76.
13. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The Effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology 2000;93:382- 94.
14. Piascik MT, Soltis EE, Piascik MM, Macmillan LB. Alpha-adrenoceptors and vascular regulation: Molecular, pharmacologic and clinical correlates. Pharmacol Ther. 1996;72:215–41.
15. Bhatia P. Dexmedetomidine: A new agent in anaesthesia and critical care practice, 2002.
16. Jung HS, Joo JD, Jeon YS, Lee JA, Kim DW, In JH, *et al*. Comparison of an intraoperative infusion of Dexmedetomidine or remifentanil on perioperative haemodynamics, hypnosis and sedation, and postoperative pain control. J Int Med Res 2011;39:1890-9.
17. Hyllested M, Jones S, Pedersen JL, Kehlet H. Comparative effect of Paracetamol, NSAIDs or their combination in postoperative pain management: A qualitative review. Br J Anaesth 2002;88:199-214.
18. Nermin Gogus, Belgin Akan, , Nurten Serger, Mustafa Baydar: The comparison of the effects of Dexmedetomidine, Fentanyl and Esmolol on prevention of hemodynamic response to intubation, Rev Bras Anesthesiology,2014;64(5):314-319.
19. Robert K Stoelting: opioid agonist and antagonists, pharmacology and physiology in anesthetic practice, 3rd edition, Lippincott Raven 1999;103-05.
20. Robert K Stoelting: Pharmacology and physiology in anesthetic practice,3 rd edition. Lippincott Raven publishers(United States of America) 1999;628:33.
21. Massad IM, Mohsen WA, Basha AS, Al-Zaben KR, Al-Mustafa MM, Alghanem SM. A balanced anaesthesia with dexmedetomidine decreases postoperative nausea and vomiting after laparoscopic surgery. Saudi Med J. 2009;30:1537– 41.