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A Prospective Randomized Double-Blind Study to Compare the Effects of Two Different Preinduction Doses of Dexmedetomidine on Hemodynamic Responses in Laparoscopic Cholecystectomy

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Abstract

Introduction: Dexmedetomidine is popular in providing stable haemodynamics, analgesia and sedation in patients undergoing laparoscopic surgeries. Two preinduction doses were compared for their effects.

Materials and Methods: 44 patients were randomly divided into 2 groups, 22each. Group D.5 received injection dexmedetomidine 0.5µg/kg, while group D1 received 1µg/kg; as intravenous bolus dose in 25ml NS over 15 min in operating room prior to induction. Parameters assessed were HR, BP, SpO2, EtCO2, RR; BIS and MAC of inhalational agent required perioperatively. Time to extubation was noted after stopping inhalational agents. In postoperative period, intravascular injection diclofenac (75mg) was used as rescue analgesic, pain and level of sedation were gauged with Numerical Rating Scale (NRS) score and Ramsay Sedation scale respectively.

Results: Requirement of induction agents was markedly reduced, hemodynamic stability, level of sedation achieved were better with Group D1. The duration of post extubation analgesia observed in group D1 was significant (P= 0.01).

Conclusion: Single preinduction bolus of 1mcg/kg adequately blunts stress response in shorter duration laparoscopic surgeries. Significantly reducing induction anesthetic dose, without delaying extubation, reducing analgesic requirement, not causing overt sedation and without increasing incidence of adverse events. So a dose of 1mcg/kg is better than 0.5mcg/kg.

Keywords: Dexmedetomidine; Laparoscopy; Pneumoperitonium; Hemodynamic Stability

Abbreviations

CO2: Carbon Dioxide; MAC: Minimum Alveolar Concentration; FDA: Food and Drug Administration; ICU: Intensive Care Unit; α 2-AR: Alpha 2 Adrenergic Receptor; IV: Intravenous Route for Drug Administration; IAP: Intra-Abdominal Pressure; ASA PS: ASA Physical Status Classification System; OT: Operation Theater; HR: Heart Rate; BP: Blood Pressure; MAP: Mean Arterial Pressure; SPO2:Oxygen Saturation; BIS: Bi Spectral Index; MAC: Minimum Alveolar Concentration; EtCO2: End

Tidal Carbon dioxide.

Introduction

Laparoscopic surgery is a minimally invasive technique that reduces operative time, decreased hospital stay, earlier return to normal activities, less pain, less postoperative ileus, small scar and hence improved cosmesis compared with the traditional open surgical procedures. Pneumoperitoneum, a pre- requisite to laparoscopic surgeries, is achieved by insufflation of CO2 in the abdominal cavity which leads to increase in systemic vascular resistance, mean arterial pressure and cardiac filling pressure [1]. This increase in blood pressure and tachycardia may increase bleeding and restrict in giving a good surgical field to the surgeon. An array of drugs like opioids, anesthetic agents, clonidine (alpha 2 agonist) [1], beta blockers and vasodilators are used to attenuate these stress responses.

Alpha2 agonists are shown to have sedative-hypnotic, sympatholytic and opioid sparing effects and overall cause reduction in anesthetic drug requirement. Dexmedetomidine is one of the newest drugs in the therapeutic armamentarium. There have been several studies where dexmedetomidine has been used to attenuate the intubation stress response, intraoperative stress response in laparoscopic surgeries [2] when given as varying doses of a single bolus or a bolus followed by infusion [3]. Even after so many studies on the drug, no consensus has been arrived on the ideal dose to be administered. Laparoscopic cholecystectomy being a short procedure we intended to use a single bolus dose of the drug. The study is an attempt to find out if 0.5mcg/kg bolus dose of dexmedetomidine is as acceptable a dose as 1 mcg/kg bolus of the same drug in attenuating the stress response.

Materials and Methods

This prospective double blind randomized comparative study was approved by the institutional ethics committee, with written informed consent obtained from all participants in the age group of 18-65yrs of age with a BMI of <=31kg/m^2 under ASA I and II Class and posted for elective laparoscopic cholecystectomy. The study aimed to observe the effects of either 0.5mcg/kg or 1mcg/kg bolus dose of dexmedetomidine administered prior to induction of anesthesia on the intraoperative hemodynamic changes and also the requirement of anesthetic agents, time to extubation, time to first analgesic request in the recovery room, and post- operative sedation.

The 44 study participants were randomly allocated into one of the two groups by using a computerized random table. Preparation of both the drugs was achieved by an anaesthesiologist not participating in the study. Blinding was achieved as the study drug was colourless. In the operation theatre (OT), the non-invasive multipara monitor was attached to the patient and baseline hemodynamic parameters were recorded and preoxygenation was given through Hudson's face mask at 4l/min. Monitoring included heart rate (HR), blood pressure (BP), electrocardiogram (ECG), oxygen saturation (SpO2), End tidal CO2 analyser or the capnograph (EtCO2) and temperature. Special Monitors: Bispectral index (BIS) (for monitoring depth of anaesthesia), MAC (Minimal Alveolar Concentration of inhalational anaesthetic agent, sevoflurane) were used.

Group D1, received 1mcg/kg dexmedetomidine and Group D.5, received 0.5mcg/kg dexmedetomidine (Xamdex, Abbott India, Ltd) diluted in 25ml NS over a period of 15mins before induction and was administered through a syringe pump inside the operation theater once monitors are attached. Preparation of both the drugs was executed by an anaesthesiologist not participating in the study also blinding was achieved as the study drug was colourless. Ringers Lactate (RL), 5ml/kg body weight was given along with the drug infusion.

The study commenced once the monitors were attached and the infusion of the prescribed drug dose was started. Parameters like HR, BP, SpO_2, BIS were monitored when the patient was awake and after inducing anesthesia additional parameters like $EtCO_2$ and MAC were monitored. Standard general anaesthesia was administered in both the groups. Intravenous Pantoprazole 40mg, Fentanyl (1mcg/kg), Propofol (until loss of eyelash reflex), Atracurium (0.6mg/kg) was given. Patients were intubated atraumatically with appropriate size of endotracheal tube after doing laryngoscopy. After intubation the patient was mechanically ventilated using Air-Oxygen mixture (50:50), Sevoflurane 1-1.5%, Fio_2 of 0.5%, a tidal volume of 6-8 ml/kg, respiratory rate of 10-12 per minute. An end-tidal CO_2 concentration of 35-45 mmHg was maintained. Orogastric tube was inserted and fixed after checking its placement in the stomach. Skin infiltration of 0.25% bupivacaine was given at port sites before incision. Prior to the commencement of Pneumoperitoneum intravenous Fentanyl (1mcg/kg) was administered. Pneumoperitoneum in standard fashion was initiated with flow rates 10-12 l/min and achieved maintaining an intra- abdominal pressure between 12-14mmHg. Inhalational anaesthetic, Sevoflurane was titrated to maintain a mean alveolar concentration (MAC) of 0.6-0.9%. BIS of 40-60 was maintained throughout. Additional propofol boluses were given for the same. Additional muscle relaxant was administered as required.

If the hemodynamic goals were not met with, rescue intervention was done and noted down.

Rescue for hypotension: Hypotension (<25%Patients

baseline systolic BP or <90 which ever being higher) a fluid bolus of 1ml/kg of crystalloid was given, a second bolus of the same was given in case the systolic blood pressure would still be low and finally a vasopressor (ephedrine 6mg aliquot i.v.) would be used.

Rescue for bradycardia: Bradycardia (HR<50bpm), a vagolytic (i.v. glycopyrrolate 0.2mg) was used.

Rescue for tachycardia and hypertension: Tachycardia (HR>100bpm) and Hypertension (>25%of patients baseline systolic BP), intravenous propofol (0.5mg/kg) aliquot was used.

All patients received 1gm paracetamol intravenous dose, as pain relief at de-sufflation (removal of pneumoperitoneum) intraoperatively. Inhalational agent was stopped at end of surgery, neuro-muscular blockade was reversed using 0.05 mg/kg neostigmine and 8 mcg/kg glycopyrrolate. Patients were extubated when standard extubation criteria were achieved. Time to extubation (since stoppage of inhalational anesthetic to extubation) was noted. In the recovery room, the patients' vital parameters were monitored and rescue analgesics were provided after assessment of pain score using Numerical rating scale (NRS) and sedation was assessed by Ramsay Sedation Scale. Intravenous diclofenac 75mg in 100ml normal saline was administered as additional pain relief for the patients complaining of pain. Study period ended when the patient was discharged from the Recovery Room (2hrs). Any patient who had any intra-operative surgical complication was excluded from the study.

Results

Taking power as 0.8 and alpha error 0.05, the sample size of 40 patients was calculated. Considering 10% dropouts, 22 patients were enrolled in each group and hence total sample size was 44. Quantitative data was presented with Mean and Std Dev, comparison among study group was done with Unpaired T test and Mann-Whitney test as per results of Normality test. Qualitative data was presented with Frequency and percentage tables, association among study group Chi-Square test (Fisher Exact test for 2*2 table). P value <0.05 was taken as level of significance.

Demographics: Group D.5 and Group D1 were comparable and the gender difference was not statistically significant. Age Distribution of both groups was comparable as the difference was not statistically significant.

Weight: The average weights of subjects in both the study groups were comparable and not statistically significant. The BMI of the subjects in both the groups was comparable and not statistically significant by applying Unpaired T test. There were 14 (63.6%) subjects of ASA PS Class I in D.5 group and 13 (59.1%) subjects in D1 group which were comparable and the difference was not statistically significant as was seen using the Pearson Chi-Square test and Fisher's Exact Test.D.5 group had 8 (36.4%) subjects belonging to ASA PS Class II and D1 group had 9 (40.9%) subjects both the groups were comparable and the difference was not statistically significant as found out using the Pearson Chi-Square test and Fisher's Exact Test.

Induction

The requirement of drug for induction, Propofol in Group D.5 was 98.18±23.02 mg (mean ± S.D.) and in Group D1 was,53.10±11.23 mg (mean ± S.D.) The difference was found out to be statistically significant using Unpaired T test (p=0.000) (Refer Table 1 and Figure 1).

Maintenance: Three patients in the D.5 group required additional bolus doses during the intra operative period.

Total Propofol Requirement: The total requirement of Propofol in D.5 Group was 102.05 ±30.34 mg (mean ± S.D.) and in Group D1 was 54.32 ±12.37 mg (mean ± S.D.). The difference was found out to be statistically significant using Unpaired T test (p=0.000).

Study Parameter	Group D.5		Group D 1		Unpaired T test	P Value
	Mean	Std. Dev.	Mean	Std. Dev.		
Propofol (Induction) mg	98.18	23.02	53.1	11.23	8.099	0
Propofol (Total) mg	102.05	30.34	54.32	12.37	6.832	0

Table 1: Comparison of the induction dose and total dose of propofol required for inducing general anesthesia.

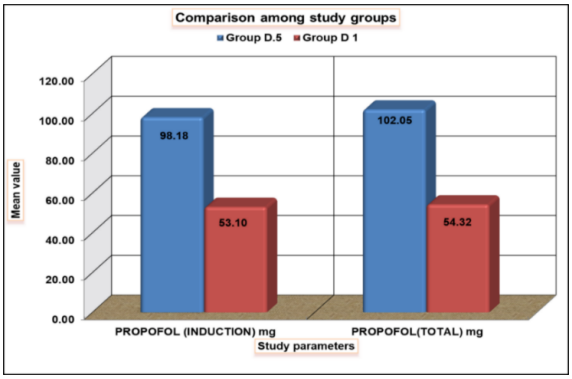

Figure 1: Comparison of the induction dose and total dose of propofol required for inducing general anesthesia.

Heart Rate: The Heart rate variations were noted at baseline, end of infusion at the 15th minute (I-15), Intubation, 5mins post intubation, Incision, at Pneumoperitoneum, 5th minute post pneumoperitoneum (P-5), P-10, P-30, P-50, P-60, at Extubation. The data collected revealed that except for baseline, the difference in all the other recordings in both the groups were significant after using Unpaired T test as shown in Table 2 and Figure 2

HR (per min)	Group D.5		Group D 1		Unpaired T test	P Value
	Mean	Std. Dev.	Mean	Std. Dev.		
Baseline	80	4.61	76.32	7.29	2.003	0.052
I-15mins	70.82	4.56	66.95	5.79	2.459	0.018
Intubation	72.27	3.99	69.41	5.06	2.085	0.043
5min	70.73	4.04	67.09	4.97	2.665	0.011
Incision	71.32	3.98	67.5	5.11	2.766	0.008
Pneumo	71.05	2.8	67	4.87	3.377	0.002
P-5	68.05	4.09	64.59	4.92	2.535	0.015
P-10	64.45	5.12	60.45	5.74	2.441	0.019
P-30	69.73	2.86	65.32	4.91	3.637	0.001
P-50	72.05	3.09	68.45	5.51	2.666	0.011
P-60	73.18	3.53	69.64	5.08	2.69	0.01
Extubation	74.77	3.77	70.5	5.03	3.189	0.003

Table 2: Comparison of Heart Rate in both the groups at different time constants.

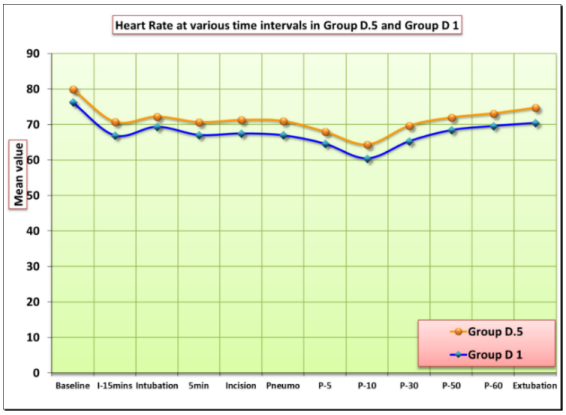

Figure 2: Comparison of Heart Rate in both the groups at different time constants.

Blood Pressure: The Mean Arterial Pressure (MAP) variations were noted at baseline, end of infusion at the 15th minute (I-15), Intubation, 5mins post intubation, Incision, at Pneumoperitoneum, 5th minute post pneumoperitoneum (P-5), P-10, P-30, P-50, P-60, at Extubation. The data collected revealed that except for baseline, P-50, P-60 and Extubation, the difference in all the other recordings in both the groups were significant after using Unpaired T test as shown in Table 3 and Figure 3.

MAP (mmHg)	Group D.5		Group D 1		Unpaired T test	P Value
	Mean	Std. Dev.	Mean	Std. Dev.		
Baseline	98.41	6.09	97.36	7.3	0.516	0.609
I-15mins	87.91	3.62	84.5	6.3	2.2	0.033
Intubation	88.05	2.65	84.59	4.38	3.165	0.003
5mins	87.09	3.22	82.91	3.31	4.248	0
Incision	87.41	3.26	83.5	3.11	4.067	0
Pneumo	86.36	3.59	82.5	4.04	3.35	0.002
P-5	85	4.15	82.09	3.82	2.42	0.02
P-10	85.77	4.69	82.86	2.85	2.486	0.017
P-30	89.32	8	85.41	2.84	2.161	0.036
P-50	87.59	2.82	86.14	2.36	1.855	0.071
P-60	88.45	2.39	87.5	2.58	1.275	0.209
Extubation	90.36	3.17	89.5	3.08	0.916	0.365

Table 3: Comparison of Mean Arterial Pressure in both the groups at different time constants.

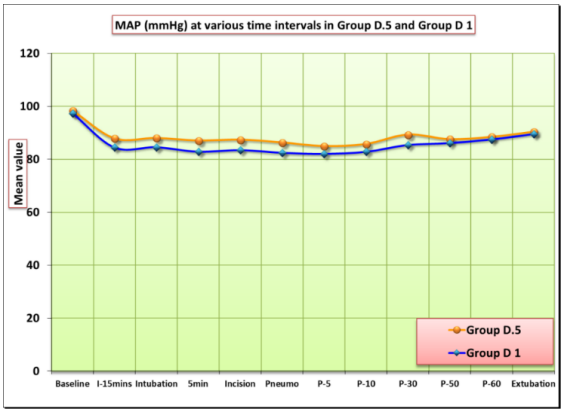

Figure 3: Comparison of Mean Arterial Pressure in both the groups at different time constants.

ECG, SPO_2, $ETCO_2$ recordings in all patients were within normal limits during the intraoperative period. BIS in all patients was maintained between 40-60 in the intra-operative period.

Time to Extubation: Time to extubation (defined as the time from stoppage of inhalational agent, Sevoflurane to adequately reversing the patient in order to be able to remove oral endo tracheal tube) was 10.73 ±1.42 minutes (mean ± S.D.) in D.5 Group, and was 11.41 ±2.59 minutes (mean ± S.D.) in D1 Group which was not statistically significant as

seen by using Unpaired T test.

Recovery Room Parameters

Heart Rate: The difference in the heart rates compared within the two groups in the recovery room at all time constants was significant as was found out by using Unpaired T test. As seen in Figure 4.

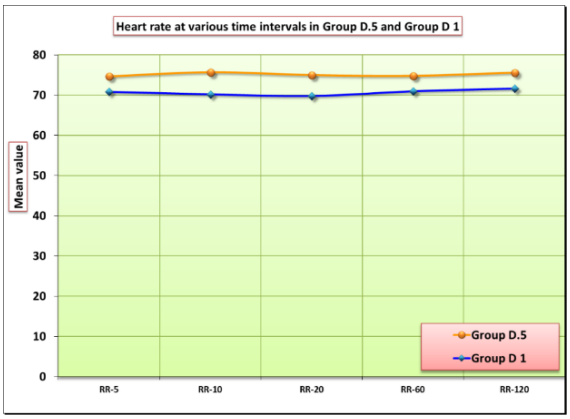

Figure 4: Heart Rate in both the groups at different time constants in the recovery room.

Blood Pressure: The difference in the Mean Arterial Pressure (MAP) compared within the two groups in the recovery room was significant (except at the 5th minute in the recovery room) as was found out by using Unpaired T test. Seen in Figure 5.

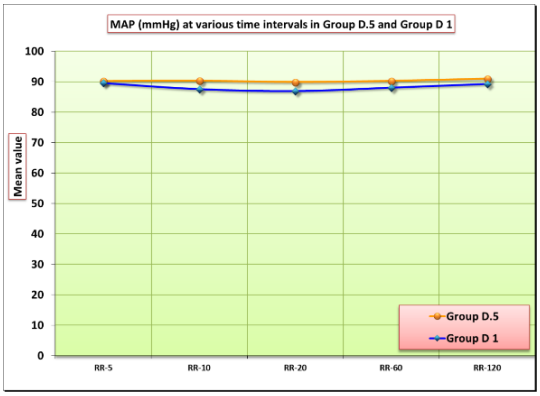

Figure 5: Comparison of Mean Arterial Pressure in both the groups at different time constants in the recovery room.

Pain Assessment and Rescue Analgesia

In the recovery room after shifting the patients from the operation theatre it was observed that 6 patients (27.3%) from the D.5 group complained of pain and had to be given 75mg of Diclofenac dissolved in 100ml of Normal saline.as against of 1patient (4.5%) from the D1 who had to be given rescue analgesic in the recovery room.

Pain was assessed using the, Numerical Rating Scale (NRS) verbal assessment (Figure 6 and Figure 7).

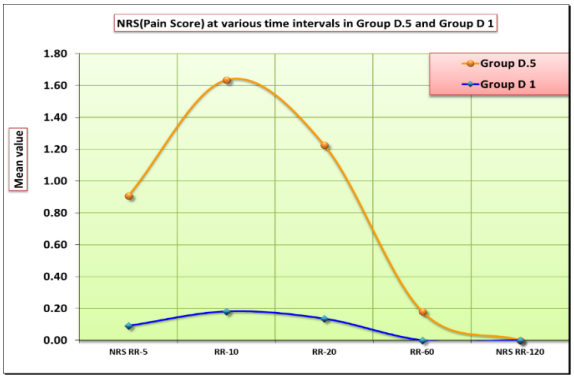

Figure 6: NRS, Pain scores of both groups.

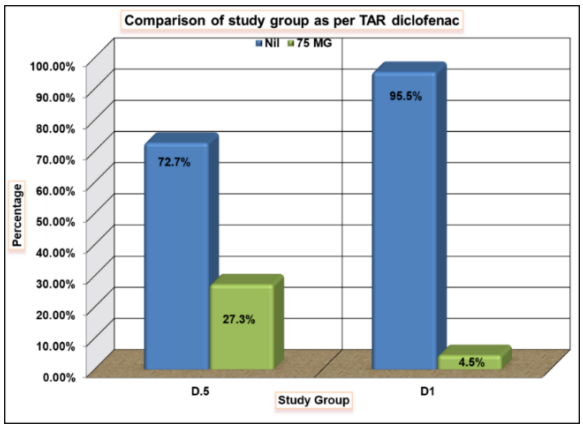

Figure 7: Total Analgesic Requirement (Diclofenac) in the post-operative recovery room in both groups.

The time to first attempt for rescue analgesic in the recovery room was found to be ranging from 5-10mins after being shifted to the recovery room.

Sedation Score: The patients in the group D1 were marginally sedated in comparison to D.5 group as seen in the table in the first five minutes in the recovery room, difference being significant (p =0.038).

The sedation was mild and patient responded to verbal commands and no intervention was required (Figure 8).

The study period ended once the patient was shifted from the recovery room at the end of his/her 2-hour observation period.

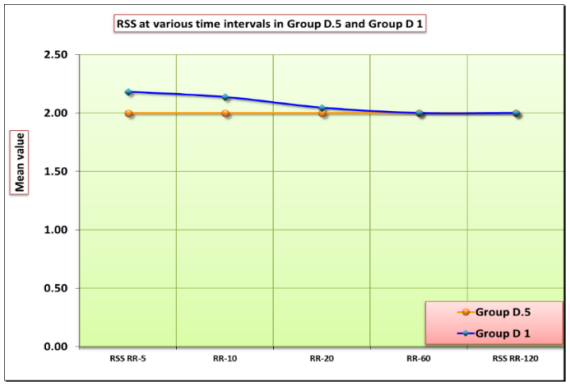

Figure 8: Comparison of Sedation in both the groups using Ramsay Sedation Score.

Discussion

The study was carried out with the primary aim of studying the effects of the 0.5mcg/kg and 1mcg/kg doses of dexmedetomidine given as a single bolus dose on the intraoperative hemodynamic changes and the secondary aims of studying the requirement of anesthetic agents, time to extubation, time to first analgesic request in the recovery room and post-operative sedation. Control group was not included in view of the fact that dexmedetomidine is an established drug used for the same purpose. Dexmedetomidine was chosen as it is a highly selective alpha 2 agonist having a significant sympatholytic property, causes dose-dependent decrease in heart rate and blood pressure. Dexmedetomidine has been used as a single bolus, infusion form with or without bolus dose to assess its effect on hemodynamic responses in patients undergoing laparoscopic surgeries. We used a single preinduction dose in short duration laparoscopic cholecystectomy to check for the attenuation of the stress response.

In a previous study, Kulkarni TM, et al. [4], in their study on patients undergoing middle ear surgeries under local anesthesia used a single bolus dose of 1mcg/kg and concluded that dexmedetomidine was the best drug out of the 'sedo-analgesics' tested producing a near bloodless microscopic surgical field with better surgeon and patient satisfaction.

Yildiz M, et al. [5], have evaluated the effect of a single pre-induction intravenous dose of dexmedetomidine 1mcg/kg on cardiovascular response resulting from laryngoscopy and endotracheal intubation, in patients undergoing minor surgeries under general anesthesia. They concluded that single dose of dexmedetomidine in preoperative period decreases blood pressure and heart rate during laryngoscopy.

Shin HW, et al. [6], evaluated the effect of pre-anesthetic dexmedetomidine, 1 μg/kg single infusion on sedation, hemodynamics, anesthetic consumption, and recovery profiles during anesthesia and concluded that it is a good anesthetic adjuvant method for general anesthesia that can attenuate the hemodynamic response to tracheal intubation and have the advantage of saving anesthetic consumption without the change of recovery profiles.

A few studies that used single bolus followed by infusion of Dexmedetomidine. Soliman R, et al. [7], demonstrated that a loading dose of 1mcg/kg over 15 min before induction and maintenance with 0.3mcg/kg/h of dexmedetomidine infusion was safe for cardiac patients undergoing laparoscopic cholecystectomy. It attenuated the changes in heart rate and blood pressure and decreased the total dose of fentanyl and end-tidal sevoflurane and the requirement for medications in high-risk cardiac patients.

Acharya G, et al. [2], in their study gave loading dose of 0.5mcg/kg over 15 mins before induction followed by an infusion of 0.3/0.6mcg/kg of dexmedetomidine and found that dexmedetomidine effectively attenuates hemodynamic stress response during laparoscopic surgery, but in a dose-dependent manner.

In other studies where only, an infusion of dexmedetomidine without a preceding bolus was used. Manne GR, et al. [3] used low dose infusion of dexmedetomidine at the rate of 0.4mcg/kg/h without any bolus dose, in patients undergoing laparoscopic cholecystectomy. They found that the drug serves as a very useful anesthetic adjuvant to control hemodynamic stress response to intubation, pneumoperitoneum and extubation. It also provides lighter sedation and reduces the postoperative analgesic requirements without any significant adverse effects.

A higher dose caused severe hypotension and bradycardia, Lawrence and De Lange have investigated the effect of a single pre-induction intravenous dose of dexmedetomidine 2μg/kg on anesthetic requirements and peri-operative hemodynamic stability in patients undergoing minor orthopedic and general surgery. They have found that the hypotension and bradycardia occurrence has been more frequently after dexmedetomidine. In a study conducted by Yildiz M, et al. [5], a single pre-induction bolus dose of 1mcg/kg was found to be safe and effective.

We found that varying doses are used in varying modes either a single bolus, with or without infusion and for various procedures from monitored anesthesia care [4] to major surgeries lasting for more than two hours (Laha et al)[11], there is no standardized recommendation on how it should be administered so we have tried here to compare two doses, 0.5mcg/kg and 1mcg/kg in surgery lasting for not more than 1-1.5hrs, laparoscopic cholecystectomy.

Dexmedetomidine potentiates anesthetic effects of all intraoperative anesthetics, regardless of the method of administration. The profound reduction in anesthetic requirement is mediated through central alpha 2 adrenergic receptors. Ghodki PS, et al. [8], have monitored the Depth of Anesthesia (DOA) using entropy in the patients undergoing laparoscopic surgeries under general anesthesia. They used a loading dose of dexmedetomidine as 1mcg/kg for 15 minutes and maintenance infusion of 0.2mcg/kg/hr and found a 62.5% reduction (0.75mg/kg) in the induction dose of propofol. They concluded that Dexmedetomidine is an effective anesthetic adjuvant that could be safely used in laparoscopy.

Laha A, et al. [9], similarly showed a decrease in the requirement of propofol for induction. In our study we found that the induction dose of propofol in Group D.5 was 98.18±23.02 mg (mean ± S.D.) and in Group D1 was,53.10±11.23 mg (mean ± S.D.) The difference was found to be statistically significant using Unpaired T test (p=0.000). We observed that dexmedetomidine significantly reduces induction dose of propofol when compared to the traditional induction dose of propofol (2 mg/kg). We observed a 65% reduction in dose of propofol in the 1 mcg/ kg group and a decrease of 30% in the 0.5mcg/kg group.

In our study, we recorded heart rate at baseline, 5mins after beginning dexmedetomidine infusion (I-5), 10th minute (I-10), 15th minute (I-15), at intubation, 1min after intubation, 5th minute after intubation, at pneumoperitoneum, P-5 (5th minute after pneumoperitoneum), P-10 (10th minute of pneumoperitoneum), P-20, P-30, P-40, P-50, P-60 and at Extubation. The heart rate control achieved in the D1 group was better as was observed in the D.5 group. The difference in both groups was significant at all point of times except at baseline, as was observed after application of the Unpaired T test (Table 2). Similar conclusions were drawn in studies conducted by Manne GR, et al. [3], where they found that a higher dose (0.4mcg/kg) dose achieved a better hemodynamic control than a lower dose of (0.2mcg/kg)

Acharya G, et al. [2], also found better hemodynamic control in 0.6mcg/kg group as against the 0.3mcg/kg group in their study.

The heart rate was well controlled at the significant time points that is intubation extubation and pneumoperitoneum. In our study we also observed considerable fall in the heart rate at end of infusion of dexmedetomidine at the 15th minute (I-15) and between P-5 and P-10. 2 patients of the D1 group and 1 patient in D.5 group experienced bradycardia which was reviewed after a single dose of rescue medication, intravenous injection of Glycopyrrolate (0.2mg).

Blood pressure was also measured at the same point constants as Heart rate and the observations were that better hemodynamics were observed in the D1 group as against the D.5 group (Figure 3). Was well controlled at significant time points of intubation and pneumoperitoneum.

It was found that except for baseline and at P-50, P-60 and at extubation the difference between both groups was statistically significant as found by the Unpaired T test (Table 3). Although the mean arterial pressure values at P-50 were par the values achieved at end of drug infusion and those at P-60 and at extubation were below baseline the hemodynamics were well controlled and we can state that even at P-50, P-60 and extubation the values were well attenuated. The possible reason being the wearing of the effect of dexmedetomidine by the end of the surgery. Hemodynamics were better achieved in the D1 group but a good control was also observed in the D.5 group (Table 3).

The Time to Extubation i.e. time recorded from stoppage of inhalational agent to adequate reversal of neuromuscular blocking agent and extubation was found to be statistically not significant by using Unpaired T test. This is suggestive that patients in the D1 group were not overtly sedated as compared to the D.5 group.

The Patients were observed for a period of 2 hours in the recovery room. Vital parameters like heart rate, blood pressure, oxygen saturation, ECG, pain assessment using NRS score and sedation assessment using Ramsay sedation score were recorded.

In the recovery room both the heart rate control and mean arterial pressure were measured at RR-5 (5th in recovery room), RR-10, RR-20, RR-30, RR-60 and RR-120 and was found that overall hemodynamic control was better in the D1 group as compared to D.5 group (Figure 4 and Figure 5).

The difference in heart rate in both groups was statistically significant using Unpaired T test.

The overall difference between both the groups was statistically significant with regards to mean arterial pressure. Probably attributable to some residual effect of dexmedetomidine in the body.

In the recovery room, 6 patients (27.3%) from the D.5 group complained of pain and had to be given 75mg of Diclofenac dissolved in 100ml of Normal saline, as against of 1patient (4.5%) from the D1 who had to be given rescue analgesic in the recovery room after grading their pain scores using the NRS (numerical rating scale) verbal assessment (Figure 6 and Figure 7). This indicates that the analgesic requirement in the 1 mcg/kg group was lesser than the 0.5mcg/kg group which was also observed in other studies including Vora KS, et al. [10], who studied the effect of 1mcg/kg bolus dose

of dexmedetomidine followed by 0.5mcg/kg continuous infusion in laparoscopic surgeries not only blunted the pressor response but also minimized analgesic requirement. Manne GR, et al. [3], also observed a reduction in requirement of analgesia in their study conducted in patients undergoing laparoscopic cholecystectomy.

In our study we observed that in the few patients requiring analgesics in the first two hours in the recovery room, the mean time of first administration of analgesic in recovery room was around approximately between the 5th and 10th minute after being shifted from operation theatre. A single dose of 75mg Diclofenac in 100 ml normal saline was sufficient for pain relief and no other analgesic was required until the study period was over in the recovery room. In our study, dexmedetomidine in a dose of 1μg/kg has provided better pain relief and sedation than at the dose of 0.5μg/kg.

Sedation was assessed in the recovery using the Ramsay Sedation score. In our study we found that patients in the group D1 were marginally more sedated in comparison to D.5 group only in the first five minutes in the recovery room (p =0.038) (Figure 8). The sedation was acceptable and patient responded to verbal commands and no intervention was required. For the major period of their stay in the recovery room, there was no statistically significant difference in the sedation scores.

Hall JE, et al. [11] in their research have determined the safety and efficacy of two small dose infusions (0.2 and 0.6mcg/kg) of dexmedetomidine by evaluating sedation, analgesia, cognition, and cardiorespiratory function. Dexmedetomidine infusions have resulted in reversible sedation and mild analgesia without cardiorespiratory compromise.

We observed that dexmedetomidine in a dose of 1μg/kg could effectively attenuate the vasopressor response of laryngoscopy, and intubation and the sympathoadrenal response occurring with pneumoperitoneum. This is in agreement with other studies demonstrating similar favorable hemodynamic response to stimulation during laryngoscopy with dexmedetomidine.

Dexmedetomidine has reduced duration of mechanical ventilation compared with midazolam and has improved patients' ability to communicate pain compared with midazolam and propofol as demonstrated in the MIDEX and PRODEX trials respectively [12]. Dexmedetomidine allows eliminating Benzodiazepines from the pre-operative induction agent requirements and this may be desirable given unfavorable recovery characteristics (poor swallowing/pharyngeal muscle weakness, pharyngeal clearance and laryngeal protection) associated with Midazolam and similar benzodiazepines [13]. In this era of ERAS, it would be very useful to have Dexmedetomidine in our armamentarium with its proven benefits of allowing reduction of the doses of induction agents, opioids and analgesics, a good hemodynamic profile and excellent recovery when used in appropriate doses in suitable clinical settings.

Conclusion

Laparoscopic surgeries are associated with pressor stress response to the pneumoperitoneum which can be blunted by using many drugs one of them being, dexmedetomidine. A single preinduction bolus dose of 1mcg/kg body weight is adequate to blunt the stress response in shorter duration surgeries, like laparoscopic cholecystectomy. It also significantly reduces the requirement of induction dose of intravenous anesthetic agent, propofol. It also doesn't delay the time to extubation, reduces analgesic requirement in the post-operative period and doesn't cause overt sedation. A dose of 0.5mcg/kg body weight of dexmedetomidine also achieves the similar effects but to a lesser extent as compared to 1mcg/kg body weight. Finally, proper patient selection, exercising caution in patients with low baseline heart rates due to any reason, monitoring vital parameters and being watchful for bradycardia and hypotension can help us use this drug for better patient care.

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Conflict of Interest

There was no conflict of interest.

Declarations

Ethical approval: Ethical approval from the Hospital Institutional Ethics Committee was obtained prior to initiation of the research work. This study was approved by the Ethics Committee under submission number: IEC/2017/TH/09, Dated: 31/07/2017. All procedures followed were in accordance with the ethical standards of the responsible committee.

Informed consent: Informed consent was obtained from all patients included in the study.

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