The Effects of Preanesthetic Single Dose Dexmedetomidine on Induction, Haemodynamic and Cardiovascular Parameters in Laparoscopic Cholecystectomy

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ABSTRACT

Introduction: Dexmedetomidine is an α2 adrenergic receptor agonist with high selectivity for the α2 receptor. It is a good preanesthetic medication for surgical procedures. The purpose of this study was to investigate the effects of a single IV dose of dexmedetomidine on hemodynamics, and cardiovascular parameters in patients undergoing elective laparoscopic cholecystectomy.

Material and Methods: This prospective study was done in the department of Anesthesiology at Osmania General Hospital, Afzalgunj, Hyderabad. Fifty patients were divided into two groups of 25 each. One group (test group) received dexmedetomidine and the other group (control group) received normal saline at predetermined time intervals. The heart rate, systolic, diastolic mean arterial blood pressures were compared for both groups.

Results: The systolic pressures were maintained and diastolic pressures were on lower side in the dexmedetomindine group as compared to control group. The hemodynamics were maintained stable in dexmeditomidine group when compared to control group.

Conclusion: It can be concluded from this study that dexmedetomidine provides a good haemodynamic control when used in such procedures with good monitoring.

Keywords: Dexmedetomidine, Preanesthesia, Induction of Anesthesia, Intraoperative Vitals Monitoring

INTRODUCTION

Dexmedetomidine is an α2 adrenergic receptor agonist with high selectivity for the α2 receptor. The α2 adrenergic mechanism causes dose-dependent reduction in blood pressure (BP) and heart rate (HR). Dexmedetomidine exhibits analgesic, anxiolytic, and sedative effects with intravenous (IV) administration. The α2 adreno-receptors give rise to the hypnotic response. These properties make dexmeditomidine an ideal preanesthetic medication for surgical procedures.[1]

The α2 agonists, including clonidine and dexmedetomidine, decrease central sympathetic outflow and modify intraoperative cardiovascular responses to surgical stimuli and laryngoscopy. The reduction in tachycardia, hypertension, and sympathetic activity may be of benefit in patients at risk of myocardial ischemia.[2]

Dexmeditomidine is proved to have antinociceptive effects and reduces the neurohumoral properties.[1]

The purpose of this study was to investigate the effects of a single IV dose of dexmedetomidine administered 10 minutes before induction of anesthesia on hemodynamics, and cardiovascular parameters in patients undergoing elective laparoscopic cholecystectomy.[2-4]

During laparoscopic cholecystectomy, CO_2 pneumoperitoneum results in ventilatory, respiratory haemodynamic changes. Pneumoperitoneum decreases thoracopulmonary compliance.

Peritoneal insufflation induces alterations of haemodynamics, characterized by decrease in cardiac output, elevation of arterial pressure, and increase of systemic and pulmonary vascular resistances. Haemodynamic changes are accentuated in high-risk cardiac patients.[5,6]

The pathophysiologic haemodynamic changes can be attenuated or prevented by optimizing preload before pneumoperitoneum and by vasodilating agents, α_2-adrenergic receptors agonists, high doses of opioids, and β-blocking agents.[6]

Study aimed to see the efficacy of preanesthetics ingle dose dexmedetomidine on induction, haemodynamic and cardiovascular parameters

MATERIAL AND METHODS

The present study was undertaken in department of Anesthesiology at Osmania General Hospital, Afzalgunj, Hyderabad, during the period of 2011- 2014.

Selection of patients

After approval from the institutional ethics committee and written informed consent from the patients, a randomized study was conducted on 50 adult patients (ASA I and II)

Study was undertaken in patients planned for elective laparoscopic cholecystectomy surgery. Patients were selected between 20 to 55 years who had no systemic disorders. They were divided into 2 groups of 25 each and allocated randomly to Group D(dexmeditomedine group), dexmedetomidine 1μg/kg and group P(control group), 0.9%

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normal saline.

All the patients were thoroughly investigated. All patients were explained about the procedure and its complications and informed consent was obtained. There were no significant differences in patient height, weight, age and duration of surgery.

Exclusion criteria

1. Patients unwilling for the study
2. Hypertension and diabetes mellitus
3. Obese with BMI > 30
4. Known case of coronary artery disease or cerebrovascular disease
5. Known case of pre-operative hypotension
6. Surgeries converted to open cholecystectomy

Monitors used Philips multi parameter

NIBP
Pulse oximeter
$EtCO_2$
ECG
Urine out put
Patients were allocated randomly into 2 groups.
GROUP D: Received dexmedetomidine 1 µg/kg
GROUP P: Received 0.9% normal saline

Anaesthesia machine was checked resuscitation equipment and drugs were checked and kept ready, before undertaking the procedure.

Procedure

On arrival to operation theatre, routine monitors (ECG, Pulse oximetry, NIBP) attached and baseline vital parameters like heart rate, mean arterial blood pressure (MAP) and arterial oxygen saturation (SpO_2) were recorded.

An intravenous line with 18G was secured. All patients were premedicated with Fentanyl 2 µg/kg, Glycopyrrolate 4µg/kg, Ondansetron 15µg/kg, Ranitidine 1mg/kg given slowly intravenously, 20 minutes before induction.

Patients in group D Dexmedetomidine received 1 µg/kg by slow IV infusion for 10minutes before induction. All patients were preoxygenated with 100% O_2 for 3 minutes and were induced with thiopentone sodium 5mg/kg I.V

Intubation was facilitated by using Vecuronium bromide 0.1mg/kg. The lungs were ventilated with 100% oxygen for 180 seconds. Intubation was achieved with an appropriate size oral cuffed, portex endotracheal tube by the aid of Macintosh laryngoscope blade.

CO_2 was insufflated into the peritoneal cavity (at a rate of 2 lit/min) to create pneumoperitoneum. Intra-abdominal pressure was restricted to 14mm Hg throughout the laparoscopic procedure. The patients were mechanically ventilated to keep $EtCO_2$ between 35-40 mm Hg.

Anaesthesia was maintained with Vecuronium bromide and intermittent positive pressure ventilation with nitrous oxide and oxygen in the ratio of 50: 50 with 0.5% Isoflurane using circle absorber system connected to the Boyle's anesthetic workstation.

Patients were observed for any adverse events during postoperative period in post anaesthesia care unit.

1. Patients under study were not given any benzodiazepines on the day of procedure
2. Intra-abdominal pressure was restricted to 14 mm Hg
3. $EtCO_2$ was maintained below 35 mm Hg
4. Nitroglycerin and metoprolol were kept as rescue drugs
5. Atropine was kept ready to counter any bradycardia, and inotropes were kept ready to counter untoward hypotension

The parameters recorded were Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Pulse oximetry and $EtCO_2$

The recordings were noted at various intervals as detailed below, from the study conducted

1. Pre-operatively i.e. before premedication (basal line value)
2. After Induction
3. After Intubation

At 15, 30, 45, 60, Extubation and Post-op first hour

At the end of surgery, neuromuscular blockade was reversed with neostigmine 60 µg/ kg and glycopyrrolate 10µg/kg intravenously. After satisfying the extubation criteria, trachea was extubated and patients were shifted to post-anesthesia care unit (PACU).

STATISTICAL ANALYSIS

The results were expressed as Mean+/- S.D. Mean and standard deviation were calculated for all the quantitative variables using SPSS statistical software. Comparison between two groups at a time (inter-group comparison) was done using Student's unpaired t-test. The statistical analysis was done using, student unpaired t test and SPSS software. P <0.05 was considered statistically significant, value < 0.01 was considered highly significant, value > 0.05 was considered insignificant

RESULTS

In this study, there was no significant difference in age, gender, weight and duration of surgery for both groups.

In this study, there was no significant difference in age, gender, weight and duration of surgery for both groups. Both the groups of the patients were comparable in age (table-1).

Heart rates were on lower side in dexmeditomidine group during intubtion and pneumoperitoneum compared to control group. The difference in heart rate was statistically highly significant in the groups during intubation with lower rates in the dexmeditomidine group when compared to the placebo group. There was no statistically significant difference in heart rate between both the groups in preop and post op period. Hemodynamics were maintained stable in dexmeditomidine group when compared to control group (table-2).

There was statistically significant difference in systolic blood pressure between both groups during intubation and intraoperative period. There was no statistically significant difference in systolic blood pressure between both the groups in post op period. Systolic blood pressures were maintained stable in dexmeditomidine group during intubation and

intraoperative period. Control group showed rise in systolic blood pressure during intubation, other intraoperative period when compared to dexmeditomidine group (table-3).

There was statistically significant difference in diastolic blood pressure between both groups during intubation and other intraoperative periods. Diastolic blood pressures were on lower side in dexmedetomidine group than in control group during intraoperative period. There was no significant difference in DBP between both groups during preoperative and postoperative period (table-4).

According to the un-paired t test analysis, there was a significant difference between the two groups during intraoperative period (table-5).

MAP in group D was on lower side when compared to group P during intubation and intra operative period. There was rise in MAP in group P during intubation, and intraoperative period.

There was no significant difference in mean arterial pressure between two groups during the pre-op period and the post-op period.

Mean arterial pressure and heart rate in group D was comparatively less than group P. The fall in blood pressure

Variable	Group D		Group P		P value	Significance
	Mean	SD	Mean	SD		
Age	40.5	11.35	42.56	9.3	0.4	NS
Gender (M/F)	13/12		12/13			
Weight	55.24	10.16	56.34	9.5	0.6	NS
NS - not significant						

Table-1: Demographic details

Heart rate Mean +/- SD	Group D		Group P		Statistical significance	
	Mean	SD	Mean	SD	P Value	Remarks
Pre op	81.17	10.80	83.68	8.37	0.30	NS
After induction	69.71	7.96	78.24	11.51	< 0.01	HS
After intubation	76.54	7.80	96.76	8.84	<0.01	HS
15min aft pnp	75.17	8.98	94.73	11.43	<0.01	HS
30min	76.54	8.70	91.72	6.41	< 0.01	HS
45min	76.33	8.35	94.60	7.47	< 0.01	HS
60min	76.63	6.61	92.84	8.06	< 0.01	HS
Extubation	84.67	8.66	93.08	10.14	<0.01	HS
Post op after 1 hour	90.44	6.65	88.17	8.55	0.40	NS
NS - not significant, HS – highly significant						

Table-2: Changes in heart rate (Mean ± SD)

Mean SBP± SD	Group D	SD	Group P	SD	P	Remarks
Pre op	130.00	5.62	134.6	8.24	0.06	NS
Induction	98.19	6.68	117.00	6.55	0.01	HS
Intubation	121.46	6.53	130.80	5.46	<0.01	HS
Pnp15min	121.92	3.57	132.08	4.24	0.01	HS
30min	124.81	3.38	128.04	3.27	0.01	HS
45min	122.65	4.52	129.08	4.27	<0.01	HS
60min	122.31	4.56	124.23	2.63	0.05	S
Extubation	132.00	3.94	134.08	4.18	0.01	HS
Post op after 1 hour	123.38	5.43	122.80	3.08	0.68	NS

Table-3: Changes in SBP (Mean ± SD)

Mean DBP± SD	Group D	SD	Group P	SD	P
Pre op	83.08	8.53	89.92	6.85	0.08
Induction	55	8.52	80.81	7.74	0.01
Intubation	74.35	7.31	83.81	5.58	0.001
Pnp15min	76.12	7.79	86.77	5.09	<0.01
30min	75.96	9.23	84.96	5.75	<0.01
45min	74	8.0	84.23	5.35	<0.01
60min	71	11.46	81	6.51	<0.01
Extubation	74	6.81	93.88	8.91	0.01
Post op after 1 hour	74.92	9.47	75.77	9.11	0.74

Table-4: Changes in DBP(Mean ± SD)

Mean arterial pressure ± SD	Group D		Group P			
	Mean	SD	Mean	SD	P Value	Remarks
Pre op	99.42	7.01	102.48	8.16	0.16	NS
Induction	65.17	7.48	92.68	6.56	< 0.01	HS
Intubation	89.79	5.39	99.56	5.08	< 0.01	HS
15min	92.13	5.57	101.32	4.02	<0.01	HS
30 min	92.17	6.84	99.6	4.19	<0.01	HS
45min	86.5	7.64	99.36	4.5	<0.01	HS
60 min	87.3	7.94	95.56	4.87	< 0.01	HS
Extubation	90.79		107.4		<0.01	HS
Post op after 1hour	91.44	6.56	90.79	6.74	0.06	NS
NS - not significant, HS - highly significant						

Table-5: Changes in Mean Arterial Pressure (Mean ± SD)

and heart rate with induction was more in group D than group P, might be due to the synergistic effect with propofol, and dexmedetomidine as both cause hypotension. But intubation response also was less in group D.

Intra operative period was uneventful and mean arterial pressures and heart rate were less in group D than Group P.

In post-operative period, haemodynamically there was no significant difference between both groups.

DISCUSSION

In this study, the effects of single dose dexmedetomidine on haemodynamics in patients undergoing laparoscopic cholecystectomy were studied. Dexmedetomidine is a highly selective alpha 2 adrenergic agonist that has sedative, anxiolytic, analgesic, sympatholytic and antihypertensive effects giving more favorable outcome in the test group (Group D) in reducing and maintaining the haemodynamics as compared to group P. Activation of receptors in the brain and spinal cord level inhibits neuronal firing, thereby causing hypotension, bradycardia, sedation and analgesia. Generally presynaptic activation of alpha 2 adrenergic receptors inhibits the release of norepinephrine.[7]

Decrease in production of catecholamines with pneumoperitonium has reduced the haemodynamic fluctuations. Other action of dexmedetomidine is postsynaptic activation of alpha 2 adrenergic receptors in the central nervous system that inhibits sympathetic activity and therefore can decrease blood pressure and heart rate. Combination of these effects produces sedation and anxiolysis. Dexmedetomidine does not appear to have any direct effect on heart. Effects on haemodynamics are mediated by inhibition of central sympathetic outflow. In laparoscopic surgery, CO_2 is routinely used to create pneumoperitoneum. Elevated intra-abdominal pressure induced by pneumoperitoneum and CO_2 itself produce some adverse effects on the cardiovascular system.[4,5]

Immediately after pneumoperitoneum, plasma level of norepinephrine, epinephrine and plasma renin activity is increased. Increased catecholamine level activates the renin-angiotensin aldosterone-system (RAAS) leading to some characteristic haemodynamic alterations such as decreased cardiac output (25-35%), elevated arterial pressure, increased systemic / pulmonary vascular resistance.

Laparoscopic cholecystectomy is performed in reverse Trendelenburg position. This position causes diminished venous return, which ultimately leads to further decrease in cardiac output.

Dexmedetomidine significantly reduces the release of catecholamines especially norepinephrine release, thereby, attenuating the increase in systemic vascular resistance. Dexmedetomidine improves intraoperative and postoperative haemodynamic stability by stabilizing the changes in arterial pressure, heart rate and cardiac output. Our study confirms that haemodynamic changes, mean arterial pressure was on low in dexmeditomidine group during intubation 89.79± 5.39 compared to control group 99.56 ±5.08, the heart rate 76.54±7.80 in group D when compared to 96.76± 8.84 in group P during intubation.

Thus haemodynamics (MAP, HR) are attenuated by dexmedetomidine infusion during laparoscopic cholecystectomy. In several study reports, dexmedetomidine infusion rates ranging from 0.1 to 10-µg/ kg-1 hr-1 have been used. The studies with higher infusion rates had more incidences of adverse effects like hypotension and bradycardia. Dexmedetomidine causes sedation but it does not cause delay in the recovery time.[8]

To conclude, dexmedetomidine reduces the elevation of mean arterial pressure and heart rate during intubation and intraoperative period and thereby improves haemodynamic stability during laparoscopic surgery.[2,3]

CONCLUSIONS

Laparoscopic cholecystectomy is associated with lot of haemodynamic changes due to pneumoperitonium and neuro humoral factors. Dexmedetomidine being an α2 receptor agonist decreases or inhibits the release of the catecholamines and vasopressin in response to pneumoperitonium. As it has sedative, anxiolytic, and analgesic properties, it provides a good haemodynamic control during the procedure. Dexmeditomidine attenuates intubation response and haemodynamic perturbations due to pneumoperitoneum giving better hemodynamic stability. It can be concluded that dexmedetomidine provides a good haemodynamic control when used in such procedures with good monitoring.

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