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Effects of Dexmedetomidine on Intraoperative Hemodynamics and Propofol Requirement in Patients Undergoing Laparoscopic Cholecystectomy

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ABSTRACT
During propofol-based anesthesia for laparoscopic cholecystectomy, dexmedetomidine provides

- more stable intraoperative heart rate
- more stable intraoperative SBP,DBP and MAP
- reduces recovery time and extubation time
- reduces propofol requirement for induction as well as maintenance.

The present study confirms that dexmedetomidine provides more stable intraoperative hemodynamics and reduces the requirement of propofol for induction as well as maintenance, without compromising the recovery profile. Furthermore studies need to be conducted in search of more adjuvants to reduce hemodynamic response of pnemoperitoneum.

I. INTRODUCTION:

properly conducted laparoscopic surgery , is one of the most frequently performed surgery due to myriad benefits such as reduced trauma to tissues, reduced morbidity , mortality , fast recovery and less hospital stay, with overall reduced cost of healthcare[1,2]. Despite these benefits, laparoscopic surgery poses a significant effect on cardio respiratory and other systems. It is due to combined effects of altered patient positioning(a surgical need), pneumoperitoneum and pharmological effect of CO2. Pneumoperitoneum creation (Increased Intra-abdominal pressure) is immediately followed by an increased plasma renin activity and increase in plasma level of norepinephrine and epinephrine[3].Thus renin-angiotensin-aldosterone system is also activated. All these effects lead to cardiovascular, respiratory & other queasy effects.[4].In a single sentence we can say that laproscopic surgery is minimal invasive surgery with maximum physiological change

Various agents such as isoflurane[3], propofol, β-blockers[5], and antihypertensives [6,] α_2-adrenergic agonist clonidine [7]have been used to blunt hemodynamic changes anxiolysis, and attenuate neurohumoral "stress response"of major surgery[10]

Recently Dexmedetomidine [11], an another highly selective α_2-adrenergic has been shown promising hypnotic, sedative, anxiolytic, sympatholytic, and analgesic properties without producing significant respiratory depression[12]. It also diminishes intra-operative requirement of analgesics[14] and anesthetics (including propofol)[14-18].

The anaesthetic depth can be measured and controlled by Bispectral index system(BIS) ranging from 100 to 0. BIS decreases with increasing depth of anaesthesia and adequate level of anesthesia is achieved with BIS ranging from 40 to 60.

we have undertaken the present study to assess the role of dexmedetomidine in hemodynamic stability and its correlation with instant BIS, in the patient of our locality.

II. MATERIAL AND METHOD:

The present study was conducted in the department of Anaesthesiology at Nalanda Medical College and Hospital, Patna on 100 patients of either sex scheduled for elective laparoscopic cholecystectomy, from December 2018 to March 2020, after obtaining approval from the Institutional Scientific and Ethical Committee.

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Inclusion Criteria

Patients scheduled for elective laparoscopic cholecystectomy under general anaesthesia

- Aged between 20 and 50 years
- Body weight between 40 and 70 kg
- ASA physical status I or II

Exclusion Criteria

- Patients on any drug treatment which may interfare with dexmedetomidine, or Patients on chronic β-blocker therapy
- Patients with H/O allergy to egg proteins and any drugs
- Obese ,Pregnant or lactating women
- Patients with H/O hepatic, renal, cardiac, neurological, respiratory or metabolic disease
- Patients with H/O alcohol or drug abuse
- Patients who were unwilling or unable to comply with the protocols
- Patients with anticipated difficult airway

Preparation of the Patient

- Detailed history taking, thorough clinical examination , reviewing laboratory investigation, and pre-anaestheticcheck up of the patients were taken up one day prior to schedule date. patients were explained about the study and informed consent was obtained, Patients were advised 12 hour period of absolute fasting and were premedicated with injection ranitidine 50 mg iv and injection ondansetron 4 mg iv before induction of anaesthesia. Patients under the study were randomly divided in by chit and box method in two groups of 50 patients eachi.e Group D(n=50) and Group N (n=50) .

Group D(n=50) – Each patients in this group was received dexmedetomidine preloading 1 µg/kg IV in 10 minutes followed by 0.6 µg/kg/hour IV continuous infusion.

Group N (n=50) – In this group patient was given normal saline 0.9 % IV preloading followed by infusion at similar rates.

Procedure.

Infusion was prepared by a separate anesthetist in a separate room according to the group allotted. To prepare the infusion, dexmedetomidine 1 mL containing 100 µg of the drug was diluted up to 100 mL with normal saline resulting in the final concentration of 1 µg/mL. Dexmedetomidine or normal saline infusion was given through a syringe infusion pump. Depending on patient`s weight, the infusion pump was set to deliver the targeted infusion rate. Thus, the syringe and volume of prepared solution were similar in both groups, and the assessor as well as the patient was unaware of the group. Decoding of blinding to the assessor was done only at the time of tabulation and result analysis.

A wide bore 18Gi.v. cannula was inserted for giving the i.v. fluids, and another line was taken up for the infusion pump. After taking the patient on the operation table, a multipara monitor with BIS module was attached, and the baseline heart rate (HR), systolic blood pressure (SBP), Diastolic blood pressure (DBP) and mean arterial pressure (MAP) were noted down (T – Ctrl).Test drug preloading was done over 10 min, and then, infusion pump was set to deliver targeted intraoperative infusion rate which was continued till removal of scope from the abdominal cavity. HR, SBP,DBP and MAP were noted down after

drug preloading (T – Load).Five minutes after starting the drug infusion at targeted intraoperative rate, pre-oxygenation was performed for 3 min. Patients were induced with injection propofol intavenous infused slowly 20 mg (2 mL) every 5 s till BIS value reached below 60 followed by i.v. injection vecuronium 0.1 mg/kg. PR, SBP, DBP and MAP were noted just before intubation (T – Ind). Patient was ventilated with 100% O2 for 3 to 5 minutes. Patient was intubated with appropriate size-cuffed endotracheal tube after direct laryngoscopy. Tube position was confirmed by auscultation and ETCO2. PR,SBP,DBP and MAP were recorded just after intubation (T – Int). Anesthesia was maintained with O2:N2O (50:50), injection propofol i.v. infusion titrated to maintain BIS value 55–60 and injection vecuronium i.v.as a muscle relaxant as per muscle requirement. Intra-abdominal pressure was maintained between 12 and 14 mm Hg throughoutthe laparoscopic procedure. The patients were mechanically ventilated using close circle system to keep the ETCO2 between 35 and 45 mm Hg.

After removal of scope from abdominal cavity, drug infusion and anesthetic agents were stopped .We carried out Reversal and extubation by conventional methods.

All patients were monitored intra-operatively for vital parametersat regular intervals. PR, SBP, DBP and MAP were recorded at surgicalincision (T – Inc), just after insufflation (T – Ins), 15 min afterinsufflation (T – Ins15), 30 min after insufflation (T – Ins30),at ex-sufflation (T – Exs), just after reversal (T – Rev), andjust after extubation (T – Ext).

We considered extubation as an end part of our study. Time to achieve BIS value 80 (recovery time) and time to extubate trachea (extubation time) from stoppage of anesthetic agents were also noted their own language

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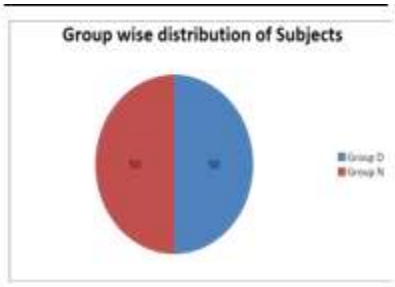
III. OBSERVATIONS

The present study "Observational study of effects of Dexmedetomidine on Intraoperative Haemodynamics and Propofol requirement on BIS guided adequate anaesthesia in patient undergoing Laproscopic cholecystectomy" was conducted amongst diagnosed cases of patients. The study comprised of 50 patients of Group D (Dexmedetomidine 1µg/ml (n=50)) between the age group of 20-50 years , study comprised of 50 patients of Group N (Normal saline 0.9% n = 50) between the age group of 20-50 years.

Various data and their analysis as obtained are given below:

Table -1(Group wise distribution of Subjects)

Sr. N0	Group	Description	No. of patients	Percentage
1	Group D	Dexmedetomidine 1µg/kg by 0.6 microgram/kg/hr	50	100%
2	Group N	Normal saline (0.9%)	50	100%

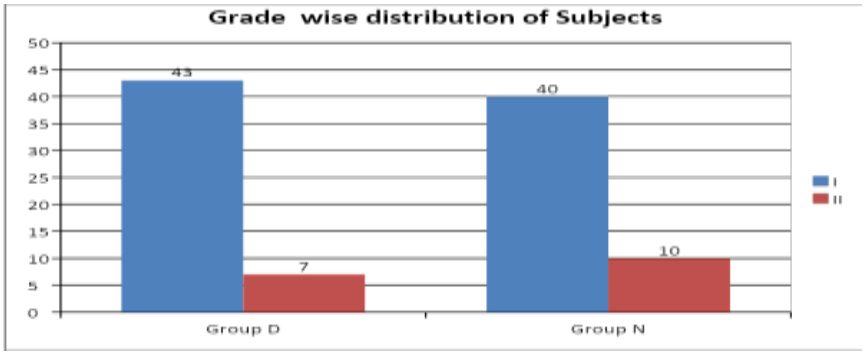


Graph 1 Shows Group wise distribution of Subjects.

Table-2 Grade wise distribution of Subjects

ASA Grade	Group D		Group N		P. Value
	N0.	%	N0.	%	
I	43	86%	40	80&	1.000
II	7	14%	10	20&	

According to Table no.-2 In Group D there were 43 (86%) grade I and 7 (14%) were grade II and group N had 40 (80%) grade I and 10 (20%) had grade II subjects



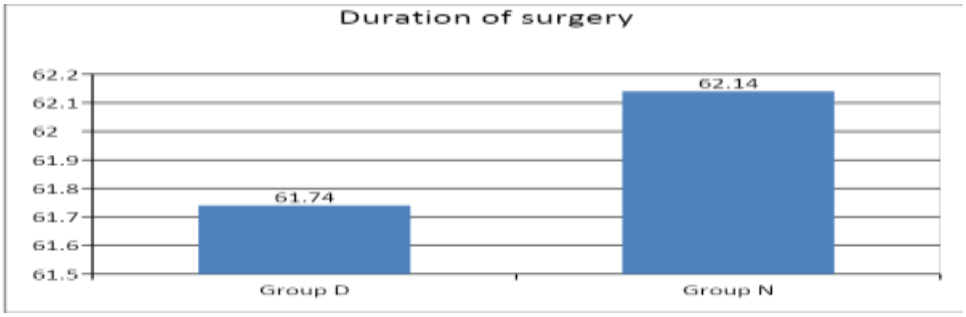
Graph 2 Shows Grade wise distribution of Subjects

International Journal Dental and Medical Sciences Research
Volume 3, Issue 4, July-Aug 2021 pp 148-157 www.ijdmsrjournal.com ISSN: 2582-6018

Table – 3 (Duration of surgery)

	Group D	Group N	't' test	P. Value
	Mean ± S.D	Mean ± S.D		
Duration of surgery	61.74±8.32	62.14±7.93	-.240	.811

The mean time to duration of surgery in Group D was 61.74±8.32 min and Group N was 62.14±7.93min. On comparing the value of duration of surgery in group D & Group N the significant difference was not found. (P. Value = 0.811).



Graph 3 Shows Duration of surgery

Table -4 Mean Heart Rate in study Groups at different time interval

	Group D		Group N		't' Value	P. Value
In Min & Hr	N	Mean±SD	N	Mean±SD		
T-Ctrl	50	87.24±7.12	50	90.26±3.86	3.121	0.127
T-Load 10 min	50	72.54±7.53	50	91.18±4.16	-17.339	< 0.0001
T-Ind	50	70.80±6.63	50	87.42±5.66	-16.781	< 0.0001
T-Int	50	76.54±8.27	50	98.02±0.820	-18.017	< 0.0001
T-Inc	50	75.92±8.95	50	95.82±2.36	-15.768	< 0.0001
T-Ins	50	79.16±9.50	50	98.04±0.832	-14.309	< 0.0001
T-Ins 15 min	50	81.54±9.79	50	96.08±2.21	-10.842	< 0.0001
T-Ins 30 min	50	79.44±9.40	50	94.52±10.75	-7.964	< 0.0001
T-Exs	50	75.78±8.23	50	92.98±9.85	-10.144	< 0.0001
T-Rev	50	86.70±6.51	50	105.06±7.40	-13.010	< 0.0001
T-Ext	50	85.78±7.98	50	101.76±8.66	-9.453	< 0.0001

In the group D (Dexmedetomidine), the basal value of mean heart rate is 87.24±7.12 bpm and we observed a decrease in mean heart rate which is 70.80±6.63 bpm from basal value at T-end. In the group N (Normal saline), the basal value of mean heart rate is 90.26±3.86 bpm and we observed a decrease in mean heart rate which is 87.42±5.66 bpm . The mean heart rate from basal to T-ctrl, T-Load 10 min, T-Ind, T- Int, T – Inc, T-Ins, T-Ins 15 min, T-Ins 30 min, T-Exs, T-Rev, & T-Ext recording is statistically significant between the groups. P. Value is <0.005.

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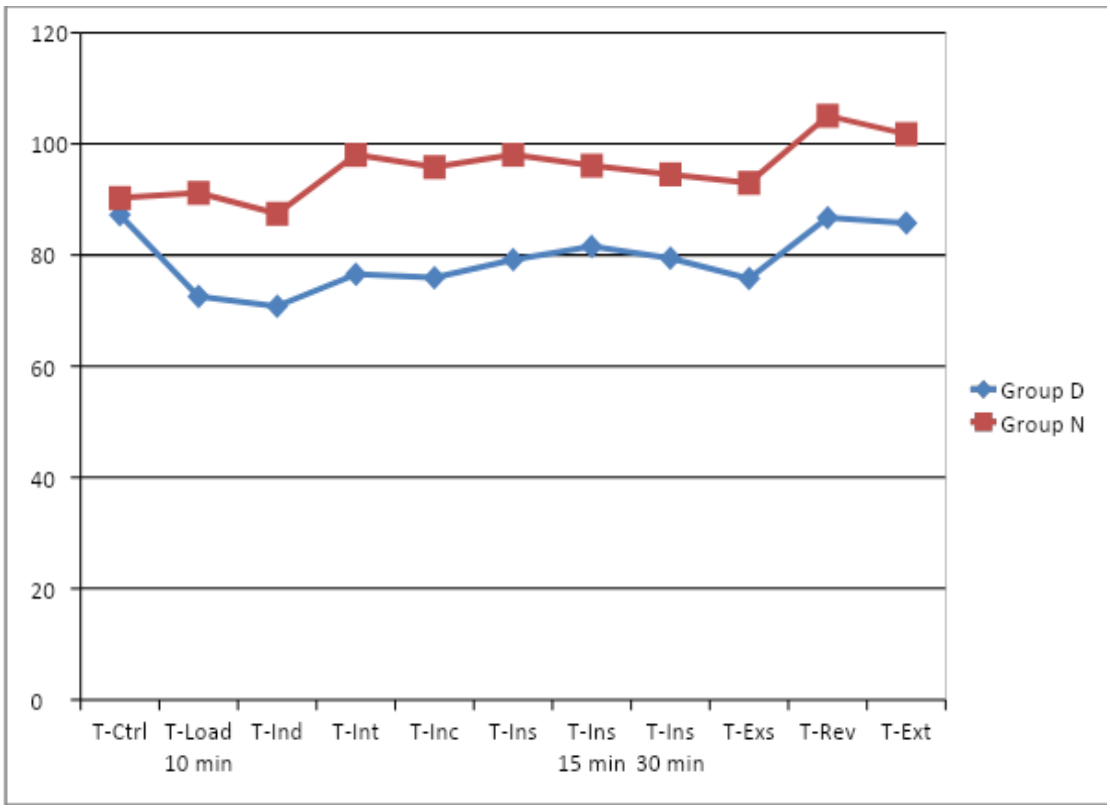


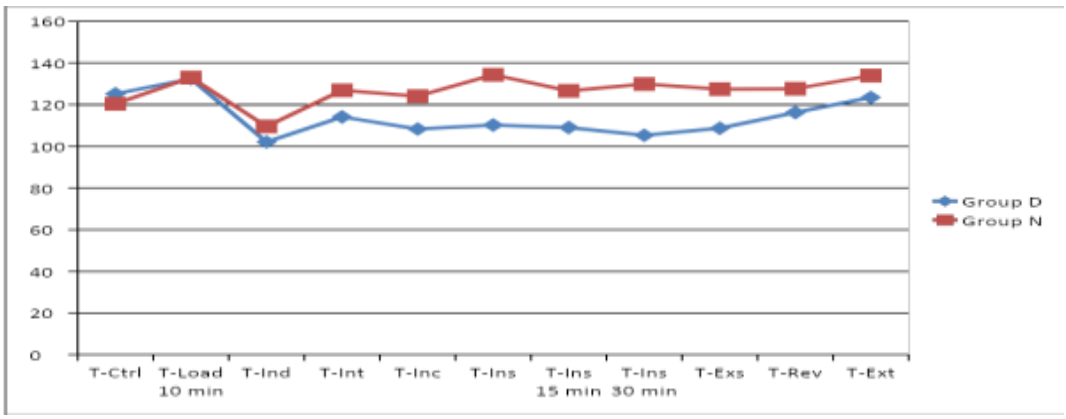
Graph 4 Shows Mean Heart Rate in study Groups at different time interval

Table -5 Systolic blood pressure in study Groups at different time interval

	Group D		Group N		't' Value	P. Value
In Min & Hr	N	Mean±SD	N	Mean±SD		
T-Ctrl	50	125.22±13.62	50	120.44±14.87	1.639	.108
T-Load 10 min	50	132.46±6.26	50	133.00±6.20	-1.717	.092
T-Ind	50	102.09±6.27	50	109.56±10.00	1.721	< 0.001
T-Int	50	114.13±15.32	50	126.88±8.48	1.379	< 0.001
T-Inc	50	108.31±10.23	50	124.08±8.17	1.607	< 0.001
T-Ins	50	110.19±11.49	50	134.34±5.08	3.212	< 0.001
T-Ins 15 min	50	109.02±10.61	50	126.64±8.76	1.209	< 0.001
T-Ins 30 min	50	105.29±13.67	50	129.92±7.37	2.189	< 0.001
T-Exs	50	108.68±10.51	50	127.46±11.59	2.197	< 0.001
T-Rev	50	116.21±15.69	50	127.64±14.92	3.262	< 0.001
T-Ext	50	123.49±6.09	50	133.96±15.64	1.177	< 0.001

In the group D (Dexmedetomidine), the basal value of systolic blood pressure is 125.22±13.62 mmHg and we observed a increase in systolic blood pressure which is 132.46±6.26 mmHg from basal value at T-Load 10 min. In the group N (Normal saline), the basal value of systolic blood pressure is 120.44±14.87 mmHg and we observed a increase in systolic blood pressure which is 134.34±5.08 mmHg . The systolic blood pressure from T-ctrl, T-Load 10 min, T-Ind, T- Int, T – Inc, T-Ins, T-Ins 15 min, T-Ins 30 min, T-Exs, T-Rev, & T-Ext, recording is statistically significant between the groups. P. Value is <0.005.

International Journal Dental and Medical Sciences Research
Volume 3, Issue 4, July-Aug 2021 pp 148-157 www.ijdmsrjournal.com ISSN: 2582-6018



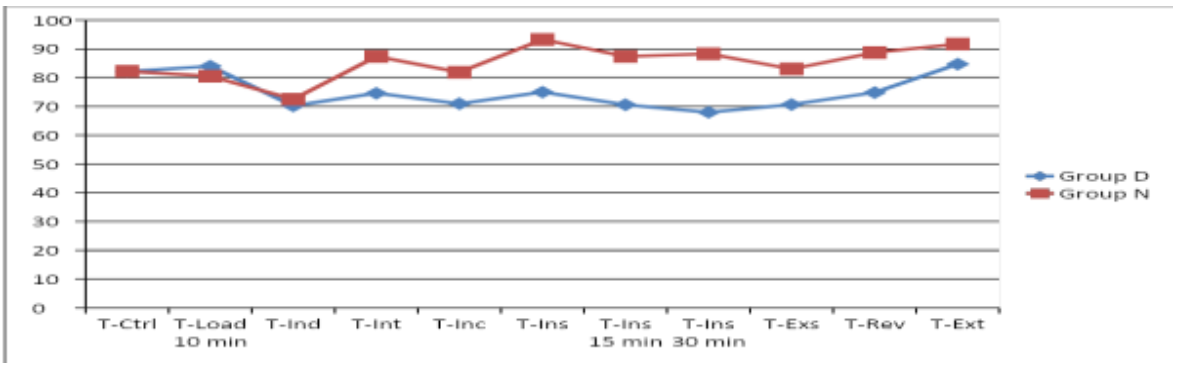
Graph 5 Shows Systolic blood pressure in study Groups at different time interval

Table -6 Diastolic blood pressure in study Groups at different time interval

	Group D		Group N		't' value	P. Value
In Min & Hr	N	Mean±SD	N	Mean±SD		
T-Ctrl	50	82.16±12.24	50	82.22±11.31	-.039	0.969
T-Load 10 min	50	83.97±6.19	50	80.52±6.09	1.259	0.172
T-Ind	50	70.21±4.71	50	72.50±9.55	3.091	< 0.001
T-Int	50	74.59±12.29	50	87.36±9.92	2.163	< 0.001
T-Inc	50	70.96±11.23	50	81.88±10.96	2.087	< 0.001
T-Ins	50	74.97±7.21	50	93.26±6.15	4.162	< 0.001
T-Ins 15 min	50	70.61±11.02	50	87.38±9.91	1.697	< 0.001
T-Ins 30 min	50	67.99±13.91	50	88.30±11.70	0.998	< 0.001
T-Exs	50	70.69±12.29	50	83.04±10.40	1.699	< 0.001
T-Rev	50	74.84±7.19	50	88.72±14.05	2.135	0.002
T-Ext	50	84.72±9.49	50	91.70±13.06	-2.997	0.004

In the group D (Dexmedetomidine), the basal value of Diastolic blood pressure is 82.16±12.24 mmHg and we observed a increase in diastolic blood pressure which is 84.72±9.49 mmHg from basal value at T-Ext.

In group N (Normal saline), the basal value of diastolic blood pressure is 82.22±11.31 mmHg and we observed a increase in diastolic blood pressure which is 91.70±13.06 mmHg . The diastolic blood pressure from T-Ind, T- Int, T – Inc, T-Ins, T-Ins 15 min, T-Ins 30 min, T-Exs, T-Rev, & T-Ext, recording is statistically significant between the groups. P. Value is <0.005.



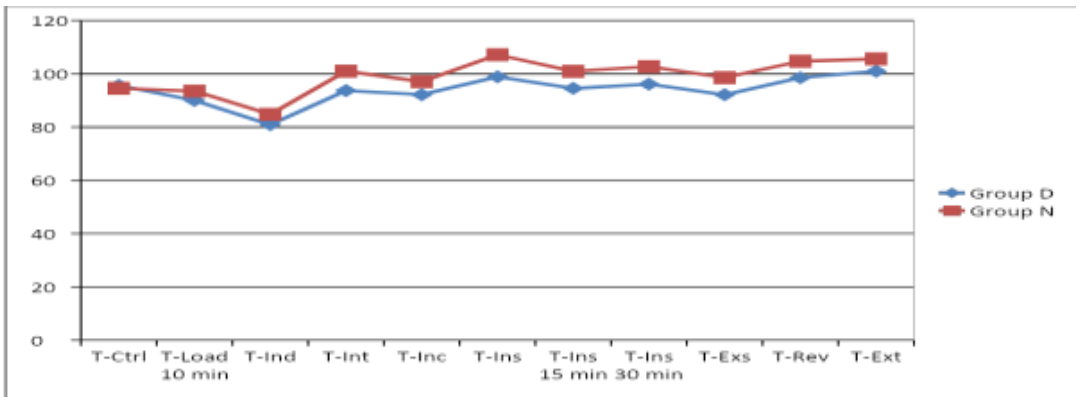
Graph 6 Shows Diastolic blood pressure in study Groups at different time interval

International Journal Dental and Medical Sciences Research
Volume 3, Issue 4, July-Aug 2021 pp 148-157 www.ijdmsrjournal.com ISSN: 2582-6018

Table -7Mean arterial blood pressure in study Groups at different time interval

	Group D		Group N		't' Value	P. Value
In Min & Hr	N	Mean±SD	N	Mean±SD		
T-Ctrl	50	95.66±9.93	50	94.56±11.16	1.309	.196
T-Load 10 min	50	90.00±5.073	50	93.50±5.17	-1.731	.094
T-Ind	50	80.91±4.27	50	84.78±9.29	3.875	< 0.001
T-Int	50	93.70±12.93	50	100.98±9.57	2.196	0.001
T-Inc	50	92.19±10.80	50	97.06±11.06	-787	0.001
T-Ins	50	98.88±11.03	50	107.16±5.45	-4.657	< 0.001
T-Ins 15 min	50	94.52±10.01	50	100.92±9.60	-1.344	<0.001
T-Ins 30 min	50	96.14±11.29	50	102.70±9.72	1.207	0.002
T-Exs	50	92.14±13.87	50	98.56±11.56	-2.725	.009
T-Rev	50	98.56±11.56	50	104.72±12.35	-4.175	<0.001
T-Ext	50	100.92±6.38	50	105.60±12.08	-2.485	.016

In the group D (Dexmedetomidine), the basal value of Mean arterial blood pressure is 95.66±9.93 mmHg and we observed a increase in Mean arterial blood pressure which is 100.92±6.38 mmHg from basal value at T-Ext. In the group N (Normal saline), the basal value of Mean arterial blood pressure is 94.56±11.16 mmHg and we observed a increase Mean arterial blood pressure which is 107.16±5.45 mmHg at T-Ins . The Mean arterial blood pressure from T-Ind, T-Int, T – Inc, T-Ins, T-Ins 15 min, T-Ins 30 min, T-Exs, T-Rev, & T-Ext, recording is statistically significant between the groups. P. Value is <0.005.



Graph7 Shows Mean arterial blood pressure in study Groups at different time interval

Table -8 Recovery time and extubation time

	Group D	Group N	't' test	P. Value
	Mean ± S.D	Mean ± S.D		
Recovery time in minutes	9.38±0.934	12.92±1.10	-16.678	< 0.001
Extubation time in minutes	10.65±1.14	14.50±1.05	-17.785	< 0.001

The recovery time in Group D was 9.38±0.934 min and Group N was 12.92±1.10 min. On comparing the value of recovery time in group D & Group N the significant difference was found. (P. Value = <0.0001).

The extubation time in Group D was 10.65±1.14 min and Group N was 14.50±1.05 min. On comparing the value of recovery time in group D & Group N the significant difference was found. (P. Value = <0.0001).

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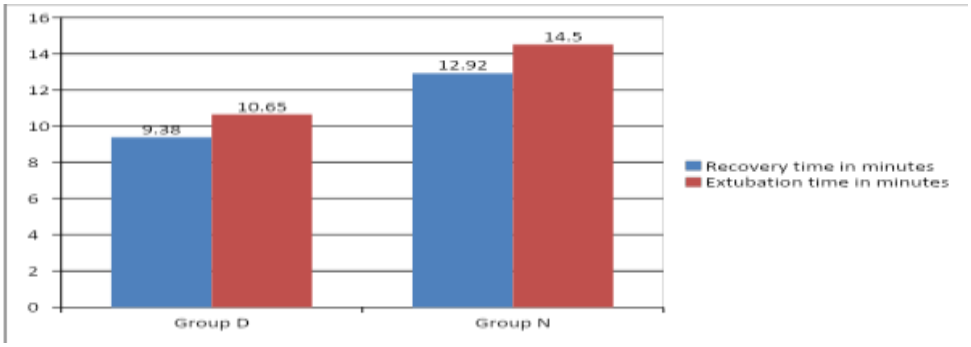


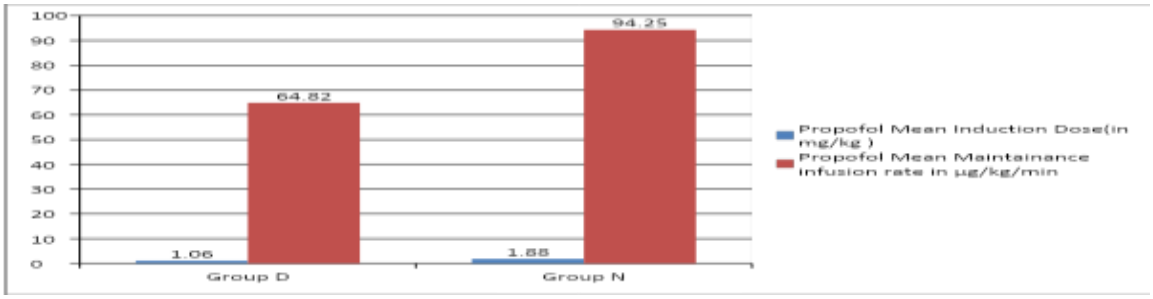
Graph8 Shows Recovery time and extubation time

Table 9 Propofol required for Induction and maintenance

	Group D Mean ± S.D	Group N Mean ± S.D	't' test	P. Value
Propofol Mean Induction Dose(in mg/kg)	1.06±0.258	1.88±0.541	-8.823	< 0.001
Propofol Mean Maintainance infusion rate in µg/kg/min	64.82±2.47	94.25±1.88	-71.116	< 0.001

The Propofol mean induction dose in Group D was 1.06±0.258 mg/kg and Group N was 1.88±0.541 mg/kg. On comparing the value of Propofol mean induction dose in group D & Group N the significant difference was found. (P. Value = <0.0001).

The Propofol mean maintainance infusion rate in Group D was 64.82±2.47 µg/kg/min and Group N was 94.25±1.88 µg/kg/min. On comparing the value of Propofol mean maintainance infusion rate e in group D & Group N the significant difference was found. (P. Value = <0.0001).



Graph 9 Shows Propofol required for Induction and maintenance

IV. SUMMARY AND CONCLUSION

In our study we found that while comparing mean heart rate in two group that is in Group D at 10 minutes after dexemedetomidine infusion and Group N at 10 minutes after normal saline infusion, we observed that there is significant decrease in mean heart rate in Group D in comparision to Group N.(P value<0.05).Throughout the course of study from induction to extubation,mean HR was significantly lower in Group D in comparision to Group N.(P<0.05)

In my study while comparing systolic blood pressure, diastolic blood pressure and mean arterial pressure in two group there is significant decrease in SBP ,DBP and MAP in group D in comparision to Group N(P<0.05) at the time of induction .Throughout the course of study from induction to extubation, SBP ,DBP and MAP was significantly lower in Group D in comparision to Group N. (P<0.05).

The recovery time was significantly less in Group D(9.38±0.934 min) compared to Group N(12.92±1.10 min).

The extubation time was significantly less in Group D(10.65±1.14 min) compared to Group N(14.50±1.05 min).

The Propofol mean induction dose was significantly low in Group D (1.06±0.26 mg/kg) in comparision to Group N (1.88±0.51 mg/kg).
The Propofol mean maintenance rate was significantly low in Group D(64.82±2.47 µg/kg/min) in comparision to Group N(94.25±1.88 µg/kg/min).

CONCLUSION

From the present study it can be concluded that during propofol based anesthesia for laparoscopic cholecystectomy, dexmedetomidine provides

- more stable intraoperative heart rate
- more stable intraoperative SBP,DBP and MAP
- reduces recovery time and extubation time
- reduces propofol requirement for induction as well as maintenance.

The present confirms that dexmedetomidine provides more stable intraoperative hemodynamics and reduces the requirement of propofol for induction as well as maintenance, without compromising the recovery profile. Furthermore studies need to be conducted in search of more adjuvants to reduce hemodynamic response of pnemoperitoneum.

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