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Effects of Dexmedetomidine on Hemodynamics in Patients Undergoing Laproscopic Surgeries under General Anaesthesia–A Comparative Study

KEYWORDS: Dexmedetomidine,hemodynamics, laparoscopic surgeries

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ABSTRACT *Background:Dexmedetomidine is a highly selective α2 agonist with properties of sedation,analgesia and anxiolysis, making it an ideal anaestheticadjuvant.We studied a randomized,double blind prospective study to evaluate the efficacy of dexmedetomidine to provide perioperative hemodynamic stability in patients undergoing elective laparoscopic surgeries.We also studied the effects of dexmedetomidine on other anaestheticagents.Material and Method:Sixty patients of either sex (18ndash;75 years)scheduled for elective laparoscopic surgeries were randomly allocated in one of the two groups containing 30 patients each.They received in a double blind manner,either a saline placebo or a dexmedetomidineinfusion.Group D received dexmedetomidine intravenous infusion at a rate of 0.4µg/Kg/hr plus fentanyl. Group C received 0.9% saline in the same rate plus fentanyl.Observation and Result:Afterpneumoperitoneum,mean value of MAP(81.53plusmn;14.19 vs 98.63plusmn;19.75 Pvaluelt;0.05)and Heart rate(73.90plusmn;10.81 vs 91.53plusmn;15.63 Pvaluelt;0.05)were significantly lower in Group D as compare to Group C.Similarly Group D blunted the tachycardic and hypertensive respose to intubation as compare to Group C (P valuelt;0.05).Furthermore Group D also provided early emergence in comparison with Group C (P valuelt;0.05).Conclusion:Dexmedetomidine as a prendash;anaestheti medication and intrandash;operative infusion is a simple,easyand economic general anaesthetic adjuvant that maintains stable hemodynamics and provides an excellent recovery profiles.*

Introduction:
Dexmedetomidine belongs to the class of $\alpha_2$agonist,has well known sedation,analgesia and opioid sparing effect.It was approved in the USA in late 1999 and gained remarkable attention for sedation and analgesia in ICU.Compared with clonidine, dexmedetomidine is about 16 times more specific for α_2 receptors[1,2]

In laparoscopic surgeries, several pathophysiological changes occur after CO_2 pneumoperitoneum and extremes of patient positioning.It leads to increased systemic and pulmonary vascular resiistance,rise of mean arterial pressure and reduced cardiac output[3].

Careful choice of the anaesthetic drug and technique must be tailored to the laparoscopic surgery.In addition to that, dexmedetomidine attenuates pressure response during direct laryngoscopy and intubation. Dexmedetomidine due to its distinct properties, can be used as an anaesthetic adjuvant in the form of Intravenous infusion[4].

We studied the use of dexmedetomidine in laparoscopic surgery and its effect on hemodynamics,anaesthetic and analgesic requirements.

Material and method:
The study protocol was approved by the institutional ethical committee.Informed consent was taken from each of the patient.Sixty ASA I nd II patients, aged 18-75 years posted for elective laparoscopic surgeries (like laparoscopic cholecystectomy, laparoscopic appendicectomy,total laparoscopic hysterectomy,diagnostic laparoscopic) were randomly assigned to one of the two groups, each containing 30 patients.Group D (Dexmedetomidine group) and Group C (control group).Patients with uncontrolled hypertension, morbid obesity,pregnancy,mental disorder and severe hepatic ,renal.endocrine and cardiac dysfunction were excluded from the study.

On arrival to recovery room,routine monitoring (ECG,SpO2,NIBP) was started and baseline vital parameters like heart rate,MAP and SpO2 were recorded.On arrival to operation theatre,baseline vital parameters like heart rate,MAP, SpO2 and EtO2 were recorded.An intravenous line was started. Group D patients :loading dose of dexmedetomidine infusion 1 µg/kg was started and continued for 15 minutes. Group C patients were given 0.9% saline in the same rate.At the end of bolus, heart rate,MAP, SpO2 and EtO2 were recorded. Dexmedetomidine infusion was given through Agilla Fresenius infusion pump.The study medication was prepared in identical 50 ml syringe. Dexmedetomidine 100 µg (1ml) was added to 0.9% saline(49 ml) making a total volume of 50 ml (resulting concentration was 2 µg / ml). Study medication was prepared by an anesthesiologists who was blinded to the computer generated randomization schedule.After 15 minutes the rate of dexmedetomidine infusion was changed to a maintenance infusion of 0.3 µg / kg/hr. Group C patients were given 0.9% saline in the same rate. Patients were premedicated with glycopyrolate 4 µg / kg,Ondansetron 4 mg and ranitidine 50 mg intravenously.All the patients received fentanyl 1 µg /kg intravenously.

Anaesthesia was induced with propofol 2 mg/kg.Endotracheal intubation was facilitated by muscle relaxant succinylcholine 1.5 mg/kg.Vasopressor response to laryngoscopy and intubation was documented by noting heart rate and MAP.All the patients were intubated with appropriate sized cuffed endotracheal tube and the placement was confirmed with auscultation and EtCO2 reading. Anaesthesia continuation was maintained with 50% : 50%, oxygen : nitrous oxide. Isoflurane concentration was adjusted to maintain systolic blood pressure within 20% of preoperative values. End tidal concentration of isoflurane was monitored.Vecuronium was used to maintain intraoperative neuroblockade.CO_2 was insufflated into the peritoneal cavity(at a rate of 2 lit/min) to create pneumoperitoneum. Intraabdominal pressure was maintained to 14 mm of hg throughout the laparoscopic procedure.The patients were mechanically ventilated to keep $EtCO_2$ between 30-35 mm of Hg.Intraoperative hypertension and tachycardia were managed by increasing the isoflurane-concentration.Heart rate and MAP response to pneumoperitoneum was documented and requirement of additional anaesthetic/analgesic noted. Dexmedetomidine infusion was continued until extubation.

Residual neuromuscular block was reversed by appropriate

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dose of neostigmine and glycopyrrolate and tracheal extubation was performed.Timing of the following events were recorded as

(1)time to tracheal extubation
(2)time to respond to simple verbal command
(3)time to orientation

Heart rate,MAP, SpO_2 and EtO_2 were recorded throughout the surgical procedure at an interval of 15 minutes and continued postoperatively.At the end of surgery,Diclofenac sodium AQ 75 mg was added to the IV fluid for post –operative analgesia.Any side effects like hypotension,bradycardia,respiratorydepression,post-operative nausea and vomiting were noted.Patient were observed for two hours in the recovery room and then shifted to the ward.

Results:
A total of sixty patients were enrolled in our study.

All the data is expressed as mean and standard deviation. All statistical analysis was conducted using http//www.graphpad.com/quickcalcs/ttestand the value of P<0.05 was considered significant and value of P<0.0001 was considered highly significant.

Table 1 depicts the demographic data.There were no significant differences between the groups with respect to patient characteristics and duration of surgery. Baseline MAP was 105±15 which fell to lowest mean of 87±14;P<0.05 after loading dose of dex(Table 2).After that minimal change was observed in MAP in post intubation and after pneumoperitoneum.However, 60 min after pneumoperitoneum no significant changes was observed in two groups.

Similarly baseline Heart rate was 86.8±14.23 which fell to lowest mean of 73.76±12.12 ;P<0.05 after loading dose of dex(Table 3).For shorter period of time, there was significant fall in Heart rate in post intubation and immediate after pneumoperitoneum.Heart rate was however sustained till end of surgery.Two three patients had sinus bradycardia (HR < 60) initially; treated with inj.Atropine 0.5 mg iv.

Postoperatively after 1 hour and 2 hour ,rapid emergence was found in dex group as compare to control group(84.93±9.69 vs 99.60±16.41 P<0.05).

Discussion:
We studied effects of dex on hemodynamic stability in patients undergoing laparoscopic surgery.

DEx is a highly selective alpha 2 adrenergic agonist with sedative, anxiolytic,analgesic,sympatholytic and antihypertensive effects.[1]

Dex, alpha 2 adrenoreceptor agonist shows a biphasic, dosedependent, blood pressure effect.

At low dose the dominant action is a reduction in sympathetic tone mediated by reduction of norepinephrine release at the neuroeffector junction and inhibition of neurotransmission in sympathetic nerves.

The net effect of dex is a significant reduction in circulating catecholamines with a slight decrease in blood pressure and moderate reduction in heart rate.

When dex is administered as a continuous infusion ,is associated with an expected and stable hemodynamic response. With continuous infusion for 24 hr,distributionhalf life of 6 min,eliminationhalf life of 2 hrs,availability of antagonistic agent Atipamezole,makedex an ideal drug for continuous infusion in the ICU, operation theatre and other areas[5].

When labour epidural analgesia could not work,in such cases intravenous dexmedetomidine infusion with systemic opioids has been successfully used[6,7].

At higher doses of dex produce an hypertensive action caused by activation of alpha 2 adrenoceptor located on vascular smooth muscle cells.

Therfore rapid injection of dex is not advised.

Dex produces analgesia effect by an action on alpha receptor within the locus ceruleus and the spinal cord.

Dex is eight times more specific for alpha 2 receptors than clonidine(alpha2 alpha 1 ratio for dex is 1620:1 and that for clonidine is 220:1)[8]

When combined with alfentanil.Dex enhances analgesia without causing further respiratory depression. Because the primary site of action is the locus cerules ,dex produce a different type of sedation compared with benzodiazepines and propofol. Central stimulation of parasympathetic outflow and inhibition of sympathetic outflow from the locus coeruleus in the brainstem plays a prominent role in the sedation and anxiolysis produced by dexmedetomidine.

The unusual subcortical form of dex induced sedation is characterized by an easy and quick arousal, resembling natural sleep. With increasing dose of dex , profound anaesthetic action have been demonstrated and this advocates that Dex could be used as total intravenous agent.

Few studies have reported use of Dexmedetomidineupto 7 days and case studies have reported use beyond 3 weeks, without any side effects.

Low and high dose of Dexmedetomidine is reported to cause a 55% and 45% decrease in Isoflurane MAC respectively.[4,9]

In our study, we observed that group D(Dexmedetomidine + fentanyl) provided more hemo stability-interaoperatively as compare to group C (NS + Fentanyl).

In addition to that, Dexmedetomidine reduced the requirement of fentanyl. Similar findings studied by B. Tufango[10]. Author used intra operative Dexmedetomidine infusion (0.2 – 0.8µg/Kg/hr) which decrease fentanyl requirement. P.E. Tanskanen also proved decreased intra operative opioid requirement.[8]

According to Hassan S[9], the intraoperative infusion of Dexmedetomidine decreased the total amount of propofol and fentanyl required to maintain anaesthesia with good hemodynamics stability and rapid recovery in morbidly obese patients undergoing laparoscopic gastric bypass.[10]

Research showed that Intraoperative Dex infusion is helpful in alleviation of post operative shivering, nausea and vomiting in gynaec laparoscopic surgery[13,14,15] We found that Group D provided better pressure attenuation response during direct laryngoscopy and intubation as compare to group C (Pvalue<0.05)

FerdiMenda[16]et al, hypothesized that in fast tarck CABG, Fentanyl 5 µg/Kg and IV dex infusion started before endotracheal intubation provided attenuation response to intubation without hemodynamic compromise.

Even In hypertensive patients, administration of dexmedetomidine before anesthesia induction blunts the hemodynamic response to tracheal intubation and reduces the thiopental dose[17,18].

In the study done by Keniya VM19et al ,dex infusion blunts the hypertensive and tachycardic response to endotracheal intubation. Systolic blood pressure was decreased in dex

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group as compare to control group (8% vs 40%).Similarly Heart rate was also decreased in dex group as compare to control group (7% vs 21%).Consumption of fentanyl, thiopentone and isoflurane was reduced with intraoperative dex infusion.

Yildiz M20 et al hypothesized that single dose of dex in preoperative period decreased blood pressure and heart rate during laryngoscopy, reduced opioid and anaestheticrequirements,rapid recovery postoperatively.

As shown in Table 2 (Heart Rate),Afterpneumoperitoneum there is a significant difference in group D as compare to Group C (73.90±10.81 vs 91.53±15.63 Pvalue<0.05). Similar findings correlated with D.P.Bhattachharjee.[21]

After pneumoperitoneum, Mean arterial pressure is also significantly decreased in Group D as compare to Group C (MAP 81.53 +14.19 Group D, 98.63+19.75 Group)P value<0.05

However, sixty minutes after pneumoperitoneum, there is no significant difference in either of Group.

(P value>0.05)

Its use is associated with a decrease in heart rate and blood pressure both in animals and humans[22].

After discontinuation of dex, rapid recovery was found in in Group D as compare to Group C.(84.93±9.69 vs 99.60±16.41 Pvalue<0.05).Hassan et al studied same findings in morbidly obese patients.[12]

According to StaffanWahlender, Dex reduces the rescue analgesia requirement in Post operative thoracic patients along with low dose epidural bupivacaine(0.125%).[23]

The activation of $\alpha_2$adrenoceptors, imidazoline-preferring receptors, or both in the ventrolateral medulla and especially in the solitarius nucleus tract by dexmedetomidine causes bradycardia. In our study we found 3 patients had episode of bradycardia. treated with inj. Atropine 0.5 mg..Similar findings have been made bycarollo DS and Lawrence CJ[24,9].

The novel therapeutic uses of this a2-AR agonist can be put safely into practice after thorough evaluation by Randomized Controlled Trials .

Conclusion:

We concluded that Dex, by the virtue of its sympatholytic ,analgesic and sedative properties,could be beneficial for a wide range of clinical conditions like ICU sedation, paediatric procedural sedation,awakefibreopticintubation,neuro,cardi ac and bariatric surgeryand the list continues to grow..

Dex appears to have promising future applications with wide safety margin….

Table 1: Demegraphic details of patients of two study groups (values in Mean±SD)

Variables	Group D	Group C
Age(years)	44.63±11.63	38.76±16.69
Weight(kg)	54.83±6.09	53.90±7.49
Duration of surgery(min)	81.66±32.67	85.83±44.14

TABLE -2

CHANGES IN MEAN ARTERIAL PRESSURE (MEAN ± SD)

	Group D	Group C	P Value
Pre operative	105.03 ± 15.48	105.03 ± 15.48	P > 0.05
Pre induction after bolus	87.26 ± 14.92	95.10 ± 11.46	P < 0.05
Post Intubation	82.70 ± 9.44	92.53 ± 16.05	P < 0.05
1 minute after intubation	80.03 ± 13.14	82.50 ± 20.24	P < 0.05
After Pneumoperitoneum	81.53 ± 14.19	98.63 ± 19.75	P < 0.05
15 minutes	84.53 ± 11.76	101.46 ± 19.21	P < 0.05
30 minutes	86.53 ± 9.34	97.96 ± 16.05	P < 0.05
45 minutes	92.22 ± 10.68	101.46 ± 17.89	P < 0.05
60 minutes	98.78 ± 10.60	101.50 ± 17.62	P > 0.05
End of Pneumoperitoneum	98.73 ± 8.96	98.70 ± 14.03	P > 0.05
POST OPERATIVE			
1 hour	84.93 ± 9.69	99.60 ± 16.41	P < 0.05
2 hour	82.70 ± 13.45	96.23 ± 15.65	P < 0.05

TABLE - 3

Changes in HR (Mean ± SD)

	Group D	Group C	P Value
Pre operative	86.80 ± 4.23	84.16 ± 14.93	P > 0.05
Pre induction after bolus	73.76 ± 12.12	94.00 ± 19.30	P < 0.05
Post Intubation	79.43 ± 10.88	97.30 ± 20.31	P < 0.05
1 minute after intubation	73.93 ± 9.80	94.23 ± 18.77	P < 0.05
After Pneumoperitoneum	73.90 ± 10.81	91.53 ± 15.63	P < 0.05
15 minutes	67.63 ± 11.27	90.00 ± 12.94	P < 0.05
30 minutes	67.89 ± 8.12	85.92 ± 14.67	P < 0.05
45 minutes	70.30 ± 9.32	84.53 ± 14.82	P < 0.05
60 minutes	75.20 ± 11.56	79.25 ± 15.27	P > 0.05
End of Pneumoperitoneum	79.37 ± 11.69	84.10 ± 14.96	P > 0.05
POST OPERATIVE			
1 hour	70.56 ± 11.10	84.46 ± 18.29	P < 0.05
2 hour	73.06 ± 12.33	84.46 ± 12.54	P < 0.05

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