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The effects on perioperative haemodynamic changes, Postoperative analgesic requirement and side effects of Dexmedetomidine infusion in patients undergoing Laproscopic cholecystectomy

Anaesthesiology

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KEYWORDS:

Introduction:-

Now-a-days most of the cholecystectomy are done laproscopically. Laproscopic surgeries has many advantages like cosmetically better, less postoperative pain, faster recovery, less hospital stay[1]. But, creation of pneumoperitoneum results in many haemodynamic changes like rise in heart rate, systemic vascular resistance, pulmonary vascular resistance and decrease in cardiac output. Reverse trendelenburg position during surgery further decreases cardiac output.[2] Stimulation of sympathetic nervous system due to hypercapnia and pneumoperitoneum leads to catecholamine particularly norepinephrine and vasopressin release.

Dexmedetomidine is a $\propto_2$ -agonist drug which acts on cardiovascular system and decreases heart rate and systemic vascular resistance. It also acts at spinal and supraspinal level and decreases intraoperative opoids requirement by modulating transmission of nociceptive signals to CNS.

Clonidine is also $\propto_2$ agonist but dexmedetomidine is more specific for $\propto_2$ receptors.[3]

The study was carried out to assess the haemodynamic changes during perioperative period as primary aim and assessment of postoperative analgesic requirement and sedation as secondary aim.

Material and Method

The study was conducted after institutional ethical committee approval. Written informed consent was taken from all the patients enrolled in study.

40 patients of either sex aged between 20 and 60 years with ASA grade 1 and 2 posted for laproscopic cholecystectomy under general anaesthesia were included in this study.

Exclusion criteria includes patients age <20 yrs and >60 yrs, diabetic, hypertensive, patients with any other comorbidity and pregnant and lactating women.

After enrollment, patients were randomly divided into two groups (20 each). Group S (normal saline) and Group D (Dexmedetomidine).

The study design was prospective randomized, double blinded and controlled.

All the patients were nil per orally for 8 hrs, premeditated with tablet ranitidine 150 mg and tablet alprazolam 0.25 mg on night before surgery and in the morning of surgery.

After taking patient on operation table a multipara monitor was attached and baseline pulse rate (PR), Systolic arterial pressure (SAP), Diastolic arterial pressure (DAP), Mean arterial pressure (MAP) and O2 saturation were recorded. Intravenous line secured with 18G cannula and infusion of ringer lactate (10 ml/kg/hr) started and injection glycopyrrlate 5 µg/kg was given to all the patients.

The study drug was prepared by other anesthetist who was not involved in this study. For group S, 50 ml normal saline was loaded in 50 ml syringe. For group D, 48 ml normal saline and 2 ml dexmedetomidine (200 µg) was loaded. Loading dose (1 µg/kg) was infused over 10 minutes and after this infusion was set 0.4 µg/kg/hr as maintenance dose.

After preoxygenation for 3 min with 100% O2, patients were induced with propofol 2 mg/kg intravenous and succinyl choline 1.5 mg/kg intravenous. Laryngoscopy and intubation done with appropriate size cuffed tube. The anaesthesia was maintained with O2: N2O (in 1:2 ratio), injection Vecuronium (0.1 mg/kg) and isoflurane (0.6 to 1%). The patients were mechanically ventilated using circle system. Throughout the procedure, end tidal CO2 was maintained between 35-45 mm Hg and intraabdominal pressure was between 12 to 14 mm Hg. Infusion of study drug, nitrous oxide and isoflurane were stopped at the end of surgery. Reversal agent neostigmine 0.05 mg/kg and glycopyrrolate 0.008 mg/kg was given intravenous and extubation done when extubation criteria met.

Vital parameters PR, SBP, MAP, DBP, SpO2 of all the patients were observed and recorded at, before starting the infusion, 10 min after starting the infusion, after induction, after intubation at 1, 3 and 5 min, after creation of pneumoperitoneum at 1 min, 15 min and then every 15 min, after release of pneumoperitoneum at 1 and 5 min, and after extubation at 1 min and then every 15 minute.

Postoperatively, the time to first rescue analgesic requirement (when pain reported by patient on visual analogue score (VAS) ≥4) and total amount of analgesic required during first 24 hrs were noted down. Injection Diclofenac sodium 1.5 mg/kg I.M was used as rescue analgesic. Sedation was assessed at every 15 min by Ramsay Sedation Score (RSS).

Intraoperatively, bradycardia (HR < 60/min) was treated with injection atropine 0.6 mg IV and hypotension (Fall in BP > 20% from baseline) was treated with inj. mephentermine 6 mg IV. Throughout the study adverse effect bradycardic, tachycardia, hypotension, hypertension, arrhythmia, dryness of mouth were observed and managed conventionally Chi-square test was used for qualitative data and paired t-test was used to compare PR, B.P etc against baseline value. $p > 0.05$ was considered insignificant, < 0.05 as significant and < 0.001 as highly significant.

Result

As shown in table 1, both groups were comparable with respect to demographic characteristics (Age, Sex, Wt. and ASA grading). Duration of anaesthesia and surgery were statistically insignificant. Mean value

of baseline PR, SBP and DBP were comparable in both groups. Mean value of PR, SBP and DBP in saline group did not show any significant change till intubation. However, there were significant rise in mean PR, SBP and DBP after intubation, during pneumoperitoneum and after extubation in saline group. (Table 2, 3, 4).

In contrast to saline group, in Dexmedetomidine group mean PR, SBP and DBP decreased significantly after intubation, during pneumoperitoneum. Even after extubation, there were significant control PR, SBP and DBP in dexmedetomidine group (Table 2, 3, 4).

In Dexmedetomidine group rescue analgesia was required late (mean 345 min) as compared to saline group (mean 57.5 min). All the patients of saline group received rescue analgesic but in dexmedetomidine group only 9 patients received rescue analgesia. In Dexmedetomidine group total analgesic requirement in first 24 hrs was 87.5 mg and in saline group requirement was 185 mg.

In postoperative period, none of the patients had RSS 5 or 6, maximum RSS in saline and dexmedetomdine group was 3 and 4 respectively. In dexmedetomdine group in 2 patients bradycardia and in 1 patients hypotension observed.

Table 1: Demographic characteristic, Duration of anaesthesia and surgery

Parameters	Group S	Group D	P Value
Age in years (Mean ± SD)	40.55 ± 6.89	41.96 ± 7.03	> 0.05
Sex Male Female	6 14	8 12	
Weight in kg (Mean ± SD)	54.65 ± 8.18	56.15 ± 7.18	> 0.05
ASA grade 1 2	19 1	18 2	
Duration of anaesthesia (in min) (mean ±SD)	92.55 ± 20.86	88.48 ± 28.41	> 0.05
Duration of surgery (in min) (mean ± SD)	77.44 ± 21.62	75.43 ± 24.63	> 0.05

P > 0.05 (Insignificant)

Table 2: Change in PR (Mean ± SD)

Time	Groups	Group D	P Value
Before starting infusion	86.9 ± 12.42	89.9 ± 10.8	> 0.05
10 min after starting infusion	88.2 ± 6.4	82.5 ± 6.9	< 0.05
1 min after induction	86.5 ± 3.43	81.2 ± 6.3	< 0.05
After laryngoscopy and intubation 1 Min 3 Min 5 Min	93.8 ± 6.3 90.1 ± 7.6 87.2 ± 4.6	84.2 ± 5.0 82.3 ± 5.9 81.5 ± 8.3	< 0.05 < 0.05 < 0.05
After pneumoperitoneum 1 Min 15 Min 30 Min 45 Min 60 Min	88.9 ± 6.43 90.2 ± 7.9 88.2 ± 9.3 86.8 ± 5.4 86.3 ± 2.3	82.3 ± 4.3 80.6 ± 10.8 81.7 ± 5.4 82.1 ± 7.3 82.9 ± 8.3	< 0.001 < 0.05 <0.05 <0.05 >0.05
After release of pneumoperitoneum 1 Min 5 Min	84.9 ± 5.6 83.2 ± 3.5	81.6 ± 4.5 81.1 ± 2.7	<0.05 <0.05
After extubation 1 Min 15 Min 30 Min 45 Min 60 Min	94.1 ± 6.8 90.2 ± 5.7 86.7 ± 8.2 85.9 ± 6.1 84.8 ± 6.6	84.6 ± 6.1 83.5 ± 3.4 80.9 ± 2.9 81.4 ± 7.2 80.8 ± 7.6	<0.001 <0.001 <0.05 <0.05 >0.05

P < 0.05 (Significant), P <0.001 (Highly Significant)

Table 3: Change in Systolic Blood pressure (SBP) (Mean ± SD)

Time	Groups	Group D	P Value
Before starting infusion 10 min after starting infusion 1 min after induction	126.3 ± 8.1 122.4 ± 6.3 117.0 ± 6.5	121.4 ± 20.4 117.3 ± 6.5 110.3 ± 9.0	> 0.05 < 0.05 < 0.05
After laryngoscopy and intubation 1 Min 3 Min 5 Min	136.3 ± 4.7 132.9 ± 7.4 131.4 ± 4.9	114.2 ± 11.3 113.6 ± 6.8 110.9 ± 10.8	< 0.001 < 0.001 < 0.001
After pneumoperitoneum 1 Min 15 Min 30 Min 45 Min 60 Min	129.3 ± 6.0 127.8 ± 9.3 123.3 ± 8.4 123.8 ± 5.8 123.5 ± 5.3	115.6 ± 10.2 114.2 ± 10.6 113.5 ± 10.4 115.4 ± 9.8 115.1 ± 13.5	< 0.001 < 0.001 <0.05 <0.05 >0.05
After release of pneumoperitoneum 1 Min 5 Min	122.8 ± 5.3 122 ± 5.9	114.0 ± 12.8 116.5 ± 8.1	<0.05 <0.05
After extubation 1 Min 15 Min 30 Min 45 Min 60 Min	132.0 ± 9.0 129.0 ± 3.5 127.0 ± 2.9 125.1 ± 9.3 123.4 ± 6.2	123.6 ± 10.8 122.5 ± 8.4 121.1 ± 9.9 119.8 ± 5.9 122.0 ± 7.4	<0.05 <0.05 <0.05 <0.05 >0.05

P < 0.05 (Significant), P <0.001 (Highly Significant)

Table 4: Change in Diastolic Blood pressure (DBP) (Mean ± SD)

Time	Groups	Group D	P Value
Before starting infusion 10 min after starting infusion 1 min after induction	79.8 ± 5.8 81.0 ± 6.3 79.8 ± 5.5	82.8 ± 6.8 76.8 ± 4.9 74.8 ± 7.6	> 0.05 < 0.05 < 0.05
After laryngoscopy and intubation 1 Min 3 Min 5 Min	94.5 ± 5.0 90.9 ± 4.6 85.4 ± 7.5	78.5 ± 8.3 75.2 ± 5.0 74.7 ± 8.2	< 0.001 < 0.001 < 0.001
After pneumoperitoneum 1 Min 15 Min 30 Min 45 Min 60 Min	84.8 ± 7.6 83.9 ± 9.6 80.9 ± 8.2 78.4 ± 6.6 77.6 ± 4.5	75.2 ± 6.3 74.5 ± 6.5 73.8 ± 5.8 73.1 ± 7.3 72.9 ± 14.5	< 0.001 < 0.001 <0.05 <0.05 >0.05
After release of pneumoperitoneum 1 Min 5 Min	77.4 ± 6.8 76.8 ± 4.5	72.1 ± 8.9 73.0 ± 6.9	<0.05 <0.05
After extubation 1 Min 15 Min 30 Min 45 Min 60 Min	82.5 ± 6.0 81.8 ± 8.2 79.9 ± 7.5 79.4 ± 6.4 78.1 ± 5.8	76.3 ± 8.9 75.7 ± 8.0 75.0 ± 5.6 75.6 ± 6.9 75.3 ± 6.0	<0.05 <0.05 <0.05 >0.05 >0.05

P < 0.05 (Significant), P <0.001 (Highly Significant)

Discussion

In patients undergoing laproscopic surgery major haemodynamic changes occur during laryngoscopy, pneumoperitoneum creation, positioning and extubation [4]. In 1947, Booker et al. studied the hemodynamic changes with pneumoperitoneum[5]. Insufflation of gas increases intraabdominal pressure resulting in decrease in venous return and hence preload due to venous compression. Systemic vascular resistance (SVR), mean arterial pressure (MAP), pulmonary vascular resistance and after load increases and cardiac

output decreases at intra-abdominal pressure 15 mm Hg[13]. At intra-abdominal pressure 16 mm Hg, significant fall in cardiac output was noted. Vasopressin and catecholamine particularly norepinephrine mediate increases in SVR during pneumoperitoneum, Joris et al[14]. Dexmedetomidine a highly selective α_2 agonist (α_2:α_1 ratio 1620:1) acts on α_2A, α_2B and α_2C receptors in brain and spinal cord. Dexmedetomidine suppress norepinephrine release by activating on α_2A receptors in brain stem. It stimulates α_2A and α_2C in locus ceruleus resulting in sedation. It also activates α_2A and α_2C receptors in spinal cord resulting in reduced release of substance P, hence decrease in pain transmission.

In our study, there was significant rise in mean PR, SBP, DBP in saline group after laryngoscopy, pneumoperitoneum and after extubation. Our results are in consistant with the study by Bhattacharjee et al., Keniya et al., Tufanogullari et al. [6,7,8].

In dexmedetomidine group, sympatholytic response was seen as observed in study done by Scheinin et al.[9]

In our study, we observed that there is an increase in the mean time of first analgesia requirement and decrease in total analgesic dose requirement in dexmedetomidine group. Similar opoid sparing effect was observed by Manne et al. .[2, 10, 11]. In our study, intraoperative bradycardia occurred in 2 patients and hypotension occurred in 1 patient in dexmedetomidine group. Bekker et al. observed that there is no significant increase in bradycaria in dexmedetomidine group [12].

Conclusion

The study confirms that dexmedetomidine effectively attenuates haemodynamic response during laproscopic surgery under general anesthesia. Dexmedetomidine reduces postoperative analgesic requirement and increase the pain free period with light sedation and minimal adverse effect.

Thus dexmedetomidine is an ideal adjuvant during laproscopy.

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