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EFFECTS OF LOW DOSE DEXMEDETOMIDINE IV INFUSION ON PERIOPERATIVE HEMODYNAMIC RESPONSE AND POSTOPERATIVE ANALGESIA REQUIREMENTS IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

Medical Science

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ABSTRACT

Laparoscopic surgeries have advantages like less postoperative pain, shorter hospitalization and associated with stress response induced by surgery, anaesthetic manoeuvres due to sympathetic stimulation. Dexmedetomidine provides hemodynamic stability, reduces requirements of rescue analgesia. We decided to study effect of low dose dexmedetomidine infusion in patients undergoing laparoscopic cholecystectomy. Randomized controlled trial involving 40 patients randomized into two groups 20 each. Group D -Dexmedetomidine infusion at the rate of 0.2 mcg/kg/h. Group C - Volume matched 0.9% NaCl. Haemodynamic stability, requirement of rescue analgesia, sedation score are compared. After 15 minutes of administration of dexmedetomidine there is reduction of pulse from 90.1 to 81.9, Mean BP from 94.06 to 81.48 , 1st dose of rescue analgesia was 187 mins in Group D which is statistically significant. Dexmedetomidine attenuates sympathetic response to laryngoscopy and intubation, stabilizes hemodynamic parameters and provides effective pain relief.

KEYWORDS

dexmedetomidine, laparoscopic cholecystectomy, analgesia

INTRODUCTION

Laparoscopic cholecystectomy is commonly practiced surgery for gall bladder diseases due to its advantages like less postoperative pain, shorter hospitalization and faster functional recovery. It also associated with stress response induced by surgery and anaesthesia, anaesthetic manoeuvres like direct laryngoscopy, tracheal intubation and extubation involves severe sympathetic stimulation[1].

During laparoscopic surgeries, there is creation of pneumoperitoneum leading to increase in systemic vascular resistance which is thought to be mediated by mechanical and neurohumoral factors such as catecholamines, the renin-angiotensin system and especially vasopressin[2]. They all are released during the presence of the pneumoperitoneum and may contribute to increase in the after load. Increase in plasma vasopressin concentrations correlate with changes in intrathoracic pressure. Mechanical stimulation of peritoneal receptors also results in increased vasopressin release, systemic vascular resistance and arterial pressure. The increase in systemic vascular resistance also explains why the arterial pressure increases but the cardiac output falls. The increase in systemic vascular resistance can be corrected by the administration of vasodilating anaesthetic agents such as Isoflurane or direct vasodilating drugs such as Nitroglycerin or Nicardipine

The α2 - adrenergic agonists such as Dexmedetomidine or Clonidine, significantly reduces the hemodynamic changes and anaesthetic requirements. Dexmedetomidine offers a unique "co-operative sedation" anxiolysis and analgesia and no respiratory depression. It's a sympatholytic and antinociceptive properties allow for hemodynamic stability at critical moments of surgery.[3] Dexmedetomidine produces dose-dependent sedation, anxiolysis, and analgesia (involving spinal and supraspinal sites) without respiratory depression.[4,5]

Dexmedetomidine is more selective alpha-2 adrenoceptor agonist, compared to clonidine, therefore it is used in higher doses for sedation and analgesia without unwanted hemodynamic effects from activation of Alpha-1 receptors. Its Intravenous use in perioperative period had found to decrease serum catecholamines levels, to blunt hemodynamic response to laryngoscopy, tracheal intubation, pneumoperitoneum and extubation, to provide sedation without respiratory depression and decrease post-operative analgesic requirements. These properties render Dexmedetomidine suitable for sedation and analgesia during the whole perioperative period as premedication, as an anaesthetic adjunct for general and regional anaesthesia, and as postoperative sedative and analgesic[6,7]

MATERIALS AND METHODS

It is prospective randomized controlled trial involving 40 patients. They were randomized by computer generated random number as 20 per group after taking informed written consent. Approval from institutional ethics committee was also taken.

Group D -Study Group-Received dexmedetomidine infusion at the rate of 0.2 mcg/kg/h (n=20)

Group C - Control Group-Received volume matched 0.9% sodium chloride (n=20)

Patients aged 35 to 65 years, ASA grade I and II, scheduled for laparoscopic cholecystectomy were included in the study. Haemodynamic parameters (Pulse, MAP), Requirement of rescue analgesia, VAS, Sedation score are compared.

PROCEDURE

All the patients underwent pre anaesthetic check-up and all the routine and specific investigations were noted. Patients were kept nil per oral for 6 hours, prior to operation patients were explained about the procedure. In OT ASA standard monitors were applied. Intravenous line secured with one 18-gauge cannula and another 20 gauge for infusion of study drug.

MATERIAL

Precedex ™, 2 ml ampoule of Dexmedetomidine was used for preparing infusion in study group. Each ml contains Dexmedetomidine hydrochloride injection equivalent to Dexmedetomidine 100µg. This 0.5ml volume containing 50 µg of drug was withdrawn in a 20 ml syringe and was diluted up to 12.5 ml with normal saline resulting a final concentration of 4 µg/ml. For each patient in Group C, 12.5ml volume of 0.9% saline solution was prepared. Dexmedetomidine or normal saline infusion was given through syringe infusion pump. Depending on weight of patient the pump was set so as to deliver the targeted infusion rate.

All patients were preoxygenated with 100% oxygen for 3 min.

Premedicated with
Inj. Ondansetron 0.15 mg/kg IV
Inj. Glycopyrrolate 0.004 mg/kg IV
Inj. Fentanyl 1 µg/kg IV

Group D patient received dexmedetomidine infusion of 0.2mcg/kg/hr 15 min prior to induction, which was continued till the end of surgery. Group C patients received the same volume of 0.9% Normal saline as saline infusion 15 min prior to induction, which was continued till the end of surgery.

Induction:
Achieved with Inj thiopentone 4 to 7 mg/kg IV. Inj. succinyl choline 2 mg/kg IV.

Maintenance:
Achieved with 0.5 to 2% (end-tidal concentration) sevoflurane, oxygen, Inj. Vecuronium loading dose (0.1mg/kg) followed by incremental dose(0.04mg/kg). In each case, the aim was to maintain mean arterial blood pressure (MAP) within 80–120% of baseline values. Mean arterial blood pressure rise of more than 20% above baseline was treated by raising the end-tidal sevoflurane concentration to 2%. Mean arterial blood pressure drop of more than 20% below baseline was treated initially with reduction of the end-tidal sevoflurane concentration to 0.5% and crystalloids. Intra-operative bradycardia (pulse rate <50) was treated with atropine 0.6 mg. Heart rate, SpO2, and MAP were recorded at specific time points during the surgical procedure. On completion of surgery Dexmedetomidine/ Saline infusions were stopped.

Reversal and Extubation:
Inj. Neostigmine 0.05-0.08mg/kg and Inj. glycopyrrolate 0.008mg /kg was given and patients extubated. All subjects were transferred to the post anaesthesia care unit (PACU), where they were monitored and received nasal O2 supplementation for 2 hours. Diclofenac sodium 2mg/kg IV was administered for rescue analgesia as a bolus dose if the pain scores higher than 5. Data for pain scores, heart rate, MAP, and sedation scores were recorded at 10, 30, 60, 90 and 120 min in the PACU. Observers who recorded data were blinded with respect to patients group allocation. The observer was never the anaesthesiologist providing clinical care of the patient. Pain intensity was assessed using a 10-point visual analogue scale (VAS) on which 0 indicated no pain and 10 indicated the worst pain imaginable.

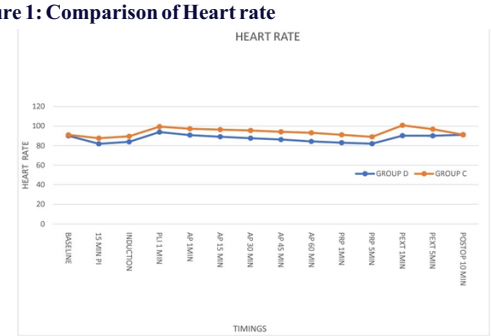
Statistical analysis:
Results obtained from the study were expressed in mean ± SD, for nonparametric data Chi square test was applied and for numeric data with continuous variables ANOVA for repeated measures with least significance difference (LSD) was performed. The software NCSS 12.0.9 was used for analysis.

RESULTS

Both the groups are comparable in baseline characteristics such as age, weight, sex ratio and duration of surgery. No significant differences have been found in these parameters.

It is evident that after 15 minutes of administration of dexmedetomidine there is significant reduction of heart rate in D group. (Group D base line 90.1 ± 4.17, 15 min after infusion 81.9± 5.12; P value <0.05). No such reduction in heart rate has been observed in saline administered C group. Heart rate has been significantly lower in dexmedetomidine group throughout the intraoperative period in comparison to saline group. (P value <0.05)

Figure 1: Comparison of Heart rate



Comparison of mean blood pressure between D and C groups at various intervals. Baseline values are similar in both the groups. After 15 of infusion of dexmedetomidine there has been fall in mean blood pressure from baseline value (Before infusion 94.06 ± 3.33,15 min after infusion 81.48 ± 2.92) (P value<0.05) but no such decrease in mean blood pressure is seen in saline administered group. (P value>0.05) Throughout intraoperative period mean blood pressure has been significantly lower in Group D as compared to Group C.

Figure 2: Comparison of Mean Blood Pressure

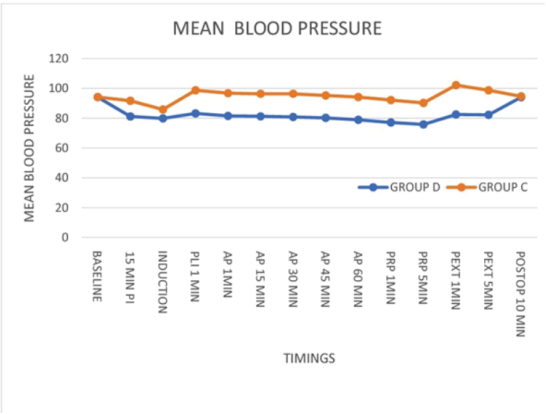


Table 1: Diclofenac requirement

No. of doses of rescue Analgesia required in 24 hrs	GROUP D	GROUP C	P value
0	0	0	0.0046
1	7	1	
2	9	4	
3	3	9	
4	1	6	

Above table shows all the subjects in both the groups required rescue analgesia during postoperative period. However, dexmedetomidine group needed significantly lesser number of doses of analgesic. (P<0.05). In D group majority of subjects 16/20 required either one or two doses of analgesic while in C group majority 15/20 required either three or four doses. This difference is statistically significant. (p<0.05).

Table 2: Comparison of time after which first dose of rescue analgesia given in both the groups.

	D group (n=20)	C group (n=20)	P value
Time to 1st dose of rescue analgesia given in postop period (mean in minutes)	187.1±6.91	56.4±5.56*	<0.0001 (S)

D group subjects have requirement of 1st dose of rescue analgesic after 187 min but control group needed it within the first 60 min of postoperative period. This difference is statistically significant (p<0.05).

Table 3: Postoperative visual analogue score (VAS):

Timings (postop)	D Group (mean± SD) (n=20)	C Group (mean± SD) (n=20)	P value
1min	0.2 ± 0.41	2.15±0.67*	<0.0001(S)
15min	0.45 ±0.51	2.3±0.47*	<0.0001(S)
30min	1.05 ± 0.22	2.8±0.76*	<0.0001(S)
45min	0.95 ± 0.39	1.9±0.71*	<0.0001(S)
60min	1.05 ±0.51	2.1±0.85*	<0.0001(S)
120min	1.15 ± 0.48	3.05±0.75*	<0.0001(S)

Visual analogue score has been significantly less throughout postoperative period among D group as compared to C group. Subjects having dexmedetomidine intraoperatively, experienced less pain and were comfortable.

During postoperative period Ramsay sedation score is more in Group D Patients in comparison to control group. This is because of sedative property of dexmedetomidine. However, the difference is not seen from 30 min (p>0.05).

DISCUSSION:

This study hypothesizes that administration of dexmedetomidine to a balanced anaesthetic technique improves perioperative hemodynamic stability and reduce postoperative analgesic requirement in patients undergoing laparoscopic cholecystectomy.

Dexmedetomidine activate receptors in the medullary vasomotor center, reducing norepinephrine turnover and decreasing central sympathetic outflow. It provides better hemodynamic and adrenergic stability via sympatholytic action, sedation, anxiolysis, decreased anaesthetics and analgesic consumption and attenuation of opioid-induced muscle stiffness, without marked ventilatory depressing effects. Sympatholytic action of α2-adrenergic agonists is not related to changes in neurotransmitter synthesis, storage or metabolism, and is reversible with vasoactive agents, antagonists of these receptors or simply by withdrawing the drug. Further dexmedetomidine decreases the need for anaesthetic agents as well as attenuates adrenergic response to tracheal intubation. After 15 minutes of starting low dose Dexmedetomidine infusion there has been a decrease in pulse rate and blood pressure in Group. This reduction in pulse rate and mean blood pressure from baseline values after starting infusion of dexmedetomidine is statistically significant($p<0.0001$).

These observations are similar with Nevriye Salman, Sennur Uzun, Fehmi Coskun, (2009)[9] and Vaddineni jagadish (2014)[8]. Neusa Maria H. Bulow, Nilda Vargas Barbosa et al[10] have also observed better hemodynamic stability with dexmedetomidine.

Bloor BC, Ward DS et al[37] have observed a biphasic effect on hemodynamic parameter after intravenous dexmedetomidine in humans, an immediate increase in blood pressure (mediated by stimulation of peripheral α2 adrenoreceptors) followed by a longer lasting reduction in pressure caused by stimulation of α2 adrenoceptors in central nervous system. Initial pressure effect is influenced by rate of intravenous infusion. They have observed this effect after giving 2μg/kg over 2 min period. But, low dose infusion of 0.25-0.5 μg/kg/hr results in monophasic response. We have not observed such biphasic response by giving low dose dexmedetomidine infusion. The activation of α2-adrenergic receptors by dexmedetomidine in the dorsal horn of the spinal cord inhibits the release of substance P, a nociceptive mediator, resulting in primary analgesic effects as well as potentiation of opioid-induced analgesia.

Our findings are similar to study done by Gurbet A et. al.[10] and Khaled Taha[11], where they proved intraoperative administration of dexmedetomidine reduced postoperative morphine requirement. Another study done by Nevriye Salman, Sennur Uzun, Fehmi Coskun, (2009)[9] also showed total number of doses of rescue analgesic reduced with dexmedetomidine usage ($P<0.0001$).

Jaakola et al.[13] evaluated analgesia after systemic administration of different doses of dexmedetomidine (0.25,0.50, and 1 mcg/kg) and fentanyl (2 mcg/kg) in healthy volunteers, and found that dexmedetomidine had a moderate analgesic effect that was maximized at 0.5 mcg/kg. In line with this, Cortinez et al.[10] showed that a 0.6 ng/mL–1 target control infusion (equivalent to 0.5 mcg/kg) of iv dexmedetomidine had analgesic effects in humans. These doses of dexmedetomidine are similar to the amounts which patients received in the current study.

Experimental pain study in human volunteers done by Ebert TJ. et al[14], used the cold pressor test after administration of dexmedetomidine different concentrations. This study indicates a significant decrease in pain VAS scores for subjects who received dexmedetomidine at doses associated with moderate to severe sedation. However conflicting results were documented in one study in an experimental model of secondary hyperalgesia, where volunteers who received clonidine at a dose known to produce moderate to severe sedation experienced no anti-hyperalgesic or anti-allodynic effects.

CONCLUSION

From our results, we conclude that Intravenous infusion of dexmedetomidine attenuates the sympathetic response to laryngoscopy and intubation and stabilizes hemodynamic parameters. Intravenous infusion of dexmedetomidine has specific analgesic properties and provides effective pain relief. We found that continuous infusion of dexmedetomidine during laparoscopic surgery significantly reduces the requirement of Diclofenac sodium as rescue analgesic in postoperative period. Thus, low dose dexmedetomidine infusion is very effective in maintaining perioperative hemodynamic stability and reducing the postoperative analgesic requirements in patients undergoing laparoscopic surgeries like laparoscopic cholecystectomy.

REFERENCES

1) Manne GR, Upadhyay MR, Swadia VN: Effects of low dose dexmedetomidine infusion on hemodynamic stress response, sedation and postoperative analgesic requirement in patients undergoing laparoscopic cholecystectomy. Indian Journal of Anaesthesia 2014;58:726-31.
2) O leary E, Hubbard K, Tormey W, Cunningham A. J: Laparoscopiccholecystectomy-haemodynamic and neuroendocrine responses afterpneumoperitoneum and changes in position; British Journal 1996 May; 76(5):640-4
3) Alex Bekker, Mary K. Sturaitis: Dexmedetomidine for Neurological surgery.Neurosurgery.2005;ONS Suppl 1]:ONS-1–ONS-10.
4) Khan ZP, Ferguson CN, Jones RM: Alpha 2 and imidazoline receptoragonists: Their pharmacology and therapeutic role. Anaesthesia .1999; 54: 146–65.
5) Maze M, Scarfini C, Cavaliere F: New agents for sedation in the intensive care unit. Crit Care Clin.2001; 17: 881–7.
6) Gertle R, Brown C, Mitchell D Et Al: Dexmedetomidine: a novel secative-analgesic agent. BUMC Proceeding; 14:13-21, 2001.
7) Ben –Abraham R, Ogorek D, Weinbroum AA: Dexmedetomidine: a promising agent for anaesthesia and perioperative care. Isr Med Assoc J 2000; 2:793-6
8) Vaddineni jagadish :A study on intraoperative and postoperative effectsof dexmedetomidine on haemodynamic stress response and anaesthetic requirements ;Perspectives in Medical Research; January- April 2014; 2(1)
9) Arcangeli A, D'Alo C, Gaspari R: Dexmedetomidine Use in GeneralAnaesthesia: Current Drug Targets 2009; 10(8);687-695(9)
10) Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, Ozcan B.:Intraoperative infusion of dexmedetomidine reduces perioperativeanalgesic requirements Canadian Journal of Anaesthesia 2006 Jul;53(7):646-52.
11) Khaled Taha: Analgesic, Sedative and Hemodynamic Effects ofDexmedetomidine Following Major Abdominal Surgeries: A Randomized,Double- Blinded Comparative Study with Morphine The Egyptian Journal of Hospital Medicine; sep 2003; 12; 113 – 120
12) Bloor BC, Ward DS, Belleville JP, Maze M: Effects of intravenousdexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology.1992 Dec;77(6):1134-42.
13) Jaakola ML, Salonen M, Lehtinen R, Scheinin H.: The analgesic actionof dexmedetomidine--a novel alpha 2-adrenoceptor agonist--in healthy volunteers. Pain; 1991 Sep;46(3):281-5.
14) Thomas J. Ebert, M.D., Ph.D.; Judith E. Hall, M.A., F.R.C.A.; Jill A.Barney, M.S.; Toni D. Uhrich, M.S.; Maelynn D. Colinco, M.D.: TheEffects of Increasing Plasma Concentrations of Dexmedetomidine in Humans. Anesthesiology 8 2000, Vol.93, 382-394