Original Research Article

Efficiency and post-operative sedation in intravenous and intrathecal clonidine in patients undergoing laproscopic assisted vaginal hysterectomy

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Abstract

Background: Intrathecal Clonidine has been used along with bupivacaine as an adjuvant for postoperative analgesia in doses from 15 to 150mcg. Higher doses have produced more sedation and hypotension. Present study was done with an aim to study the efficacy and post-operative sedation in intravenous and intrathecal clonidine in patients undergoing laparoscopic assisted vaginal hysterectomy under general anesthesia. **Material and Methods:** Patients posted for laparoscopic assisted vaginal hysterectomy under general endotracheal anesthesia are dividend in to two groups of 50 patients each. Patients assigned to group A (IV), received 50 mcg of clonidine in 50ml of normal saline over 10 minutes 10 minutes before induction. Patients assigned to group B (IT), received intrathecal clonidine 50 mcg in 1 ml of clonidine containing 150mcg was diluted to 3ml with each ml containing 50 mcg], in sitting position at L3-L4 interspace using 27G quincke's spinal needle just before induction. Intraoperative monitoring included heart rate (HR), continuous electrocardiography, noninvasive systolic (SBP), diastolic (DBP), mean blood pressure (MBP), pulse oximetry (SpO2) and EtCO2. Systolic, diastolic, mean arterial blood pressures and heart rate were recorded at regular interval. **Results:** During capnoperitoneum, mean HR values, mean SBP values, mean DBP values, mean MAP values in (IT) group B were below the baseline and that in group A (IV) were near the baseline. **Conclusion:** 50mcg of intrathecal clonidine given before induction of general anaesthesia was able to attenuate haemodynamic stress response to capnoperitoneum in adult patients posted for laparoscopic assisted vaginal hysterectomy under general anaesthesia.

Key Words: Bupivacaine, Clonidine, Mean Blood Pressure, Vaginal Hysterectomy

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INTRODUCTION

Laparoscopic surgeries are very commonly performed surgeries and they offer several advantages over open laparotomies. Although general anaesthesia is considered the choice of anaesthesia for laparoscopy, regional anaesthesia in the form of spinal anaesthesia provides unique advantages over general anaesthesia.[1-3] Several studies have been conducted to find ways for decreasing shoulder tip pain in laparoscopy under spinal anaesthesia.[4-7] Intrathecal opioids have been tried in combination with local anaesthetics for spinal anaesthesia but post-operative nausea, vomiting, and pruritis have been the limiting factor for their use. Studies have been conducted using intrathecal clonidine in doses up to 1 mcg/kg.[8-11] These doses are associated with sympatholytic side effects of clonidine along with analgesic effects disfavouring its use. Various pharmacological methods have been tried to overcome complications associated with pneumoperitoneum. Drugs like adrenoreceptor blockers, beta blockers, calcium channel blockers, opioids, magnesium sulfate, and

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vasodilators have been tried to improve quality of recover in laparoscopic procedures.[12-14] Clonidine, a centrally acting α2-adrenergic receptors agonist has sedative, anxiolytic, analgesic properties and stabilizes circulatory system. It diminishes stress response by reducing circulating catecholamines and hence increases perioperative circulatory stability in patients undergoing laparoscopic surgeries. In addition, it increases cardiac baroreflex sensitivity in hypertensive individuals, and thus, stabilizes blood pressure by enhancing the role of changes in heart rate. Clonidine through i.v route has been used as a single dose prior to induction or as continuous infusion throughout laparoscopic procedures.[14] Single dose clonidine has also been effective in attenuating haemodynamic response to capnoperitoneum. As the half-life of clonidine is 9-12 hours intravenous clonidine, single dose has been used in various doses ranging from 1mcg/kg[15,16] bodyweight to 8 mcg/kg1 bodyweight. Higher doses have produced more incidences of hypotension whereas 1 mcg/kg bodyweight was found to be effective in attenuating haemodynamic response without many side effects. Intrathecal Clonidine has been used along with bupivacaine as an adjuvant for postoperative analgesia in doses from 15 to 150mcg. Higher doses have produced more sedation and hypotension. Since in literature there are less studies comparing IV and Intrathecal clonidine we have taken up this study. Present study was done with an aim to study the efficacy and post-operative sedation in intravenous and intrathecal clonidine in patients undergoing laparoscopic assisted vaginal hysterectomy under general anesthesia.

MATERIAL AND METHODS

It's a prospective, randomized, comparative study medical sciences and Hospital at tertiary care institute of India for the duration of 1 year. Patients posted for laparoscopic assisted vaginal hysterectomy under general endotracheal anesthesia are dividend in to two groups of 50 patients each. Patients assigned to group A (IV), received 50 mcg of clonidine in 50ml of normal saline over 10 minutes 10 minutes before induction. Patients assigned to group B (IT), received intrathecal clonidine 50 mcg in 1 ml of clonidine containing 150mcg was diluted to 3ml with each ml containing 50 mcg], in sitting position at L3-L4 interspace using 27G quincke's spinal needle just before induction.

Inclusion criteria: Patient belonging to American Society of Anesthesiologists (ASA) physical status class I and II. With age of 35-60 years that are undergoing elective laparoscopic assisted vaginal hysterectomy (LAVH) under general anesthesia.

Exclusion criteria: Patients with Body mass index (BMI) >30kg/m2, Uncontrolled hypertension, cardiac disease, hepatic or renal impairment and patients receiving clonidine, methyldopa, beta blocker, benzodiazepines, MAO inhibitors and Patients recognised as, difficult for intubation and History of allergy or any drug dependence to clonidine and Any contraindications for intrathecal route of administration.

All patients were pre medicated with IV Fentanyl 2µg/kg and IV midazolam 0.03 mg/kg. The patients were pre oxygenated with 100% oxygen for 3 minutes. General anaesthesia was induced with IV propofol 2mg/kg and IV vecuronium 0.1 mg/kg. Then the patients were manually ventilated by face mask for 3 minutes with 100% oxygen and tracheal intubation will be done with 7.5 mm endotracheal tube using Macintosh laryngoscope. Capnoperitoneum was created by insufflation of CO2. Intra-abdominal pressure (IAP) will be maintained between 12-15 mmHg throughout surgical procedure. At the end of the surgery, residual neuromuscular blockade will be reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg IV after return of protective reflexes. Intraoperative monitoring included heart rate (HR), continuous electrocardiography, noninvasive systolic (SBP), diastolic (DBP), mean blood pressure (MBP), pulse oximetry (SpO2) and EtCO2. Systolic, diastolic, mean arterial blood pressures and heart rate were recorded at the following points of time: 1. Prior to induction (intrathecal or intravenous clonidine)[T0]. 2. 3 minutes after intubation [T1]. 3. Before capnoperitoneum[T2]. 4. 5 minutes after capnoperitoneum[T3]. 5. 15 minutes after capnoperitoneum[T4]. 6. 30 minutes after capnoperitoneum[T5] 7. 5 minutes after carbon dioxide release[T6]. All the episodes of circulatory derangements were recorded. Hypertension was treated with isoflurane (0.2% increments) at 2-minute intervals up to 2% if required. Tachycardia was treated with bolus dose of fentanyl 25 mcg. Hypotension was treated by 250 ml bolus dose of lactated Ringer's solution over 5 minutes followed by ephedrine 6 mg, if the patient is unresponsive. Bradycardia was be treated with atropine 0.6 mg and repeated once if necessary. Degree of sedation according to Ramsay sedation score was assessed 15 min after reaching PACU. All patients were followed for 72 hours for incidence of PDPH.

Statistical analysis: The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

RESULTS

Mean HR in group A varied from 76.68 ±9.48 to 87.74 ±10.26. Mean HR in group B varied from 74.22±10.32 to 89.30 ±13.45. During capnoperitoneum, values from 5 minutes after capnoperitoneum [T3] and 30 minutes after capnoperitoneum [T5] were not comparable. There was statistically significant difference between two groups, with mean HR values significantly lower in B group compared to A group ($p<0.05$). 5 minutes after carbon dioxide release [T6] observed after release of capnoperitoneum, showed significant variation with value lower in group B than in group A.

Before capnoperitoneum [T2] values in group B was lower than group A with significant statistical difference ($p<0.05$). During capnoperitoneum, values from 5 minutes after capnoperitoneum [T3] and 30 minutes after capnoperitoneum [T5] were not comparable. There was statistically significant variation between two groups with mean SBP values in group B significantly lower than group A. 5 minutes after carbon dioxide release [T6] observed after release of capnoperitoneum, showed significant variation with values lower in group B than in group A. 5 minutes after carbon dioxide release [T6] observed after release of capnoperitoneum, showed significant variation with values lower in group B than in group A<0.05). During capnoperitoneum, values from 5 minutes after capnoperitoneum [T3] and 30 minutes after capnoperitoneum [T5] were not comparable. There was statistically significant variation between two groups with mean SBP values in (IT) group B significantly lower than (IV) group A. 5 minutes after carbon dioxide release [T6] observed after release of capnoperitoneum showed significant variation with values lower in Group B (IT) than in (IV) group A (<0.05) Before capnoperitoneum [T2 values in (IT) group B was lower than (IV) group A with significant statistical difference. There was statistically significant variation between two groups with mean MAP values in (IT) group B significantly lower than (IV) group A.

Table 1: Comparison of mean heart rate values in both groups

Variable	Group IT ((Mean ± SD)	Group IV ((Mean ± SD)	P value
T0	89.30 ±13.45	87.05 ±11.54	
T1	84.10 ±10.84	80.31 ±7.64	
T2	77.23 ±11.14	76.68 ±9.48	
T3	80.25±11.50	87.65±10.67	
T4	79.32±10.67	87.74 ±10.26	
T5	78.11±10.67	86.25 ±9.87	
T6	74.22±10.32	80.14±7.47	

Table 2: Comparison of mean SBP (mmHg) in both groups

Variable	Group IT ((Mean ± SD)	Group IV ((Mean ± SD)	P value
T0	89.30 ±13.25	87.12 ±11.62	
T1	84.09 ±10.88	80.50 ±7.84	
T2	77.04 ±11.15	76.40 ±9.20	
T3	80.52±11.60	87.30±10.24	
T4	79.34±10.13	87.65 ±10.74	
T5	78.10 ±10.32	86.59 ±9.40	
T6	74.35±10.12	80.21±7.54	

Table 3: Comparison of mean DBP (mmHg) in both groups

Variable	Group IT ((Mean ± SD)	Group IV ((Mean ± SD)	P value
T0	89.21 ±13.10	87.32 ±11.60	
T1	84.11 ±10.87	80.54 ±7.81	
T2	77.14 ±11.23	76.64 ±9.22	
T3	80.47±11.60	87.30±10.54	
T4	79.36±10.40	87.47 ±10.87	
T5	78.23 ±10.12	86.64 ±9.82	
T6	74.45±10.22	80.35±7.51	

DISCUSSION

Laparoscopic surgeries under spinal anaesthesia are generally complicated by shoulder tip pain.[17,18]The exact aetiology of this shoulder tip pain is not known although several studies have been put forward for its explanation, the most popular one being that of diaphragmatic irritation and the shoulder tip pain being actually a referred pain and hence difficult to treat. In our study we evaluated the efficacy of low dose intrathecal clonidine to abolish the shoulder tip pain. Clonidine is a selective alpha 2 agonist and acts by inhibiting norepinephrine release from presynaptic terminals. This effect is responsible for the sympatholytic effect produced by clonidine.[19] It produces sedation and analgesia by its action on spinal cord and locus ceruleus.[20] Analgesia that is produced by clonidine is not only because of sympatholysis at peripheral level, but also due to decrease catecholamine release in brain. This results in an overall analgesic effect of clonidine. Also, it has been shown that intrathecal clonidine suppresses tumor necrosis factor α in plasma and CSF during the perioperative period which is presumed to result in analgesia.[21] All these effects may be responsible for decreasing the shoulder tip pain in laparoscopy. Demographic data between two groups with regard to age, weight, height and BMI was comparable. Duration of surgery was comparable in both groups. Base line haemodynamic data were comparable in both groups. In this study compared with Bhalerao PM *et al.*[15], Tripathi DC *et al.*[16], Kalra NK *et al.*[13]. All the mentioned studies used 1mcg/kg of intravenous clonidine and found better control of heart rate similar to our study. By comparing 2 groups (IV and IT), we observed that both the groups were able to control heart rate changes during capnoperitoneum but there was statistically significant variation between two groups with values in the intrathecal group B lower than intravenous group A. So heart rate [HR] was better

controlled in intrathecal group. In the intrathecal group B [IT], both before and after capnoperitoneum, SBP values were lower than the baseline. By comparing 2 groups we observed that, both the groups were able to control SBP changes during capnoperitoneum but there was statistically significant variation between two groups with values in the intrathecal group B lower than intravenous group A. So SBP was better controlled in intrathecal group. In the intrathecal group B [IT], both before and after capnoperitoneum, SBP values were lower than the baseline. By comparing 2 groups we observed that, both the groups were able to control SBP changes during capnoperitoneum but there was statistically significant variation between two groups with values in the intrathecal group B lower than intravenous group A. So SBP was better controlled in intrathecal group. Sympatholytic effects of intrathecal clonidine resulting in hypotension are seen with higher doses forcing the use of vasopressors.[22] There were 6 cases of hypotension in intrathecal group and 2 in intravenous group. Both were managed with ephedrine and fluid bolus there were 9 cases of hypertension in IV group and 2 in IT group. Both were managed by deepening the plane of anaesthesia using fentanyl and increments of isoflurane. In the intravenous group [IV], before capnoperitoneum, mean DBP values were lower than the baseline. In the intrathecal group B [IT], both before and after capnoperitoneum, values were lower than baseline. Both the groups were able to control DBP changes during capnoperitoneum but there was statistically significant variation between two groups with values in the intrathecal group B lower than intravenous group A. So DBP was better controlled in intrathecal group B. Intrathecal clonidine has been shown to prolong the action of spinal anesthesia when added to local anesthetic due to its multireceptor level action and also helps in providing better post-operative analgesia after intrathecal use when compared to fentanyl. [23,24] The sedation provided by Clonidine is excellent as elicited by the Ramsay sedation score, thereby decreasing the need of additional intravenous drugs. The combined property of sedation and analgesia of clonidine keeps patients pain free and comfortable. The sedation between 2 groups was compared using Ramsay sedation score. Sedation seen in both groups was comparable with no statistically significant difference between 2 groups. There was minimal sedation in both groups after extubation with no signs of respiratory depression. Sedation seen in the intravenous group A [IV] in our study compares with the studies done by Tripathi DC *et al.*[16] Kalra NK *et al.*[13]. This decreases the requirement of additional intravenous drugs. The combined property of sedation and analgesia of clonidine keeps patients pain free and comfortable. At the same time this obviates unnecessary intravenous interventions, thus serving the purpose of spinal anaesthesia. General anaesthesia in laparoscopy may be preferred in laparoscopy with prolonged pneumoperitoneum times or that involving diaphragm like laparoscopic fundoplication for hiatus hernia. Spinal anaesthesia not only provides good muscle relaxation and optimum operative field, but also facilitates better post-operative analgesia. And with adjuvants like low-dose intrathecal clonidine, stable haemodynamics along with good sedation and analgesia is provided abolishing shoulder tip pain, making the procedure more economical and comfortable to the patient.

CONCLUSION

50mcg of intrathecal clonidine given before induction of general anaesthesia was able to attenuate haemodynamic stress response to capnoperitoneum in adult patients posted for laparoscopic assisted vaginal hysterectomy under general anaesthesia. The haemodynamic stability like heart rate, mean systolic and diastolic BP, mean arterial pressure were observed better in intrathecal clonidine group. However Ramsay sedation scores were comparable in both groups.

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