



## Original Research Article

## To study the efficacy and post-operative sedation in intravenous and intrathecal clonidine in patients undergoing laparoscopic assisted vaginal hysterectomy under general anesthesia

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## ARTICLE INFO

## Article history:

Received 30-08-2020

Accepted 04-09-2020

Available online 15-03-2021

## Keywords:

Intrathecal clonidine

laparoscopic surgeries

Ramsay sedation score

## ABSTRACT

**Introduction:** Advent of Laparoscopy have benefitted patients in terms of lesser tissue damage, early ambulation, decreased duration of hospital stay and reduced analgesic needs. However capnoperitoneum and position of patient during laparoscopic procedure induces pathophysiological changes that may potentially complicate anesthetic management.

Various pharmacological methods have been tried to overcome complications associated with pneumoperitoneum. One among those drugs is Clonidine, a centrally acting  $\alpha_2$ -adrenergic receptors agonist has sedative, anxiolytic, analgesic properties and stabilizes circulatory system. It diminishes stress response hence increases perioperative circulatory stability in patients undergoing laparoscopic surgeries. In addition, it increases cardiac bar reflex sensitivity in hypertensive individuals, and thus, stabilizes blood pressure by enhancing the role of changes in heart rate.

**Objectives:** To study the efficacy and post-operative sedation in intravenous and intrathecal clonidine in patients undergoing laparoscopic assisted vaginal hysterectomy under general anesthesia.

**Materials and Methods:** Patients were divided randomly into 2 groups (A group & B group) of 30 each. Patients assigned to group a, received 50 mcg of clonidine in 50ml of normal saline over 10 minutes 10 minutes before induction. Patients assigned to group B, received intrathecal clonidine 50 mcg in 1 ml 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 (SpO<sub>2</sub>) and EtCO<sub>2</sub>. Systolic, diastolic, mean arterial blood pressures and heart rate were recorded at regular interval and plotted on graph.

**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:** Efficacy of Intrathecal route of clonidine administration during laparoscopic hysterectomy surgeries have better control of heart rate, mean systolic and diastolic blood pressure and mean arterial pressure is better during capnoperitoneum compared to intra venous clonidine. But post-operative sedation and adverse effects in both routes are statistically insignificant.

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### 1. Introduction

Advent of laparoscopy have benefitted patients in terms of lesser tissue damage, early ambulation, decreased duration of hospital stay and reduced analgesic needs. However capnoperitoneum and position of patient during

laparoscopic procedure induces pathophysiological changes that may potentially complicate anesthetic management. Pneumoperitoneum can alter acid base balance, cardiovascular complications like increase arterial pressure and systemic vascular resistance, pulmonary vascular resistance and result in reduced tissue perfusion.<sup>1</sup>

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Various pharmacological methods have been tried to overcome complications associated with pneumoperitoneum. Drugs like adrenoceptor blockers, beta blockers,<sup>2</sup> calcium channel blockers, opioids, magnesium sulfate,<sup>3</sup> and vasodilators<sup>4</sup> have been tried to improve quality of recover in laparoscopic procedures.

Clonidine, a centrally acting  $\alpha_2$ -adrenergic receptors agonist has sedative, anxiolytic, analgesic properties and stabilizes circulatory system. It diminishes stress response by reducing circulating catecholamines<sup>1</sup> 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.

Many studies have shown effectiveness of intravenous clonidine in attenuation of hemodynamic response during laparoscopy<sup>1,3,5</sup> Intrathecal clonidine used as adjuvant for bupivacaine during laparoscopic cholecystectomies shown prolonged post-operative analgesia and sedation.<sup>6</sup>

Clonidine through i.v route has been used as a single dose prior to induction or as continuous infusion throughout laparoscopic procedures.<sup>4</sup> 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<sup>7,8</sup> bodyweight to 8 mcg/kg<sup>1</sup> 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.

## 2. Aims and Objectives

Comparing intravenous with intrathecal clonidine 50mcg in adult patients posted for laparoscopic assisted vaginal hysterectomy under general endotracheal anesthesia regarding efficacy in attenuation of hemodynamic response to capnoperitoneum and the postoperative sedation in between two groups.

## 3. Materials and Methods

It's a prospective, randomized, comparative study between Jan 2019 to December 2019 at BGS Global institute of medical sciences and Hospital, Bangalore.

Patients posted for laparoscopic assisted vaginal hysterectomy under general endotracheal anesthesia are divided in to two groups of 30 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[1ml 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.

The above procedure was done by anaesthesiologist who was involved in the randomization of patient. Another anaesthesiologist who was the observer then entered the operation theatre and induced the patient and also recorded haemodynamic changes and post op sedation. Thus the observer was blinded to the procedure.

### 3.1. Inclusion criteria

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

### 3.2. Exclusion criteria

Patients with Body mass index (BMI) >30kg/m<sup>2</sup>, Uncontrolled hypertension, cardiac disease, hepatic or renal impairment and patients receiving clonidine, methyl dopa, 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 2 $\mu$ g/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 CO<sub>2</sub>. 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 (SpO<sub>2</sub>) and EtCO<sub>2</sub>. 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)[T<sub>0</sub>].
2. 3 minutes after intubation [T<sub>1</sub>].
3. Before capnoperitoneum[T<sub>2</sub>].

4. 5 minutes after capnoperitoneum[T<sub>3</sub>].
5. 15 minutes after capnoperitoneum[T<sub>4</sub>].
6. 30 minutes after capnoperitoneum[T<sub>5</sub>]
7. 5 minutes after carbon dioxide release[T<sub>6</sub>].

All the episodes of circulatory derangements were recorded. Hypertension (defined as SBP >20% of basal) was treated with isoflurane (0.2% increments) at 2-minute intervals up to 2% if required. Tachycardia (defined as heart rate >100 beats/min) was treated with bolus dose of fentanyl 25 mcg. Hypotension (defined as SBP <20% of basal) 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 (defined as heart rate <50 beats/min associated with hypotension) 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. Level of sedation score is as follows:

**Table 1:**

1	Patient is anxious and agitated or restless, or both
2	Patient is co-operative, oriented, and tranquil
3	Patient responds to commands only
4	Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5	Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus
6	Patient exhibits no response

All patients were followed for 72 hours for incidence of PDPH.

### 3.3. Statistical analysis

The descriptive procedure displays univariate summary statistics for several variables in a single table and calculates standardized values (z scores). Variables can be ordered by the size of their means (in ascending or descending order), alphabetically, or by the order in which the researcher specifies.

Following descriptive statistics were employed in the present study—mean, standard deviation, frequency and percent. Collected data was analyzed and presented in forms of tables, figures, graphs and diagrams where ever necessary. The analyzed data was discussed and compared with the data of other similar studies conducted elsewhere based on objectives of the present study.

In all the test the “p” value of less than 0.05 was accepted as indicating statistical significance. Data analysis was carried out using Statistical Package for the Social Sciences (SPSS) package (version 20.0).

## 4. Results

Mean HR in group A varied from  $76.86 \pm 9.34$  to  $87.50 \pm 10.9$ . Mean HR in group B varied from  $74.10 \pm 10.08$  to  $89.43 \pm 13.30$ . During capnoperitoneum, values from 5 minutes after capnoperitoneum[T<sub>3</sub>] and 30 minutes after capnoperitoneum[T<sub>5</sub>] 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[T<sub>6</sub>] observed after release of capnoperitoneum, showed significant variation with value lower in group B than in group A ( $p < 0.05$ ).

Before capnoperitoneum[T<sub>2</sub>] values in group B was lower than group A with significant statistical difference ( $p < 0.05$ ). During capnoperitoneum, values from 5 minutes after capnoperitoneum[T<sub>3</sub>] and 30 minutes after capnoperitoneum[T<sub>5</sub>] were not comparable. There was statistically significant variation between two groups with mean SBP values in group B significantly lower than group A ( $p < 0.05$ ). 5 minutes after carbon dioxide release[T<sub>6</sub>] observed after release of capnoperitoneum, showed significant variation with values lower in group B than in group A ( $p < 0.05$ ).

Before capnoperitoneum [T<sub>2</sub>] values in group B were lower than group A with significant statistical difference ( $p < 0.05$ ). During capnoperitoneum, values from 5 minutes after capnoperitoneum [T<sub>3</sub>] and 30 minutes after capnoperitoneum[T<sub>5</sub>] 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 ( $p < 0.05$ ). 5 minutes after carbon dioxide release [T<sub>6</sub>] observed after release of capnoperitoneum showed significant variation with values lower in Group B (IT) than in (IV) group A ( $< 0.05$ ).

Before capnoperitoneum [T<sub>2</sub> 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.

## 5. Discussion

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 [HR, SBP, DBP, and MAP] were comparable in both groups.

In this study compared with Bhalariao PM et al<sup>7</sup> [clonidine group], Tripathi DC et al.<sup>8</sup> [group II], Kalra NK et al.<sup>3</sup> [group C1]. 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

**Table 2:** Comparison of mean heart rate values in both groups

	Group IT(Mean ± SD)	Group IV(Mean ± SD)	t value	p value
T <sub>0</sub>	89.43 ±13.30	87.03 ±11.77	0.740	0.462
T <sub>1</sub>	84.00 ±10.99	80.63 ±7.98	1.357	0.180
T <sub>2</sub>	77.00 ±11.01	76.86 ±9.34	0.051	0.960
T <sub>3</sub>	80.16±11.75	87.46±10.30	-2.557	0.013
T <sub>4</sub>	79.20±10.23	87.5 ±10.95	-3.032	0.004
T <sub>5</sub>	78.0 ±10.40	86.83 ±9.60	-3.416	0.001
T <sub>6</sub>	74.20±10.08	80.00±7.70	-2.503	0.015

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

	Group B (IT clonidine)(Mean± SD)	Group A(IV clonidine)(Mean± SD)	t value	p value
T <sub>0</sub>	133.13±14.38	134.73±11.16	-0.481	0.632
T <sub>1</sub>	124.43±12.96	124.33±13.96	0.029	0.977
T <sub>2</sub>	110.96±14.01	119.83±10.73	-2.752	0.008
T <sub>3</sub>	125.36±13.99	140.96±13.01	-4.471	0.000
T <sub>4</sub>	123.23±13.42	140.56±14.06	-4.882	0.000
T <sub>5</sub>	123.00±13.78	140.86±13.35	-5.100	0.000
T <sub>6</sub>	112.16±13.75	123.63±12.40	-3.390	0.001

**Table 4:** Comparison of mean DBP (mmHg) in both groups

	Group IT(Mean± SD)	Group IV(Mean± SD)	t value	p value
T <sub>0</sub>	80.66±9.23	83.06±7.31	-1.115	0.269
T <sub>1</sub>	75.06±10.93	77.53±9.29	-0.941	0.350
T <sub>2</sub>	68.30±11.16	75.13±7.59	-2.771	0.007
T <sub>3</sub>	73.70±7.74	86.76±6.35	-7.145	0.000
T <sub>4</sub>	72.86±9.36	85.66±8.61	-5.509	0.000
T <sub>5</sub>	72.53±7.35	86.33±8.04	-6.936	0.000
T <sub>6</sub>	71.93±11.40	78.76±8.52	-2.629	0.011

**Table 5:** Comparison of mean MAP (mmHg) in both groups

	Group IT(Mean± SD)	Group IV(Mean± SD)	t value	p value
T <sub>0</sub>	98.15±9.51	100.29±7.29	-0.980	0.331
T <sub>1</sub>	91.51±10.75	93.13±10.11	-0.598	0.552
T <sub>2</sub>	82.51±11.26	90.03±7.53	-3.036	0.004
T <sub>3</sub>	91.00±9.08	104.80±7.90	-6.279	0.000
T <sub>4</sub>	89.65±10.16	103.96±9.95	-5.508	0.000
T <sub>5</sub>	89.35±9.07	104.50±9.38	-6.359	0.000
T <sub>6</sub>	85.34±11.77	93.71±9.04	-3.091	0.003

**Table 6:** Comparison of Ramsay Sedation Scores [Rss] in both groups

RSS	Group IV		Group IT		Total		p-value
	No	%	No	%	No	%	
1	5	16.7%	7	23.3%	12	20%	<b>0.590</b>
2	17	56.7%	18	60%	35	58.3%	
3	8	26.7%	5	16.7%	13	21.7%	
Total	30	100%	30	100%	60	100%	

**Table 7:** Adverse effects profile

	IT	IV
Hypertension	1	6
Hypotension	4	1
Tachycardia	0	2
Bradycardia	0	0

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. Since this is a new study, we couldn't compare this with the result of any other study.

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. We couldn't compare IT group with any other study as no such previous study has been done.

There were 4 cases of hypotension in intrathecal group and 1 in intravenous group. Both were managed with ephedrine and fluid bolus there were 6 cases of hypertension in IV group and 1 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.

In the intravenous group A [IV], before capnoperitoneum, mean MAP values were lower than the baseline. In the intrathecal group B [IT], both before and after capnoperitoneum mean MAP values were lower than baseline.

We couldn't compare IT group B with any of the previous studies because no study has been done using intrathecal clonidine alone in laparoscopic surgeries.

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,<sup>8</sup> Kalra NK et al.<sup>3</sup>

## 6. Conclusion

In this study, we found that 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 score was comparable in both groups.

## 7. Source of Funding

None.

## 8. Conflict of Interest

The authors declare that there is no conflict of interest.

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**Cite this article:** Asha G, Masamaddi GS, Amith S. To study the efficacy and post-operative sedation in intravenous and intrathecal clonidine in patients undergoing laparoscopic assisted vaginal hysterectomy under general anaesthesia. *Indian J Clin Anaesth* 2021;8(1):24-28.