Original Article

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Evaluation of Two Doses of Intrathecal Clonidine on Analgesia and Haemodynamic Profile in Elderly Patients Undergoing Endoscopic Bladder Surgeries- A Randomised Clinical Trial

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ABSTRACT

Introduction: Endoscopic bladder surgeries like Transurethral Resection of Prostrate (TURP) and Transurethral Resection of Bladder Tumour (TURBT) are performed preferably under spinal anaesthesia, using local anaesthetic like bupivacaine along with an adjuvant. Of these adjuvants used, clonidine is gaining popularity because of its safety and various advantages associated with its use. However its effect on haemodynamics, effect on block characteristics and analgesia in elderly patients has not been studied extensively.

Aim: To evaluate the analgesic efficacy and safety of clonidine 30 µg and 50 µg, in elderly patients undergoing endoscopic bladder surgeries.

Materials and Methods: It was a double blinded randomised clinical study, conducted in Department of Anaesthesia, University College of Medical Sciences, Delhi, India, from September 2008 to October 2011. Total 60 American Society of Anaesthesiology (ASA) grade I and II patients, of age 50-80 years, undergoing endoscopic bladder surgeries, were randomly allocated into three groups of 20 each. Group C received 12.5 mg of 0.5% heavy bupivacaine (2.5 mL) without clonidine, while group A and group B received 30 µg and 50 µg, respectively of clonidine. Intraoperative non invasive and invasive haemodynamic monitoring was done. The duration of analgesia (the time from the intrathecal injection to Visual Analog Scale (VAS) score greater than 0 and Bromage Scale 3), quality of anaesthesia and haemodynamic were compared between the three groups. Analysis of variance (ANOVA) for repeated measures was used for analysing the collected data. Tukey's Honest Significant Difference (HSD) test was applied as post hoc test whenever applicable.

Results: The mean duration of complete analgesia was 3.32±1.80 hours in group A, 6.30±1.45 hours in group B, and 2.22±0.92 hours in group C. The duration of complete analgesia was significantly longer in group A and B, when compared to group C. The mean duration of effective analgesia was 6.05±0.88 hours in group A, 8.65±1.75 hours in group B, and 4.68±1.77 hours in group C. The duration of effective analgesia was significantly longer in group A and B, as compared to group C. Following intrathecal injection, there was no significant difference in heart rate, Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP), cardiac output, stroke volume, systemic vascular resistance in between groups. There were no significant side effects in any of the groups.

Conclusion: Intrathecal clonidine in a dose of 30 µg and 50 µg provides faster onset, better quality and prolonged duration of block with stable haemodynamic and minimal side effects in patients undergoing endoscopic bladder surgeries.

Keywords: Geriatric, Transurethral resection of prostate, Transurethral resection of bladder tumours

INTRODUCTION

Minimally invasive endoscopic bladder surgeries like Transurethral Resection of Prostate (TURP) and Transurethral Resection of Bladder Tumours (TURBT) are commonly performed surgeries under spinal anaesthesia using bupivacaine [1,2].

Patients undergoing these surgeries are often elderly and have associated co-morbid conditions. Their autonomic homeostasis is impaired and compensatory haemodynamic responses are reduced leading to increased incidence of systemic hypotension and bradycardia than the younger population [3-5]. The anatomical and physiological changes due to ageing lead to altered nerve block characters following spinal anaesthesia. The maximal height of subarachnoid block has been shown to increase with age when using hyperbaric bupivacaine [6].

Hence, it is desirable to decrease the dose of bupivacaine. Various adjuvants have been added to bupivacaine to prolong the duration, improve the quality of analgesia and decrease its dosage. Clonidine, an alpha 2 agonist has been used extensively as an adjuvant to bupivacaine for spinal anaesthesia as it lacks the side effects of opioids like pruritis, nausea, vomiting and respiratory depression [7-11]. However due to its alpha 2 agonist properties intrathecal clonidine is also known to produce hypotension and bradycardia when given in conventional doses. Low dose clonidine (less than 1 µg/kg) has shown promising results in augmenting sensory and motor blockade with low incidence of hypotension bradycardia and sedation [12]. The efficacy and safety of low doses has not been extensively studied in elderly patients.

Based on above consideration, this study was designed with the aim of evaluating the efficacy and safety of addition of clonidine in small doses of 50 µg and 30 µg to 12.5 mg intrathecal hyperbaric bupivacaine in patients undergoing endoscopic bladder surgeries. The primary objectives were to study the characteristics of subarachnoid block and the duration of post operative analgesia and secondary objectives were to study the haemodynamic changes occurring intraoperatively in these patients and to observe for any side effects.

MATERIALS AND METHODS

This double blind, randomised clinical study was conducted in University College of Medical Sciences, Delhi, India, from

September 2008 to October 2011, following approval from Institutional Ethics Committee (Academic and Ethical Committee, Guru Teg Bahadur Hospital, Delhi, India). Written informed consent from each patient was taken.

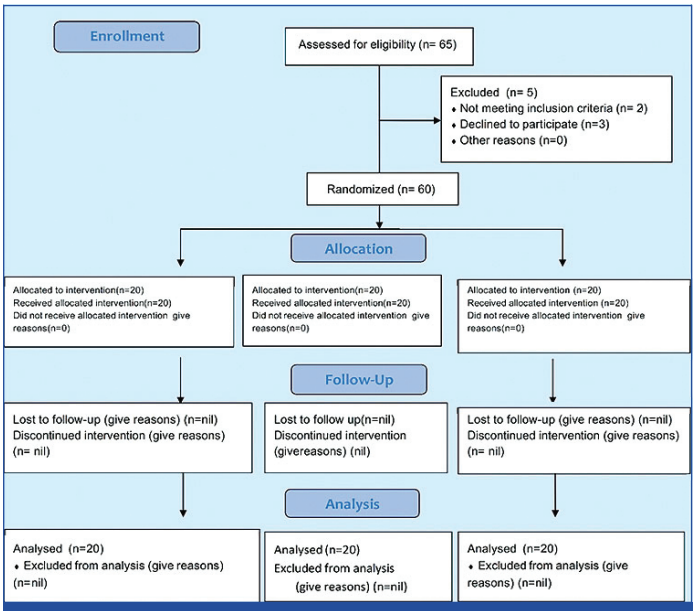
Inclusion criteria: Patients aged 50-80 years of ASA grade I-II undergoing endoscopic bladder surgeries such as transurethral resection of prostate and bladder tumours were included.

Exclusion criteria: Patients were excluded in case of any contraindications to spinal anaesthesia, local anaesthetic or clonidine allergies, insufficient cognitive ability and on treatment with drugs that might interact with clonidine i.e., Monoamine Oxidase (MAO) inhibitors or antidepressants.

Sample size calculation: Sample size was calculated considering SD=0.51 and SD2=0.72 in the bupivacaine group and in the clonidine 50 µg group. To study a difference of 0.65 in the mean values of VAS score at 90% power and alpha value of 5%, a sample size of 20 cases in each group was required.

Study Procedure

Routine pre anaesthetic assessment was done and the procedure including the use of invasive monitoring and use of VAS was explained to all the patients. Patients were premedicated with oral alprazolam 0.5 mg on the night before surgery and in the morning of surgery. Using the sealed envelope technique, patients were randomly allocated to three groups each comprising of 20 patients [Table/Fig-1]. Patients in group A received 12.5 mg of 0.5% heavy bupivacaine (2.5 mL)+30 µg of clonidine (1 mL). Patients in group B received 12.5 mg of 0.5% heavy bupivacaine (2.5 mL)+50 µg of clonidine (1 mL) and patients in group C received 12.5 mg of 0.5% heavy bupivacaine (2.5 mL)+Normal saline (1 mL). The total drug volume remained 3.5 mL in each group.



[Table/Fig-1]: CONSORT 2010 flow diagram.

Test solution was prepared under all aseptic precautions by the anaesthesiologist who was otherwise not involved in the study. Each mL of the 100 µg/mL (0.1 mg/mL) concentration contains 100 µg of clonidine hydrochloride, 0.3 mL+0.7 mL normal saline for 30 µg and 0.5 mL+0.5 mL Normal Saline (NS) for 50 µg. The dose of bupivacaine and the volume of drug injected intrathecally was kept constant for randomisation purpose according to protocol.

Intraoperative monitoring included continuous electrocardiography, pulse oximetry, invasive haemodynamic monitoring and intermittent Non Invasive Blood Pressure (NIBP). After shifting the patient to operation theatre either left or the right radial artery was cannulated using 20 G arterial cannula and Vigileo cardiac output monitor attached to it. A peripheral long line to measure the Cardiac Venous Pressure (CVP) (to derive Systemic Vascular Resistance) was also placed in the right arm brachiocephalic vein. Invasive arterial monitoring of cardiac output and stroke volume were carried out using the Vigileo monitor at every five minutes for first 30 minutes and then every 10 minutes till the end of surgery. Trend of changes in these indices were also recorded.

Preloading was done with 10-15 mL/kg of lactated Ringer's solution over a period of 10-15 minutes before the subarachnoid block. Under all aseptic precautions subarachnoid block was given in the L2-L3 or L3-L4 interspace with 25G pencil point needle via midline approach with patients in sitting position. Patients received the study drug according to the group allocation. The total volume of subarachnoid injectate was 3.5 mL in each group. Patients were returned to supine position after the completion of the block. Lactated ringer solution was administered at the rate of 2 mL/kg/hr as maintenance fluid. Blood loss was replaced using crystalloid in the ratio of 3:1. Hypotension was defined as systolic blood pressure below 90 mmHg or decrease in systolic blood pressure of more than 20% from the baseline value. It was treated with additional boluses of intravenous fluids or intravenous increment of 3 mg mephentermine i.v. Oxygen at the rate of 2-4 litre per minute was administered through simple face mask throughout the surgery. The onset and duration of sensory block were assessed by loss of pinprick sensation to a 23G hypodermic needle and dermatome level was tested every 5 minutes until level is stabilised for four consecutive tests and then every 15 minutes till the point of two segment. The onset and duration of motor block was assessed and graded every 5 minutes until complete block was achieved and then every 30 minutes till full recovery using modified Bromage criteria [12] {0=no block (the ability to flex the knees and feet), 1=partial block (the ability to flex the knees and with movement of the feet), 2=nearly complete block (the inability to flex the knees retaining ability to flex the feet) 3=complete block (the inability to move the legs or feet)}.

Pain was evaluated using standard 10 cm VAS with 0 corresponding to no pain and 10 to the worst imaginable pain. Pain score was recorded postoperatively every 30 minutes for two hours and then every four hours till the end of 24 hours. Duration of complete analgesia was defined as the time from intrathecal injection to VAS greater than 0 and the duration of effective analgesia was defined as the time to reach a VAS greater than or equal to 3, at which time patient received Injection tramadol 50 mg IM or i.v as a rescue analgesic. Sedation scoring was done intra operatively using a four point rating score every 15 minutes until patient was fully awake (0=fully awake 1=somnolent, responds to call, 2=somnolent, responds to tactile stimuli, 3=deep sedation, responds to painful stimuli) [13].

The patients were evaluated for haemodynamic changes intraoperatively using non invasive monitoring of Heart Rate (HR) and NIBP. Side effects such as nausea, vomiting, shivering or sedation were also noted.

STATISTICAL ANALYSIS

Data was analysed using Statistical Package for the Social Sciences (SPSS) version 21.0. Continuous variables were expressed in means and standard deviation, while categorical data was expressed in percentages. Statistical significance for continuous variables was assessed by unpaired T-test while for categorical variable, was calculated using the Chi-square test. Analysis of Variance (ANOVA) for repeated measures was used for analysing the collected data. Tukey's HSD test was applied as post hoc test whenever applicable. The power of one-way ANOVA was found to be 1.00 for detecting the difference in the average time to first analgesic administration. A p-value less than 0.05 was considered statistically significant.

RESULTS

A total of 65 patients were enrolled, out of which five were excluded as three did not give consent and two patients were on

antidepressants. So, finally, a total of 60 patients were included with 20 in each group. The mean age, weight and height were comparable among all the patients in the three groups [Table/Fig-2].

Parameter	Group A (n=20)	Group B (n=20)	Group C (n=20)	p-value (repeated values of ANOVA)
Age (years)				
Range	52-80	50-75	50-78	0.625
Mean±SD	64.45±7.82	62.15±6.48	63.80±8.63	
Weight (kgs)				
Range	42-65	50-65	40-73	0.645
Mean±SD	56.10±6.83	57.35±4.89	58.10±8.25	
Height (cms)				
Range	150-170	160-170	150-170	0.515
Mean±SD	164.65±6.38	166.40±3.13	164.80±5.78	

[Table/Fig-2]: Demographic profile.
NS: Not significant

Characteristics of block: The mean time of onset of action was significantly earlier in group B as compared to group A (p-value=0.002) and also significantly earlier in group A and B as compared to group C (p-value=0.001) [Table/Fig-3].

The maximum block height achieved was T6 and minimum block height was T10 in all three groups. The mean height in group B was significantly higher than group [Table/Fig-3].

Time to reach Bromage 3 ranged between 4-8 minutes in group A while it ranged between 3-5 minutes in group B and in group C it ranged between 4-9 minutes [Table/Fig-4]. The mean time of onset was significantly earlier in group A and B as compared to group C.

The mean time to two segment regression was significantly longer in group A as compared to group C significantly longer in group B as compared to group C and also significantly longer in group B as compared to group A [Table/Fig-3].

Parameter	Group A (n=20)	Group B (n=20)	Group C (n=20)	p-value (repeated values of ANOVA)
Onset (minutes)				
Mean±SDs	3.28±0.89	2.35±0.51	5±0.91	0.001 (group A and C) 0.002 (group A and B) 0.001 (group B and C)
Maximum block height (median)				
Mean±SD	T6 9.00±1.21	T6 8.10±1.21	T6 9.30±1.17	0.001 (group B and C)
Time to two segment regression				
Mean±SD	96.75±10.29	123.75±16.7	82.50±21.49	0.001 (group B and C) 0.001 (group B and A)

[Table/Fig-3]: Comparison of sensory block characteristics in the three groups.

The mean duration of motor blockade was significantly longer in group B as compared to group A and group C (p-value=0.001) [Table/Fig-4].

Parameter	Group A (n=20)	Group B (n=20)	Group C (n=20)	p-value (repeated values of ANOVA)
Onset (minutes)				
Range	4-8	3-5	4-9	0.001 (group A and C) 0.001 (group Band C)
Mean±SD	4.78±1.18	3.98±0.78	6.80±1.39	
Duration (minutes)				
Mean±SD	135.00±15.39	186.00±18.46	127.50±13.32	0.001 (group A and B)

[Table/Fig-4]: Comparison of motor blockade characteristics in the three groups.
p-value <0.05 was taken as significant

The duration of complete analgesia was defined as the time from the intrathecal injection to VAS score greater than 0. The mean duration of complete analgesia was 3.32±1.80, 6.30±1.45 and 2.22±0.92 hours in group A, group B, group C, respectively. The duration of complete analgesia was significantly longer in group A and B [Table/Fig-5] as compared to group C, and in group B as compared to group A. The duration of effective analgesia was defined as the time to VAS ≥3. The mean duration of effective analgesia was 6.05±0.88, 8.65±1.75 and 4.68±1.77 hours in group A, group B, group C respectively. The duration of effective analgesia was significantly longer in group A and B [Table/Fig-5] as compared to group C, and in group B as compared to group A [Table/Fig-5].

Parameter	Group A (n=20)	Group B (n=20)	Group C (n=20)	p-value (repeated values of ANOVA)
Complete analgesia (hours)				
Mean±SD	3.32±1.80	6.30±1.45	2.22±0.92	0.001 (group A and C) 0.001 (group A and B)
Effective analgesia (hours)				
Mean±SD	6.05±0.88	8.65±1.75	4.68±1.77	0.001 (group A and C) 0.001 (group A and B)

[Table/Fig-5]: Comparison of duration of complete and effective analgesia in the three study groups.
p-value <0.05 is taken as significant

Haemodynamic parameters: Following intrathecal injection there was a decrease in heart rate, SBP and DBP in all the three groups which was significant after 10, 15, 20, 25, 30 minutes as compared to baseline value. However, there was no significant difference in between groups [Table/Fig-6-8]. None of the patients in any groups developed significant bradycardia or hypotension necessitating treatment. In all the groups there was a significant decrease in cardiac output at various time intervals after intrathecal injection as compared to baseline value. However on intergroup comparison there was no significant difference and the trends in all the three groups were comparable [Table/Fig-9]. Similarly an analysis of cardiac index [Table/Fig-10], stroke volume [Table/Fig-11] stroke volume index [Table/Fig-12], systemic vascular resistance and systemic vascular resistance index, [Table/Fig-13,14], also show a similar trends. On intra group analysis there is a significant fall from initial baseline values however the fall is not significant on intergroup analysis and the trends in all the three groups were comparable.

Time (minutes)	Group A (n=20) (Mean±SD)	Group B (n=20) (Mean±SD)	Group C (n=20) (Mean±SD)	p-value (repeated values of ANOVA)
Preoperative	80.85±19.08	73.90±11.67	77.55±17.33	0.470
5	77.30±20.36	71.80±12.44	76.40±18.47	0.472
10	74.25±21.46	69.55±11.18	74.90±18.28	0.472
15	73.00±21.52	68.50±12.84	73.70±17.28	0.474
20	74.20±20.22	67.60±12.81	72.45±15.21	0.475
25	74.35±20.64	67.25±13.01	71.05±14.16	0.473
30	73.30±20.02	66.75±12.70	71.80±15.42	0.471

[Table/Fig-6]: Comparison of heart rate (beats/minute) at varying time intervals in the three groups.
NS: Not significant

Time (minutes)	Group A (n=20)	Group B (n=20)	Group C (n=20)	p-value (repeated values of ANOVA)
Preoperative	128.25±14.26	137.25±13.32	131.25±19.52	0.558
5	122.60±13.91	127.55±12.87	121.25±19.00	0.557
10	122.00±14.89	126.50±17.24	122.90±18.26	0.556
15	119.30±14.37	122.95±16.39	119.65±18.00	0.552
20	117.60±19.59	119.90±16.32	118.25±19.73	0.553
25	116.45±15.38	118.70±14.51	117.60±19.59	0.554
30	112.90±16.57	119.55±17.15	116.20±15.28	0.555

[Table/Fig-7]: Comparison of systolic blood pressure (mmHg) at varying time intervals.
NS: Not significant

Time (minutes)	Group A (n=20) (Mean±SD)	Group B (n=20) (Mean±SD)	Group C (n=20) (Mean±SD)	p-value (repeated values of ANOVA)
Preoperative	80.60±6.85	79.05±8.74	75.75±13.52	0.783
5	74.25±8.07	74.40±10.50	70.40±11.23	0.785
10	73.10±7.32	73.05±10.51	72.00±13.84	0.784
15	72.00±7.44	73.50±9.01	72.55±13.49	0.787
20	71.65±7.24	71.55±8.93	71.70±13.71	0.785
25	70.45±10.03	71.00±8.98	69.55±12.47	0.782
30	72.70±9.57	69.90±10.06	69.95±9.79	0.781

[Table/Fig-8]: Comparison of diastolic blood pressure (mmHg) at varying time intervals.
NS: Not significant

Time (minutes)	Group A (n=20) (Mean±SD)	Group B (n=20) (Mean±SD)	Group C (n=20) (Mean±SD)	p-value (repeated values of ANOVA)
Preoperative	5.54±1.17	6.15±1.35	6.13±1.36	0.263
5	5.01±1.17	5.59±1.33	5.66±1.55	0.264
10	4.93±1.07	5.34±1.25	5.48±1.30	0.262
15	4.63±1.16	5.22±1.22	5.23±1.22	0.266
20	4.49±1.04	4.95±1.20	5.00±1.19	0.269
25	4.49±1.09	4.93±1.11	4.80±1.17	0.264
30	4.42±1.00	4.73±1.09	4.91±1.13	0.265

[Table/Fig-9]: Comparison of cardiac output (L/min) at varying time intervals in the three groups.

Time (minutes)	Group A (n=20) (Mean±SD)	Group B (n=20) (Mean±SD)	Group C (n=20) (Mean±SD)	p-value (repeated values of ANOVA)
Preoperative	3.34±0.75	3.73±0.82	3.77±0.90	0.46
5	3.13±0.80	3.36±0.78	3.48±1.01	0.47
10	3.06±0.65	3.24±0.72	3.40±0.84	0.47
15	2.92±0.78	3.15±0.74	3.14±0.84	0.48
20	2.83±0.69	3.00±0.65	3.11±0.74	0.45
25	2.85±0.72	2.98±0.69	2.97±0.68	0.44
30	2.77±0.64	2.86±0.68	3.02±0.66	0.43

[Table/Fig-10]: Comparison of cardiac index (L/min/m^2 BSA) at varying time intervals.

Time (minutes)	Group A (n=20) (Mean±SD)	Group B (n=20) (Mean±SD)	Group C (n=20) (Mean±SD)	p-value (repeated values of ANOVA)
Preoperative	72.10±15.68	82.60±15.07	82.85±22.81	0.121
5	69.75±15.31	78.00±13.91	74.60±21.29	0.122
10	69.80±15.98	74.85±11.96	75.00±22.22	0.123
15	65.20±14.96	74.75±11.52	73.35±22.38	0.125
20	62.80±16.53	72.55±12.84	71.80±19.22	0.126
25	62.55±15.34	73.30±11.85	70.40±17.49	0.124
30	60.80±13.32	71.55±13.92	71.00±17.97	0.123

[Table/Fig-11]: Comparison of stroke volume (mL/beat) at varying time intervals.

Time (minutes)	Group A (n=20) (Mean±SD)	Group B (n=20) (Mean±SD)	Group C (n=20) (Mean±SD)	p-value (repeated values of ANOVA)
Preoperative	44.90±10.83	50.00±9.74	51.20±16.42	0.342
5	43.95±11.41	47.10±8.59	46.95±15.69	0.343
10	43.75±11.82	45.25±7.75	46.95±15.69	0.344
15	40.95±11.28	45.60±7.68	45.30±15.45	0.345
20	39.70±12.23	44.20±8.07	44.95±13.67	0.341
25	39.40±11.30	44.55±8.10	43.75±11.42	0.344
30	38.45±9.41	43.30±9.13	44.05±11.89	0.346

[Table/Fig-12]: Comparison of stroke volume index (mL/beat/m^2 BSA) at varying time intervals.

Time (minutes)	Group A (n=20) (Mean±SD)	Group B (n=20) (Mean±SD)	Group C (n=20) (Mean±SD)	p-value (repeated values of ANOVA)
Preoperative	1607.35±317.18	1470.45±346.95	1341.20±319.95	0.095
5	1452.30±288.81	1359.25±265.78	1244.55±309.33	0.097
10	1381.40±277.91	1345.50±212.52	1217.05±273.90	0.094
15	1335.65±256.13	1304.40±209.61	1217.45±241.54	0.093
20	1374.60±234.33	1286.50±236.99	1201.50±235.30	0.091
25	1371.50±231.43	1255.85±200.34	1200.30±240.59	0.092
30	1280.15±273.80	1205.45±208.12	1207.70±213.10	0.098

[Table/Fig-13]: Comparison of systemic vascular resistance (dyne/seconds/cm^5) at varying time intervals.

Time (minutes)	Group A (n=20) (Mean±SD)	Group B (n=20) (Mean±SD)	Group C (n=20) (Mean±SD)	p-value (repeated values of ANOVA)
Preoperative	2604.95±506.70	2429.05±552.23	2123.45±543.73	0.097
5	2315.80±516.12	2244.45±433.66	1981.45±537.09	0.095
10	2206.10±514.51	2223.95±349.10	1943.60±487.04	0.093
15	2117.35±495.23	2158.45±341.97	1943.50±443.65	0.094
20	2207.40±436.26	2127.25±396.59	1911.25±431.90	0.092
25	2194.60±433.27	2076.70±334.69	1912.25±441.66	0.091
30	2057.45±447.40	1997.05±358.46	1925.50±390.46	0.098

[Table/Fig-14]: Comparison of systemic vascular resistance index (dyne.sec/cm^5/m^2 BSA) at varying time intervals.

Side effects: Three patients in clonidine 30 µg (15%) group and 4 (20%) patients in clonidine 50 µg group were sedated [Table/Fig-15]. Only 1 (5%) patient reported shivering in the control group which subsided by itself and did not require any medication, while none of the patient reported nausea or vomiting.

Side effects	Group A	Group B	Group C
Nausea/vomiting	Nil	Nil	Nil
Sedation	3	4	0
Shivering	0	0	1

[Table/Fig-15]: Comparison of side effects.

DISCUSSION

Clonidine is a commonly used adjuvant to intrathecal bupivacaine. It is safe and lacks side effects like respiratory depression, nausea and pruritis which are commonly associated with opioids. It prolongs duration of sensory and motor block by depressing the release of C-fibre transmitters in pre synaptic neurons and hyperpolarisation of postsynaptic dorsal horn neurons. It also binds to motor neurons in the dorsal horn and may prolong motor block. Clonidine has been used in doses ranging from 1-3 µg/kg [9-11]. When used in higher dosages, it prolongs sensory block. Bonnet F et al., reported a significantly prolonged duration of sensory block in patients receiving clonidine 150 µg as adjuvant to 15 mg of 0.5% hyperbaric bupivacaine as compared to bupivacaine alone during orthopaedic surgery under spinal anaesthesia [14]. We used much lower dosages of clonidine and observed a similar prolongation of sensory and motor block as our patients belonged to elderly age group and the surgical procedure was of limited duration and caused lesser surgical trauma. This is similar to study by Kanazi GE et al., and Singh G et al., who found a significantly earlier onset of motor block and prolonged duration of action in patients receiving 30 µg of clonidine with bupivacaine as compared to those receiving bupivacaine alone or combined with fentanyl during transurethral resection of prostate or bladder tumour [8,9]. Agarwal D et al., also conducted a similar study using 15 and 30 µg clonidine as an adjuvant in intrathecal bupivacaine in patients undergoing lower limb procedures with bupivacaine and concluded that intrathecal clonidine prolongs duration of effective analgesia and sensory block without significant haemodynamic

changes [15]. They however used a lower dose of bupivacaine and supplemented surgical anaesthesia with epidural bupivacaine. Krishna K et al., demonstrated 30 µg to have better analgesic efficacy in patients undergoing infra umbilical surgeries Chopra P and Talwar V, also showed similar results on addition of 30 µg clonidine as an adjuvant to intrathecal bupivacaine in gynaecological surgeries [16,17]. Decrease in heart rate due to spinal anaesthesia induced sympathetic blockade is well documented in literature. Clonidine when used intrathecally is known to cause a reduction in heart rate as well as myocardial contractility [18], however in present study there was no significant difference in decrease in heart rate from baseline this could be due to low doses of clonidine used and is similar to results of Kanazi GE et al., [8]. Another study also did not report any significant difference in heart rate when clonidine was used in dose of 37.5 to as high as 150 µg intrathecally as adjuvant to bupivacaine as compared to bupivacaine alone [19].

Intrathecal administration of clonidine causes activation of postsynaptic alpha 2 adrenoceptors in the brain stem and inhibits sympathetic presynaptic alpha 2 adrenoceptors neurons in the spinal cord [15]. In a systemic review, the authors reported a 31% incidence of hypotension in patients receiving 15-150 µg of clonidine as compared to 20% in control groups [20]. Some studies have concluded that large doses of local anaesthetics mask the hypotensive effects of clonidine while large doses of clonidine with small doses of local anaesthetics reveal the hypotensive effect [21,22].In the present study, incidence of hypotension was not increased with use of 30 µg and 50 µg clonidine and none of the patients developed hypotension requiring treatment probably because of smaller doses of clonidine and better haemodynamic monitoring and the administration of adequate fluid. It is known that for the same level of block, the systemic vascular resistance decrease to a greater extent than fall in cardiac output in elderly patients as compared to younger patients [23,24]. Intravenous clonidine also causes a decreases in cardiac index, stroke volume and SVR [21]. De Negri P et al., reported that addition of clonidine to hyperbaric bupivacaine prolongs the duration of block and postoperative analgesia without significant variations of cardiovascular parameters (cardiac output, stroke volume, systemic vascular resistance) in patients undergoing minor surgical procedure (spermatic vein ligature) under spinal anaesthesia [24].

There is a paucity of literature documenting the effect of intrathecal clonidine on haemodynamic parameters by invasive cardiac monitoring in elderly patients. Evans JWH et al., found that heart rate and stroke volume decreased progressively over first 30 minutes of surgery, resulting in steady reduction in cardiac output during transurethral prostatectomy under spinal anaesthesia [25]. In present study there was significant decrease in all the haemodynamic indices on intrathecal injection in all the three groups but the trend was similar in all the three groups and there was no statistically significant difference among the three groups. There was no significant hypotension requiring treatment with vasopressor in any of the groups. This could be because of fluid co-loading and strict intraoperative monitoring of SVR cardiac output and blood pressure. This proves that intrathecal clonidine in low doses is a safe adjuvant even in elderly undergoing surgeries like TURP which involve fluid shifts. We found a significantly longer duration of post operative analgesia in patients receiving either clonidine 30 µg or clonidine 50 as compared to control group. The results are similar to those of Singh G et al., who also observed a significant prolongation of analgesia in patients receiving clonidine 30 µg as adjuvant to bupivacaine as compared to those receiving bupivacaine alone during TURP under spinal anaesthesia [9]. Several other authors have reported significant prolongation of postoperative analgesia using similar doses of, clonidine [26]. Patients receiving clonidine showed a higher degree of sedation but it was not significant when compared to control group. Total 3 (15%) patients in clonidine 30 µg group and 4 (20%) patients in clonidine 50 µg group were sedated. This was in accordance with a study conducted by Strebel S et al., who found that there was no significant difference in the sedation score in patients receiving clonidine as adjuvant to bupivacaine as compared to the bupivacaine alone during orthopaedic surgery under spinal anaesthesia [27]. Only one patient (5%) reported shivering in the control group which subsided by itself and did not need any medication, while none of the patients reported nausea or vomiting.

Limitation(s)

Only ASA I and ASA II patients were studied hence the results of the study may not be applicable to elderly patients with co-morbidities. Secondly only one dose of bupivacaine with clonidine was studied same dose of clonidine may be evaluated with smaller doses of bupivacaine.

CONCLUSION(S)

It can be concluded that intrathecal clonidine in a dose of 30 µg and 50 µg provides faster onset, better quality and prolonged duration of block with stable haemodynamics and minimal side effects in patients undergoing endoscopic bladder surgeries. It is recommended to validate our findings of haemodynamic changes and characteristics of block with clonidine in elderly patients during spinal anaesthesia with further studies using a larger sample size and in geriatric patients with co-morbidities.

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