

Study to Evaluate the Efficacy and Safety of Oral Clonidine in Controlling of Shivering in Patients Undergoing Elective Urological Surgeries under Subarachnoid Block- A Comparative Study

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ABSTRACT

BACKGROUND

Shivering is a very unpleasant, physiologically stressful sensation for the patient undergoing surgery. Spinal anaesthesia impairs the thermoregulatory control, increasing the sweating threshold and decreasing vasoconstriction and shivering threshold.¹ The combination of anaesthetic induced thermoregulatory impairment and exposure to a cool environment makes most unwarmed surgical patients hypothermic. Around 40-60% of patients under regional anaesthesia develop shivering.^{2,3} The aim of this study was to evaluate the efficacy and safety of oral clonidine in the control of shivering in patients undergoing elective urological surgeries under subarachnoid block.

METHODS

The study was an observational study including 100 patients fulfilling the inclusion criteria who had given a written informed consent. Patients were divided into study and control groups of 50 each with the test group receiving 150 mcg of oral clonidine 90 mins prior to the surgery. Grading of shivering was done as per the grading in the study of Wrench et al (1997) for six 10 min. intervals for first hour of surgery and sedation was assessed using Modified Ramsay Sedation Scale⁴ for 30 min intervals for the first 3 hours following onset of surgery.

RESULTS

The overall incidence of shivering was significantly low ($p < 0.0001$) across all the time periods in the Clonidine group. The severity of shivering was also significantly low in Clonidine group across all time periods. No statistically significant difference in sedation was seen among the two groups across all time intervals.

CONCLUSIONS

Oral clonidine at a dose of 150 µg administered 90 minutes before subarachnoid block in urological surgeries affected a significant reduction in the intensity and severity of post subarachnoid block shivering.

KEYWORDS

Clonidine, Shivering, Sub-Arachnoid Block, Sedation

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DOI: 10.18410/jebmh/2020/31*

*Financial or Other Competing Interests:
None.*

How to Cite This Article:

Divya SS, Aswathy S. Study to evaluate the efficacy and safety of oral clonidine on control of shivering in patients undergoing elective urological surgeries under subarachnoid block- a comparative study. J. Evid. Based Med. Healthc. 2020; 7(4), 148-152. DOI: 10.18410/jebmh/2020/31

*Submission 01-01-2020,
Peer Review 06-01-2020,
Acceptance 17-01-2020,
Published 21-01-2020.*



BACKGROUND

Regional anaesthesia is a safe and popular anaesthetic technique for various surgeries. However around 40-60% of patients under regional anaesthesia develop shivering.^{2,3} In homoeothermic species a thermo regulatory system coordinates defences against cold and heat to maintain internal body temperature within a narrow range of 0.2°C of 37°C, thus optimizing normal physiological and metabolic functions.⁴ Spinal anaesthesia impairs the thermoregulatory control, increasing the sweating threshold and decreasing vasoconstriction and shivering threshold.¹ The combination of anaesthetic induced thermoregulatory impairment and exposure to a cool environment makes most unwarmed surgical patients hypothermic leading to shivering. Shivering occurs frequently 40-60% after regional anaesthesia and remains poorly understood.^{2,3,5} Shivering is a potentially serious complication, resulting in increased metabolic rate; increased oxygen consumption (up to 100-600%) along with raised carbon dioxide (CO₂) production; ventilation and cardiac output; adverse postoperative outcomes, such as wound infection; increased surgical bleeding; and morbid cardiac events. It causes arterial hypoxemia, lactic acidosis, increased intraocular pressure (IOP), increased intracranial pressure (ICP); and interferes with pulse rate, blood pressure (BP) And electrocardiographic (ECG) monitoring.^{1,5,6} Customarily, we just treat shivering rather than prevent it. Prevention using physical measures like forced air warming blankets however is less efficient than pharmacological interventions using drugs like Pethidine, Tramadol, Clonidine, Doxapram, Ketanserin, Nefopam, etc.^{7,8} Clonidine is a selective partial α₂ adrenergic receptor agonist, which has both central as well as peripheral effects. This drug is primarily used as an antihypertensive agent but also has sedative and analgesic properties. Clonidine is an established anti shivering drug.^{9,10,11} It is also cheap and easily available. Urology patients are at a relatively high risk of hypothermia and its consequences. They tend to be elderly and as such at higher risk for perioperative complications.^{12,13}

METHODS

After obtaining Local Ethics and Research Committee approval and written informed consent from patients an observational study was performed. One hundred patients undergoing urological procedures under sub arachnoid block from 1st April 2018 to 31st March 2019, at Sree Gokulam Medical College were enrolled in the study.

Inclusion Criteria

1. Patients undergoing elective urological surgeries between the age group of 20 to 80 yrs.
2. ASA I/II.

Exclusion Criteria

1. Patients with hypotension.
2. Severe atrio ventricular Conduction block or bradycardia.
3. Chronic clonidine exposure.

Details regarding age, sex, contact information, comorbidities and ASA class were recorded. Oral Clonidine in a dose of 150 µg administered 90 minutes prior to subarachnoid block. All baseline values are recorded (heart rate, oxygen saturation, non-invasive BP). All patients are preloaded with 15 ml/kg of normal saline. Under strict aseptic precautions lumbar puncture is performed at the L3-L4 level. After 5 minutes patient positioned according to the surgical procedure. Patients were monitored for the presence and severity of shivering from the onset of subarachnoid block up to 3 hrs postoperatively. Patients were also be monitored for bradycardia, hypotension at 5 minutes interval for the initial 15 minutes thereafter till 3 hours postoperatively. Degree of sedation was monitored every 15 minutes. Bradycardia, hypotension and vomiting if present are treated with atropine, ephedrine and metoclopramide respectively.

The incidence of shivering, hypotension, bradycardia and sedation was compared between 2 groups.

Grading of Shivering

(as per grading in the study of Wrench et al¹⁴)

Grade 0: no shivering.

Grade 1: one or more of the following piloerection peripheral vasoconstriction, peripheral cyanosis with but without visible muscle activity.

Grade 2: visible muscle activity confined to one muscle group.

Grade 3: visible muscle activity in more than one muscle group

Grade 4: gross muscle activity involving the whole body.

Hypotension as systolic Blood pressure of < 100 mm of Hg using a mercury sphygmomanometer and bradycardia as pulse rate <60 beats per minute. Sedation of the patient was assessed as per Modified Ramsay Sedation Scale.¹⁵

0 - Anxious, agitated, restless.

1 - Co-operative, oriented, tranquil.

2 - Responds to commands only.

3 - Brisk response to light glabellar tap or loud noise.

4 - Sluggish response to light glabellar tap or loud noise.

5 - No response.

The data was analysed using Statistical Package for the social sciences (SPSS) version 21.0. Data for statistical analysis are presented as mean ± standard deviation. Comparison of shivering at different time intervals was done using Mann-Whitney U test and comparison of sedation at different time intervals was done using Fisher Exact Test.

RESULTS

Figure 1 shows the consort diagram for the flow of participants through each stage of the study. Hundred patients completed the study and were analysed for the study. There were no statistically significant differences regarding the demographic data among the 2 groups (P >0.05) (Table 1). Comparison of Shivering in the intraoperative period showed statistically significant reduction of shivering in the study group which received preoperative Clonidine. (Figure 2; Table 2).

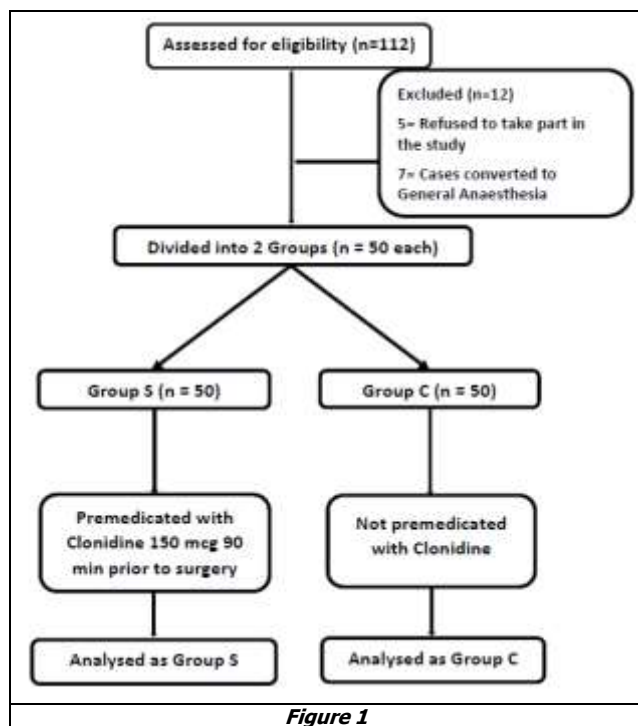


Figure 1

Parameters	Group S	Group C	p-Value
Age	45.9 ± 13.8	48.2 ± 12.4	0.380
Weight	65.5±6.5	67.1±8.0	0.259

Table 1. Demographic Variables

Group S: Study Group; Group C: Control Group

Shivering Grade	Group A		Group B		Z#	P
	Count	Percent	Count	Percent		
0-10 Min	Nil	42	84.0	22	4.43**	0.000
	Grade I	7	14.0	11		
	Grade II	0	0.0	10		
	Grade III	1	2.0	7		
10-20	Nil	42	84.0	21	4.27**	0.000
	Grade I	4	8.0	12		
	Grade II	2	4.0	9		
	Grade III	2	4.0	8		
20-30	Nil	42	87.5	26	3.63**	0.000
	Grade I	5	10.4	6		
	Grade II	1	2.1	8		
	Grade III	0	0.0	6		
30-40	Nil	28	96.6	24	2.18*	0.029
	Grade I	1	3.4	5		
	Grade II	0	0.0	2		
	Grade III	0	0.0	0		
40-50	Nil	17	100.0	16	0	1.000
	Grade I	0	0.0	0		
	Grade II	0	0.0	0		
	Grade III	0	0.0	0		
50-60	Nil	4	100.0	3	0	1.000
	Grade I	0	0.0	0		
	Grade II	0	0.0	0		
	Grade III	0	0.0	0		

Table 2. Comparison of Shivering in the Intraoperative Period

Mann-Whitney U Test

The incidence of shivering was maximum in the initial 30 minutes after SAB in Group B; 56% of the patients in the first 10 minutes, 58% in the 10-20 minute and 43% in the 20-30 minute period. Only 22% of the patients in 30-40 minutes had shivering and none in the 40-50 minutes and 50-60 minutes had shivering. As compared to Group B in Group A, only 16% had shivering in the 1st 10 minutes (vs. 56% in controls), 16% in 10-20 minutes (vs. 58%) and 3% in 20-30-minute group (vs. 43%). None in the 30-40 minute (vs. 22%) and 40-50 minutes had shivering. Thus the overall incidence of shivering was significantly low (p<0.0001) across all the time periods in the Clonidine group. The severity of shivering was also significantly low in Clonidine group across all time periods. The incidence of sedation was 4% in the first 90 minutes and 2% in 90 -180 minutes among clonidine group and sedation was not seen in the control group and the result was not statistically significant (p>.05) (Table 3).

		Group S		Group C		p
		Count	Percent	Count	Percent	
0-30	Grade I	48	96.0	50	100.0	p>0.05
	Grade II	2	4.0	0	0.0	
30-60	Grade I	48	96.0	50	100.0	p>0.05
	Grade II	2	4.0	0	0.0	
60-90	Grade I	48	96.0	50	100.0	p>0.05
	Grade II	2	4.0	0	0.0	
90-120	Grade I	49	98.0	50	100.0	p>0.05
	Grade II	1	2.0	0	0.0	
120-150	Grade I	49	98.0	49	100.0	p>0.05
	Grade II	1	2.0	0	0.0	
150-180	Grade I	49	98.0	50	100.0	p>0.05
	Grade II	1	2.0	0	0.0	

Table 3. Comparison of Sedation Score

No statistically significant difference was noted in Heart rate or Blood Pressure in the two groups

HR	Group S			Group C			T	p
	Mean	SD	N	Mean	SD	N		
0-10 min	68.0	10.2	50	71.1	9.4	50	1.59	0.115
10-20	67.7	11.2	50	69.6	16.9	50	0.65	0.518
20-30	69.9	8.5	48	73.8	11.2	46	1.94	0.055
30-40	70.3	7.0	29	72.4	10.4	29	0.9	0.370
40-50	69.7	6.8	18	72.0	9.0	15	0.84	0.406
50-60	66.2	7.9	5	66.0	12.5	3	0.03	0.978

Table 4. Comparison of Heart Rate

BP	Group S			Group C			T	p
	Mean	SD	N	Mean	SD	N		
0-10 min	115.4	10.3	50	114.6	10.1	50	0.39	0.696
10-20	102.2	10.9	50	106.6	11.6	50	0.20	0.649
20-30	111.7	7.1	48	112.1	8.2	46	0.27	0.791
30-40	116.2	6.6	29	115.0	7.9	29	0.65	0.520
40-50	121.1	7.0	17	119.9	9.4	15	0.41	0.686
50-60	118.0	5.1	5	124.7	12.2	3	1.11	0.308

Table 5. Comparison of Blood Pressure

DISCUSSION

This study attempts to evaluate the efficacy and safety of oral clonidine as premedication on control of shivering in patients undergoing elective urological surgeries under subarachnoid block. Several studies indicate that Clonidine reduces post anaesthetic shivering and the associated increases in oxygen consumption and carbon dioxide production.¹⁶ This drug may prevent post anaesthetic shivering in a dose-dependent fashion when administered

during surgery. However, the optimal timing for the drug administration (maximum ant shivering effect and minimum side effects) has not been identified. Treatment of visible post anaesthetic shivering may be insufficient because even invisible shivering may significantly increases oxygen consumption. In the present study age, sex, weight, ASA type of surgery and duration of surgery did not statistically defer among both groups. Maximum number of patients in group A and Group B were in the 24-60 yrs. age group (48% vs. 50%, p 0.38). Males predominated in both groups (90% vs. 80%, p 0.372) which are in concurrence to previous studies of Dhorigol et al¹⁶ Anurag Tiwari et al.¹⁷ In the preoperative period before giving Clonidine as premedication the mean heart rate and BP in the 2 groups did not defer significantly comparable with the studies of Anurag Tiwari, Katyal. S et al¹⁷ There was no significant variation in the blood pressure intraoperatively in two groups ($p < 0.01$) though nine patients in Clonidine and eight in control group required Ephedrine as comparable with studies of Dhorigol et al¹⁶ There was no significant variation in the heart rate intraoperatively in two groups ($p < 0.01$) though eight patients in the Clonidine group and seven in the control group required atropine. This was not clinically significant and is comparable to other studies Dhorigol et al.¹⁶ Incidence of shivering after subarachnoid block is 40-60% as per studies conducted by Devitte al; Sessler et al.² The incidence of shivering was maximum in the initial 30 minutes after SAB in Group B; 56% of the patients in the first 10 minutes, 58% in the 10-20 minute and 43% in the 20-30 minute period. Only 22% of the patients in 30-40 minutes had shivering and none in the 40-50 minutes and 50-60 minutes had shivering. As compared to Group B, in Group A, only 16% had shivering in the 1st 10 minutes (vs. 56% in controls), 16% in 10-20 minutes (vs. 58%) and 3% in 20-30-minute group (vs. 43%). None in the 30-40 minute (vs. 22%) and 40-50 minutes had shivering. Thus the overall incidence of shivering was significantly low ($p < 0.0001$) across all the time periods in the Clonidine group. Not only the incidence, but the severity of shivering was significantly low in Clonidine group across all time periods. This was in comparison with Buggy. D et al in which 60 patients scheduled for elective orthopaedic surgery under general anaesthesia, clonidine 150 µg iv was given before induction and it was observed that it reduces the incidence of shivering and patients subjective perception of cold on emergence from anaesthesia.¹⁸ As per earlier studies by Sia et al Clonidine is an effective drug when use prophylactically at 1µg/kg IV to control shivering under neuraxial block¹⁹ In one study that was conducted by Mao et al with oral clonidine in 100 patients undergoing surgery under spinal anaesthesia it was concluded that preanaesthetic medication with oral clonidine 150 µg significantly reduced the incidence and severity of shivering.¹² Another study by Delaune et al in which hypothermia induced in volunteers using ice cold saline infusion made the authors conclude that 75 µg iv bolus of Clonidine not only decreased the thermoregulatory threshold for shivering but also decreased the magnitude once triggered that Clonidine decreases the

thermoregulatory thresholds because of generalized impairment of thermoregulatory control is supported by the comparable decreases in the thresholds triggering cutaneous vasoconstriction and shivering²⁰ As per the present study the sedation of the patient was assessed by Modified Ramsay sedation scale,⁴ Clonidine has sedative properties and may reduce post anaesthetic shivering by sedation of the patients. And the sedative effect of Clonidine may be due to reduced tonic activity of Locus ceruleus which modulates the stimuli arriving from the central nervous system. The incidence of sedation was 4% in the first 90 minutes and 2% in 90 -180 minutes among Clonidine group and sedation was not seen in the control group and the result was not statistically significant ($p > .05$) as per the study of Anurag Tiwari; Sunil Katyal et al.¹⁷ There was a fall in systolic blood pressure among Clonidine group in the first 90 minutes postoperatively which was statistically significant but none of the patients were hemodynamically unstable.

CONCLUSIONS

Oral clonidine at a dose of 150 µg administered 90 minutes before subarachnoid block in urological surgeries affected a significant reduction in the intensity and severity of post subarachnoid block shivering without producing any significant adverse effects. Besides, since oral clonidine is cheap and easily available than its intravenous counterpart. It might be an ideal preventive medication before subarachnoid block, to prevent post subarachnoid block shivering.

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