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ORIGINAL ARTICLE

Efficacy of Prophylactic Clonidine in Preventing Postanesthetic Shivering in Laparoscopic-assisted Vaginal Hysterectomy

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ABSTRACT

Objective: Postanesthetic shivering occurs in up to 60% of patients following general anesthesia and is associated with deleterious consequences. Various drugs have been used to prevent or treat postanesthetic shivering, but the ideal one has not yet been found. In this study, we have studied the efficacy of prophylactic clonidine in preventing postanesthetic shivering.

Meterials and methods: Sixty ASA (American Society of Anesthesiologists) I and II patients scheduled for laparoscopic-assisted vaginal hysterectomy (LAVH) were randomly allocated to receive either clonidine 2 μg.kg^{-1} (group C, n = 30) or normal saline (group S, n = 30) intravenously at the time of vault closure. Core body temperature (nasopharyngeal) along with NIBP, heart rate and ECG were monitored at regular intervals. The severity of shivering was assessed according to a five-point scale (0 to 4).

Results: Significantly less shivering occurred in clonidine group 5 (17%) compared to normal saline group 20 (67%). The recovery time (between end of anesthesia and extubation) was significantly longer in the clonidine group (12.5 ± 4.3 minutes) compared with normal saline group (8.0 ± 4.5 minutes). Mean arterial blood pressure and heart rate were significantly lower in the clonidine group compared with saline group.

Conclusion: Prophylactic clonidine is effective in the prevention of postanesthetic shivering. Following clonidine administration, the recovery time was prolonged and incidence of bradycardia and hypotension were more than placebo.

Keywords: Shivering, Clonidine, Postanesthetic complications, Laparoscopic hysterectomy.

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INTRODUCTION

Along with postoperative nausea and vomiting, postanesthetic shivering is one of the most frequent problems in the early recovery phase following anesthesia.[1,2] Previous studies have found that shivering occurs in the postoperative period in up to 60% of patients[1-3] and varies according to age, gender, drug used for anesthesia and the duration of surgery.

In a survey on 33 clinical problems, anesthesiologists ranked postanesthetic shivering eighth when its frequency was considered.[4] In a shivering patient, oxygen consumption may increase by 200 to 500%.[5] Also hypothermia may trigger vasoconstriction and thus increase vascular resistance. Thus, in a patient with already limited myocardial oxygen supply because of atherosclerosis, shivering may further compromise myocardial function. Shivering may also increase intraocular and intracranial pressure, and it may contribute to increased wound pain.[6]

A number of pharmacological interventions have been studied for the prophylaxis and the treatment of shivering. The relative efficacy of these different agents remains unclear. The aim of this randomized, double-blind, placebo-controlled study was to investigate the efficacy of intravenous clonidine in preventing/reducing the incidence of postanesthetic shivering in comparison with placebo in the gynecological operative model of laparoscopic-assisted vaginal hysterectomy (LAVH).

MATERIALS AND METHODS

After obtaining approval from the institutional ethical committee and written informed consent from the patients, a prospective, randomized, double-blind, placebo-controlled study was conducted in the Department of Obstetrics and Gynecology, Medical College and Hospitals, Kolkata, from July 2010 to December 2011. Sixty women of ASA (American Society of Anesthesiology) physical status I and II who were scheduled for LAVH were enrolled. The following groups of patients were excluded from the study: those with cardio-respiratory problem, those with a known allergy to study medication, patients with fever (temperature >37.5°C), those with known muscle disease or alcohol abuse.

The patients were randomly (envelope randomization) allocated to receive normal saline (group S, n = 30) or clonidine 2 μg. kg^{-1} (group C, n = 30) intravenously at the time of vault closure. The treatment drugs were prepared, diluted to a volume of 5 ml with normal saline and presented as coded syringes by an anesthesiologist who was not involved in the management of patients.

All patients were kept fasting for at least 6 hours preoperatively and received alprazolam 0.5 mg orally 2 hours prior to the induction of anesthesia. Anesthesia was induced using propofol (1%) and fentanyl 2 μg.kg^{-1}. Vecuronium (0.1 mg. kg^{-1}) was administered to facilitate tracheal intubation. General anesthesia was maintained using isoflurane (0.8-1% inspired concentration) and nitrous oxide 60% in oxygen, in all patients. Ventilation was adjusted to maintain end-tidal carbon dioxide concentration between 35 and 45 mm Hg. Intraoperatively, the patients were not actively warmed but were covered with sheets. The entire operation was done in a lithotomy position. One umbilical port and three side ports were made for laparoscopic entry. The laparoscopic part of the hysterectomy was done up to the level of uterine artery and

rest of the operation was done vaginally. Residual neuromuscular blockade was antagonized using neostigmine 0.05 mg kg^{-1} and atropine 0.02 mg kg^{-1}. When respiratory effort of the patients was adequate and she responded to verbal commands, the trachea was extubated. Patients in all groups received diclofenac (100 mg) rectally at the start of surgery. Postanesthetic recovery was graded using the established Aldrete score[7] on arrival in the PACU.

In the recovery room, all patients were monitored, received oxygen via a facemask and covered with a cotton blanket. An anesthesiologist unaware of the study drug observed the patient for shivering, pain, nausea and vomiting. Shivering was graded using a scale similar to that validated by Tasi and Chu[8] (as shown in the following Table 1):

Table 1: Scale of shivering

Grade/score	*Clinical signs*
0	No shivering
1	Piloerection or peripheral vasoconstriction but no visible shivering
2	Muscular activity in only one muscle group
3	Muscular activity in more than one muscle group but not generalized
4	Shivering involving the whole body

A score of 3 or more was considered as a failure of prophylaxis, 25 mg pethidine (an established antishivering drug)[9,10] was given intravenously as rescue medication and repeated once, if necessary. Heart rate, noninvasive blood pressure, oxygen saturation and nasopharyngeal temperature were measured and recorded on admission to the recovery room and every 5 minutes thereafter throughout her stay in the recovery room.

The incidence of shivering and side-effects were compared using the chi-square test. The results were reported as mean ± standard deviation. $p < 0.05$ was considered statistically significant. The power of the study was calculated based on the number of patients who shivered. Setting a significance level of $p = 0.05$, it was calculated detection of a difference between groups with a power of 80%.

RESULTS

The two groups were comparable with regard to age, weight, ASA physical status, and gender (Table 2). Duration of surgery and anesthesia were comparable in the study groups. The recovery time between the end of anesthesia and extubation was significantly longer in the clonidine-treated patients (12.5 ± 4.3 minutes) than in the placebo group (8.0 ± 4.5 minutes). However, the Aldrete score at arrival and at discharge from PACU were similar as shown in Table 2.

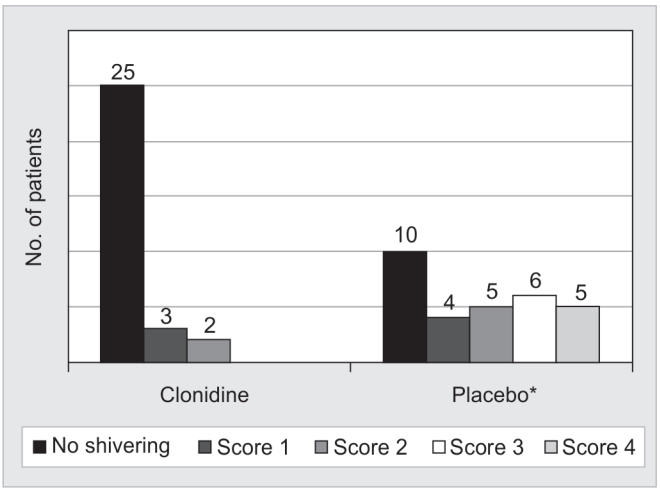
The incidence of postanesthetic shivering (See Table 2) was significantly lower ($p < 0.01$) in the clonidine 5 (17%) than for patients receiving placebo 20 (67%). The degree of postanesthetic shivering was significantly greater ($p < 0.01$) in the placebo group (Graph 1).

Mean arterial pressure and heart rate decreased significantly in the clonidine patients 15 and 30 minutes after extubation compared with placebo treated patients (Table 3). However, no patient in any group needed a therapeutic intervention with regard to hemodynamic effects of study medication.

The time of first analgesic requirement in the postoperative period in group S (mean 16 ± 9.5 minute) was significantly shorter than that in group C (mean 28 + 12 minute) ($p < 0.05$). None of the patients had episodes of oxygen desaturation or respiratory depression during the study.

DISCUSSION

In this study, we have observed the efficacy of clonidine for the prevention of postanesthetic shivering following LAVH.



Graph 1: Severity of postanesthetic shivering. 0 : no shivering; 1 : piloerection or peripheral vasoconstriction; but no visible shivering; 2 : muscular activity in one muscle group; 3 : muscular activity in more than one muscle group but not generalized; 4: shivering involving the whole body (*$p < 0.01$)

Table 2: Demographic characteristics, perioperative data and incidence of postanesthetic shivering

	Clonidine (2 μg. kg^{-1}) (n = 30)	*Placebo (n = 30)*
Age (yrs)	43 (21-64)	45 (21-66)
Weight (kg)	57 ± 6	55 ± 9
Duration of surgery (minute)	93 ± 36	91 ± 28
Duration of anesthesia (minute)	125 ± 30	128 ± 25
ASA I/II	25/5	26/4
Extubation time (minute)	12.5 ± 4.3	8.0 ± 4.5
Incidence of shivering (n)	5 (17%)	20(67%)*
Aldrete score arrival at PACU	7.0 (6-10)	8.0 (6-10)
Discharge at PACU	10.0 (9-10)	10.0 (8-10)

Data are presented as mean (SD) and as median (range): PACU : postanesthetic care (recovery) unit ; * $p < 0.01$

Table 3: Mean arterial blood pressure (MAP), heart rate (HR) and nasopharyngeal temperature (NPT)

	Clonidine			*Placebo*		
	MAP	*HR*	*NPT*	*MAP*	*HR*	*NPT*
After induction	88.3 (16.4)	76.3 (15.6)	36.7	90.7 (15.6)	74.4 (10.6)	36.6
15 minutes after extubation	90.2 (14.6)*	70.5 (10.6)*	35.7	111.6 (16.4)	90.6 (14.2)	35.8
30 minutes after extubation	93.2 (15.0)*	73.6 (9.9)*	36	101.5 (13.2)	88.0 (13.0)	36.1

*$p < 0.01$

Postanesthetic shivering is a common phenomenon and, in our placebo group, the incidence was 67%, a figure that is in accordance with other studies.[1,11] Shivering not only causes patient's discomfort and wound pain but can also lead to adverse effects, including increased oxygen consumption, lactic acidosis, raised carbon dioxide production and increased left ventricular systolic work index.[12] Because these physiological responses follow shivering, prevention would seem prudent, especially in vulnerable patients.

Current thermoregulatory theory does not completely explain the mechanisms of shivering following general anesthesia or regional anesthesia. Postanesthetic shivering is mostly due to a thermoregulatory effect in response to core and skin hypothermia and vasoconstriction in the perioperative period.[13] Active warming is one important intervention to prevent postanesthetic shivering in patients during surgery and maintain normothermia.[14] However, shivering occurs in normothermic patients as well.[15] The activity of thermoregulatory center is modulated by input from temperature receptors found in the skin, viscera and various levels of neuraxis.[13] Volatile anesthetic like isoflurane has been shown to produce shivering like tremor by modulation of the shivering threshold.[16,17] During anesthesia, patients are protected against thermoregulatory responses by lowering of the threshold for shivering and vasoconstriction. During recovery from anesthesia, thermoregulatory mechanism is no longer inhibited and shivering is triggered and becomes apparent when temperature is below the thermoregulatory threshold.[18] This effect was seen in this study, with patients who had not received any shivering prevention having a high 67% incidence of shivering. This is consistent with previous data.[11]

Clonidine is an established antishivering drug[19,20] and is one of the most frequently used substance in the prophylaxis and treatment of shivering. In several studies, sedative and cardiovascular effects of clonidine were noticed when a dose of 3 $\mu g.\ kg^{-1}$ was used.[11, 20] Other studies have shown that lower doses were also effective in the reduction of shivering.[1,12,21] Therefore, to minimize adverse effects, we decided to administer 2 $\mu g.kg^{-1}$ clonidine. This lower dose of clonidine used in the present study was effective in the prevention of shivering. Time spent in recovery room was similar in both groups and there were no significant differences on the Aldrete score on discharge.

A limitation of this study is that a dose-ranging of clonidine (3 $\mu g.kg^{-1}$, 2 $\mu g.kg^{-1}$, one dose of >3 $\mu g.kg^{-1}$ and one smaller dose <2 $\mu g.kg^{-1}$) regarding its optimal antishivering effect in this subset of patients have not been performed. Future studies may find the optimal dose of clonidine for this purpose.

From this study, we conclude that prophylactic administration of clonidine 2 $\mu g.kg^{-1}$ is effective and significantly decreases the incidence of postanesthetic shivering in patients undergoing LAVH. However, the sedative effects of clonidine prolonged the initial recovery time, when compared with placebo groups.

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