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Intravenous Pethidine versus Diclofenac Suppository in Shivering after Cesarean Section under Spinal Anesthesia

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ABSTRACT

Introduction: One of the most common surgeries on women is a cesarean section. Shivering is a prevalent adverse effect of spinal anesthesia following surgery. This study aimed to evaluate the effect of intravenous pethidine and diclofenac suppository on shivering after cesarean section under spinal anesthesia.

Methods: This double-blinded randomized clinical trial was conducted on 130 patients aged 20 to 40 years with ASA I, and II elective cesarean section candidates. Patients were randomly assigned to one of two groups receiving intravenous pethidine (group A) and diclofenac suppository (group B). Patients' shivering incidences using VAS measuring instrument at times; entry to the recovery room was measured at 30 and 60 minutes in recovery and 2, 4, and 6 hours after surgery.

Results: The incidence of shivering was significantly different between both groups at the beginning of recovery and 30, 60, and 120 minutes after surgery, and also its mean was lower in the group receiving suppository, but the severity of shivering was not significantly different between the two groups.

Conclusion: The results of the present study revealed that the diclofenac suppository significantly reduces shivering incidence and has a more appropriate effect than intravenous pethidine. Therefore, it is recommended to use a diclofenac suppository to reduce the incidence of shivering in subjects who have undergone a cesarean section.

GRAPHICAL ABSTRACT



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Introduction

Throughout various pregnancies, a cesarean section may be required due to a variety of circumstances. As a result, it's critical to select a low-risk, acceptable, and cost-effective anesthetic approach for the mother and infant. This surgery is performed using a multitude of techniques. One of the anesthesia methods is spinal anesthesia. This method has many advantages such as patient comfort, elimination of risks due to general anesthesia, shorter hospital stay, and postoperative pain control [1-2]. Shivering is among the adverse effects of spinal anesthesia, with an estimated incidence of 40% to 70% [3-4]. During shivering, increased oxygen consumption up to 600%, increased release of catecholamine's, followed by increased cardiac output, increased carbon dioxide production, and increased intraocular and intracranial pressure might happen [5-7]. Many pharmacological and non-pharmacological methods are used during cesarean section to control pain, nausea, vomiting, and shivering [8-11]. Increased oxygen demand of up to 600%, escalating catecholamine release, increased cardiac output, increased carbon dioxide generation, and elevated intraocular and intracranial pressure may occur during shivering [12]. Pharmacological methods in the treatment of shivering are the use of drugs such as nefopam, clonidine, physostigmine, ketanserin, magnesium sulfate, diclofenac sodium, and opioids, especially pethidine [13]. The results of studies have indicated the beneficial effect of drugs in controlling shivering and in some cases, the process of action of these drugs is different from the main effect of the drug [14]. Ebrahimi et al. compared the effects of diclofenac and pethidine on the frequency of shivering in individuals undergoing spinal anesthesia, figuring that diclofenac is more effective in preventing shivering [15]. Considering the ways to prevent shivering in C-section surgery is very important. This can be helpful in better treatment planning. Considering that there have been few studies on the comparison of the effect of intravenous pethidine with diclofenac suppository on shivering after cesarean section under spinal anesthesia in Iran,

in this study, we decided to evaluate this objective with the aspiration of providing effective steps towards improving the safety of mothers in C-section.

Methods

This was a double-blind randomized clinical trial recruiting 130 patients aged 20 to 40 years old with ASA I, II, who were candidates for elective cesarean delivery in Hormozgan Persian Gulf Hospital, in 2018. All patients were given the relevant details regarding the study after receiving authorization from the ethics committee of Hormozgan University of Medical Sciences (IR.HUMS.REC.1397.201). If they wished to participate in the trial, each individual signed an informed consent form. All ethical considerations related to the Helsinki principles were taken into account in this study. Patients who for any reason did not consent to the study had taken analgesics before surgery, contraindications to spinal anesthesia (high ICP, coagulation disorders, anticoagulants, and patients who had contraindications to NSAIDs or pethidine); ASA \geq 3, intraoperative hemorrhage, hysterectomy, and emergency patients were excluded. The sample size of 65 patients in each group was calculated based on the study of Sarvari et al. (16). Using a random number table, the patients were randomly assigned to one of two groups: intravenous pethidine (group A) or diclofenac suppository (group B), as displayed in Figure 1.

All patients underwent standard Non-invasive Blood Pressure (NIBP) recording, pulse oximeter, electrocardiogram, and capnograph monitoring before the onset of spinal anesthesia and after being placed on the operating table, and baseline hemodynamic parameters were measured and recorded. After intravenous administration, all patients were administered 7 cc/kg ringer serum at room temperature. The type of serum received was crystalloid and the operating and recovery room temperature was maintained at 21-23 °C. Then, the patients underwent spinal anesthesia by an anesthesiologist in a sitting position with 12.5 mg (2.5 cc) of marcaine 0.5% of the L4-L5 space with needle number 25. After the baby was born, group A received 0.5 mg/kg of intravenous

pethidine in a slow injection and group B was given a 100 mg diclofenac suppository. Before surgery, during surgery, and after surgery, arterial blood pressure, heart rate, and arterial blood oxygen saturation were measured and recorded every 5 minutes. 5 mg of intravenous ephedrine was prescribed for patient SBP<100 mmHg and 0.5 mg intravenous atropine for HR>60 mg. The study checklist included demographic variables (age, weight, and sex) and systolic and diastolic blood pressure, before and after surgery, and the incidence and severity of shivering at the time of entry into recovery, 30 and 60 minutes in recovery and 2, 4, and 6 hours after the operation

was measured. The extent of shivering was measured based on the visual instrument. The amount of shivering is further based on whether there is no vibration (zero), hair spiking or peripheral vasoconstriction (first degree), the presence of muscle shivering in only one muscle group (second degree), muscle shivering in more than one muscle group that occurs in a generalized way and does not stop (grade 3) and whole-body tremor (grade 4). The shivering assessment was conducted by an anesthesia resident who did not know the group of patients and was recorded in the ward by a midwife.

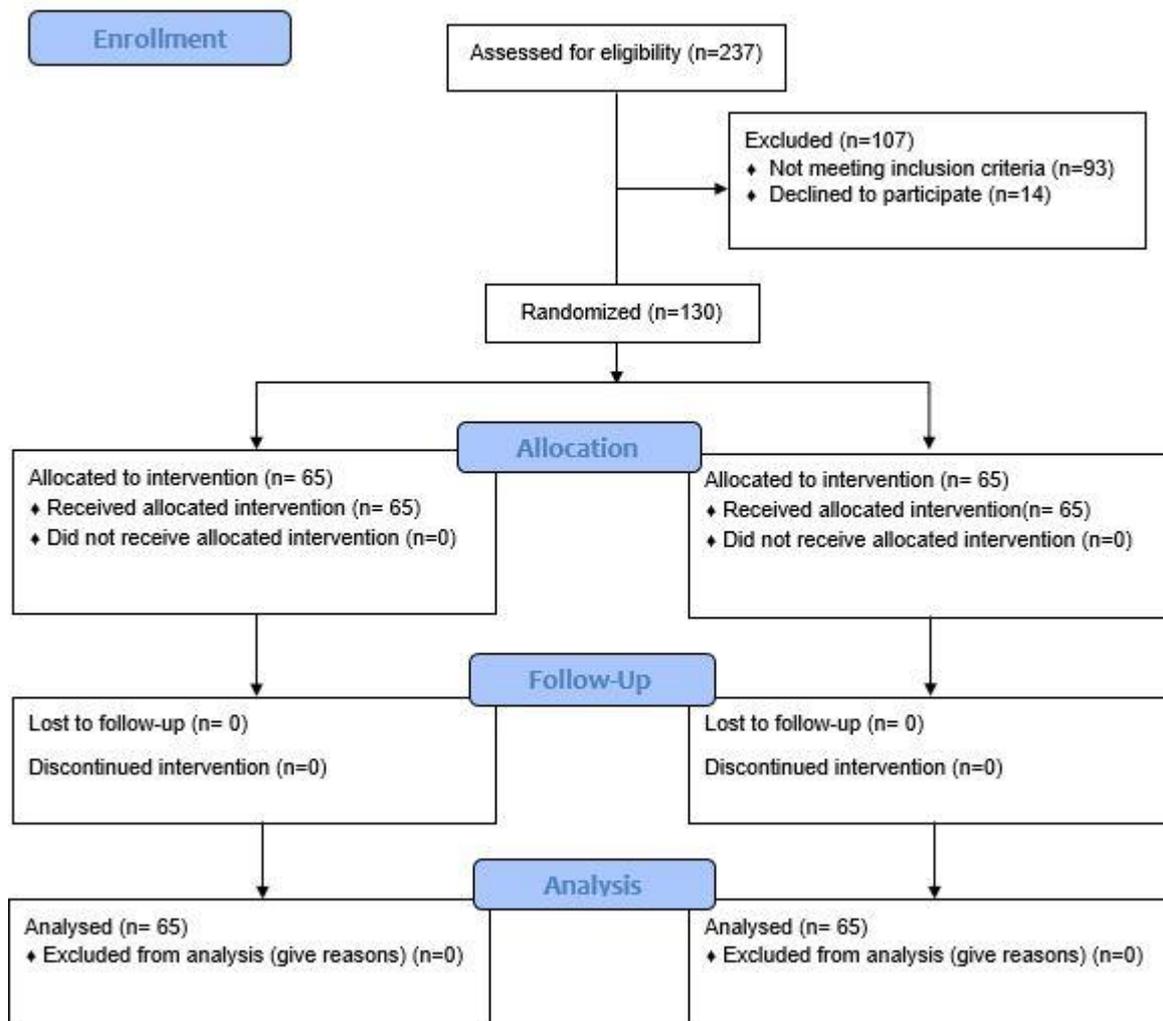


Figure 1: CONSORT flowchart of study

Data were analyzed using SPSS software version 19 and descriptive statistics (mean-standard deviation-percentage, etc.) and independent t-test, one-way ANOVA with repeated measures,

and chi-square. P-value <0.05 was considered the significant level.

Results

At the time of entering recovery, 16 patients in group A experienced shivering and 49 did not

have shivering. However, 7 patients in group B reported shivering and 58 patients did not have shivering, which was statistically significant between the two groups (P-value = 0.039). At 30, 60, and 120 minutes after surgery, there was a

significant difference in terms of shivering between the two groups (P-value <0.05). The average shivering were lower than those of pethidine (Table 1).

Table 1: Comparison of shivering at different postoperative times between the two groups

Shivering		Group				P-value
		Pethidine		Diclofenac		
		Number	Percent	Number	Percent	
Enter Recovery	No	49	75.4%	58	89.2%	0.039*
	Yes	16	24.6%	7	10.8%	
30 minutes after surgery	No	40	61.5%	55	84.6%	0.003*
	Yes	25	38.5%	10	15.4%	
60 minutes after surgery	No	31	47.7%	46	70.8%	0.007*
	Yes	34	52.3%	19	29.2%	
2 hours after surgery	No	39	60.0%	50	76.9%	0.038*
	Yes	26	40.0%	15	23.1%	
4 hours after surgery	No	46	70.8%	51	78.5%	0.314
	Yes	19	29.2%	14	21.5%	
6 hours after surgery	No	55	84.6%	59	90.8%	0.286
	Yes	10	15.4%	6	9.2%	

The mean intensity of shivering ranged from 1.38±0.62 in pethidine group and 1.43±0.53 in diclofenac group at entrance to recovery room (P=0.689) to 1.10±0.32 in pethidine and 0 in diclofenac group six hours after surgery

(P=0.439). There were no difference between the groups in mean intensity of shivering at any other times of 30 minutes, 2, and 4 hours after the surgery (P>0.05) (Table 2).

Table 2: Comparison of shivering in different postoperative times between the two groups

Intensity of shivering	Group				P-value	Test
	Pethidine		Diclofenac			
	Mean	SD	Mean	SD		
Enter Recovery	1.38	0.62	1.43	0.53	0.689	Mann-Whitney
30 minutes after surgery	1.52	0.51	2.40	2.72	0.548	Mann-Whitney
60 minutes after surgery	2.12	2.14	3.26	2.77	0.173	Mann-Whitney
2 hours after surgery	1.35	0.89	2.20	2.04	0.114	Mann-Whitney
4 hours after surgery	1.21	0.42	1.50	0.85	0.437	Mann-Whitney
6 hours after surgery	1.10	0.32	1.00	0.00	0.439	Mann-Whitney

In terms Operation time, Anesthesia time, and the number of pregnancy, there was no significant difference between the two groups. However,

when it comes to the average recovery time, there was a considerable difference between the two groups. As a result, group A spent more time recovery (Table 3).

Table 3: Investigation and comparison of other studied parameters in the two groups

Parameters	Group				P-value	Test
	Pethidine		Diclofenac			
	Mean	SD	Mean	SD		
Operation time	60.00	7.71	60.46	5.50	0.261	Mann-Whitney
Anesthesia time	71.69	6.81	69.85	5.52	0.250	Mann-Whitney
Recovery time	23.23	5.11	21.08	4.80	0.010*	Mann-Whitney
Number of pregnancy	2.26	1.09	2.14	1.03	0.603	Mann-Whitney

Discussion

Shivering after surgery and anesthesia is one of the unfavorable adverse events which can occur following both general and spinal anesthesia. Numerous studies have been conducted and several medications have been used in important to dissolve this problem and its negative consequences [16-20]. Shivering after spinal anesthesia can be caused by a drop in central body temperature caused by sympathetic system blockage, followed by dilatation of peripheral arteries and loss of percutaneous heat, or by a cool operating, recovery, or administration in room environment. In some cases, shivering happens after quick infusion of intravenous fluids [21].

The results of the proposed study indicated that the incidence of shivering was significantly different between the two groups at the beginning of recovery and 30, 60, and 120 minutes after surgery.

The most similar study was the one by Ebrahimi *et al.* that revealed better efficacy of diclofenac [15]. Bandari *et al.* indicated that diclofenac sodium suppository is effective in reducing postoperative shivering after cesarean section [22]. The effect of diclofenac suppository on shivering after general anesthesia in elective cesarean section was studied by Rostaminezhad *et al.* Their findings showed that diclofenac suppository group had much less shivering than the control group [23]. The findings of prior studies are consistent with the findings of this one. When compared to intravenous pethidine, diclofenac suppository dramatically reduced the incidence of shivering after cesarean surgery in this study. Diclofenac sodium appears to reduce shivering by suppressing the production of vasoconstrictors and cytokines, which are thought to be the cause of shivering. Diclofenac sodium suppresses

shivering by lowering the temperature difference between the core and the surface of the body [24].

The results of Sultan *et al.* study illustrated that pethidine is superior to diclofenac in reducing shivering [25]. Tilahun *et al.* compared the pethidine and tramadol on the incidence of postoperative shivering in the cesarean section under spinal anesthesia. The results of this study revealed that both tramadol and pethidine effectively control shivering in women undergoing cesarean section [26]; while Sahmeddini *et al.* indicated the better efficacy of tramadol in general anesthesia setting [27] as well as what Mohammadian Erdi *et al.* found [28]. In the comparison of pethidine, clonidine, and fentanyl, in the treatment of shivering after spinal anesthesia for elective cesarean section, pethidine had the best performance [29]. But Jabalameli *et al.* indicated better effects of intravenous dexamethasone than pethidine under spinal anesthesia [30].

The findings of the mentioned previous investigations contradict those of the current study. Pethidine did not lower the occurrence of shivering in this trial. Pethidine was shown to be either more or less effective than other medicines in reducing shivering in other studies that necessitate a network pooled analysis of the effects to rate medications.

Medications that interact with opioid receptors raise the shivering threshold. Shivering is influenced more by opioid receptors than by other receptors. Pethidine has a stronger antagonistic action on the κ -receptor and reduces shivering better than μ -receptor agonists like morphine, fentanyl, alfentanil, and sufentanil at identical dosages. As a result, pethidine's unique anti-vibration impact is linked to its effect on the opioid receptor [31].

Conclusion

Diclofenac suppository greatly lowers the incidence of shivering following intravenous pethidine and has a more suitable impact, according to the findings of this study. As a result, it is suggested that individuals who have had a cesarean section take a diclofenac suppository to prevent shivering.

Limitations

While we have recruited a good number of patients as our sample size, the baseline characteristics like the gestational age, gravida, and any factor related to the mother's emotional and psychological status might have biased the study that should be justified for further studies.

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Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

There are no conflicts of interest in this study.

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