ORIGINAL RESEARCH

Effects of perioperative administration of acetaminophen on postoperative shivering

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ABSTRACT
Shivering manifests as long-lasting fasciculation of the jaw, head, face or muscle hyperactivity. Post anesthetic shivering is a relatively common complication that can be stressful for patients and is occasionally associated with negative outcomes. Shivering increases oxygen consumption and the risk of hypoxemia. Data collection included a detailed history and a thorough clinical examination, and entry of information into the designed proforma. Patients were subjected to routine laboratory investigations (CBC, LFT, RFT, RBS, HIV, and HbsAg) and radiological investigations (Chest X-ray and ECG). There is no statistically significant difference between both groups regarding body temperature measured at forehead (BTF) at various intervals.

Key words: Perioperative administration, acetaminophen, postoperative shivering

INTRODUCTION

Shivering is a response characterized by oscillatory involuntary contractions of skeletal muscles that occurs during the early stages of recovery from anesthesia. Shivering is a frequent side effect of anesthesia and specific targeted temperature modulation[1]. Previous research has found an occurrence of 15% to 65% following general anesthesia and 30% to 33% following epidural procedures[2]. Shivering manifests as long-lasting fasciculation of the jaw, head, face or muscle hyperactivity[3]. Post anesthetic shivering is a relatively common complication that can be stressful for patients and is occasionally associated with negative outcomes[4]. Shivering increases oxygen consumption and the risk of hypoxemia.

A distinct rhythm in a typical cold tremor in the electromyography usually manifest in the form of grouped discharges. Shivering efferent signals descend along the medial forebrain bundle. Shivering occurs when there is cooling of hypothalamic preoptic region. The final pathway for shivering response and coordinated movement is through spinal alpha motor neurons along with their axons[5]. With consistent cold stimulation of the cutaneous skin or spinal cord, increasing size of motor neurons are recruited, beginning with small gamma motor neurons, then small alpha motor tonic neurons and lastly larger alpha motor phasic neurons[6,7].

Forced patient warming and medication use are the two methods for reducing shivering. Several therapies, including intravenous opioids, physostigmine, dexmedetomidine, ketamine, ondansetron, granisetron, clonidine, tramadol, dexamethasone, doxapram and ephedrine, have been researched for reducing shivering. Paracetamol lowers the hypothalamus temperature set point by a prostaglandin blockade that is centrally mediated[8].

Surgical patients who are unwarmed may become hypothermic due to anesthetic-induced thermoregulatory dysfunction and exposure to a cool environment. Hypothermia usually causes shivering. In the perioperative period, shivering may occur in normothermic patients. While cold-induced thermoregulatory shivering is the most obvious cause, the phenomenon has been linked to a variety of other factors, including pain, disinhibited spinal reflexes, decreased sympathetic activity, respiratory alkalosis, pyrogen release, and adrenal suppression[9]. Muscle activity may rise even in the post-surgery period despite retaining normothermia, indicating that causes other than heat loss and the resulting reduction in core temperature may be associated in the development of shivering.

Different frequencies have been recorded for shivering, which can occur as a thermoregulatory reaction tocold or muscleexcitation with clonic or tonic patterns. Postoperative shivering is linked to the surgical wound's release of pyrogenic mediators. Post-anesthetic shivering risk factors include young age, core hypothermia, and endoscopic surgery[10].
Perioperative hypothermia is described as a core body temperature of 33°C to 35°C, while in the non-anesthetized shivering threshold is about 35.5°C. Anesthetic drugs raise the thresholds to heat while decreasing thresholds to cold, increasing the normal inter-threshold range (hypothalamic set-point)[11]. Shivering is precipitated bypain in postanesthetic patients and also in women experiencing spontaneous term labour. The thermoregulation mechanism is inextricably linked to various homeostatic systems like pain control. Pain and temperature sensation are transmitted by synaptic fiber signals in the dorsal horn. The rostral ventromedial medulla controls cooling-induced thermoregulation and peripheral heat, as well as analgesia in reaction to painful stimuli. Through gating the communication of neuronal signals at the dorsal horns level, the rostral ventromedial medulla is important for modulating the amount of pain and temperature feedback ascending from the spinal cord [12].

METHODOLOGY

STUDY POPULATION

Those scheduled for lower abdominal procedures under spinal anesthesia.

STUDY DESIGN

Randomized control trial.

SAMPLE SIZE

60 patients (30 in each group).

MODE OF SELECTION OF SUBJECTS

60 patients are randomly allotted into 2 groups, who fit into the inclusion criteria.

Group "A": Acetaminophen group.

Group "P": Placebo group.

INCLUSION CRITERIA

1. ASA Grade 1 & 2 patients.
2. Patients scheduled for gynecology, lower abdominal and orthopedic surgeries under spinal anesthesia who have given consent.

EXCLUSION CRITERIA

1. Patients having liver dysfunction (Aspartate transaminase >35 IU/L; Alanine transaminase >35 IU/L)
2. Patients having obesity (BMI - >35kg/m²)
3. Patients allergic to acetaminophen.

EQUIPMENT UTILIZED

1. Thermometer.
2. Multi parameters measuring monitors (SpO2, NIBP, HR, PR).
3. Acetaminophen and Normal Saline 0.9%.

STUDY METHODS

- **PATIENT SCREENING AND OBTAINING INFORMED CONSENT**

All the patients posted for gynecology, lower abdominal and orthopedic surgeries under spinal anesthesia during the study period were evaluated. Patients were explained about the study being performed and informed written consent obtained.

- **STUDY PROFORMA AND BASELINE INVESTIGATIONS**

Data collection included a detailed history and a thorough clinical examination, and entry of information into the designed proforma. Patients were subjected to routine laboratory investigations (CBC, LFT, RFT, RBS, HIV and HbsAg) and radiological investigations (Chest X-ray and ECG).

- **PATIENT ALLOCATION PROCEDURE**

Patients were subjected to systematic block randomization and divided into 2 groups.

1. **Group A:** Acetaminophen administered as a test drug.
2. **Group P:** Placebo (Normal Saline) administered as a test drug.

After randomization, all 60 patients were allocated into one of the following groups of 30 each, after giving spinal anesthesia,

- Group A (n = 30) was given intravenous acetaminophen of 15 mg/kg over 15 minutes.
- Group P (n = 30) was given intravenous 0.9% normal saline of 15 ml/kg over 15 minutes.

The BTF and BTA were recorded using the thermometer as follows:
T0 - Before anesthesia (spinal anesthesia) induction.
T1 - At the initiation of surgery.
T2 - At the end of surgery.
T3 -At the initiation of postoperative observation in the PACU.
T4 - 30 minutes after T3.
T5 - At 1 hour after T4 (i.e., time 5 [T5]).

Postoperative shivering was estimated using the shivering score.

RESULTS

Table 1: Comparison of OT/PACU temperatures among the groups

	Acetaminophen group (n=30)		Placebo group (n=30)		P-value
	Mean	SD	Mean	SD	
T0	24.53	2.19	24.45	1.80	0.87
T1	24.53	2.19	24.46	1.82	0.88
T2	24.53	2.19	24.45	1.80	0.87
T3	28.33	3.65	27.43	2.90	0.29
T4	28.46	3.72	27.43	2.84	0.23
T5	28.46	3.72	27.43	2.84	0.23

- The mean OT/PACU temperature for the acetaminophen group is 26.86 $\pm$ 3.67 ºC.
- The mean OT/PACU temperature for the placebo group is 26.24 $\pm$ 2.86ºC.
- There is statistically no significant difference between both groups regarding themaintenance of OT/PACU temperature at any measurement time.

Table 2: Comparison of shivering score among the groups

	Acetaminophen group (n=30)		Placebo group (n=30)		P-value
	Mean	SD	Mean	SD	
T0	0	0	0.06	0.25	0.15
T1	0.06	0.25	1.26	1.08	<0.001
T2	0.16	0.59	1.16	0.98	<0.001
T3	0.03	0.18	0.5	0.62	<0.001
T4	0	0	0.06	0.25	0.15
T5	0	0	0	0	

Thereisstatisticallysignificantdifferenceregardingshivering score with acetaminophen group showing less score compared to placebo group.

Table 3: Comparison of severe shivering among the groups

	Acetaminophen group (n=30)	Placebo group (n=30)	P-value
Severe Shivering	3	21	<0.001
No Shivering	27	9	

There is statistically significant difference regarding severe shivering with shivering more in placebo group compared to acetaminophen group.

Table 4: Comparison of BTF among the groups

	Acetaminophen group (n=30)		Placebo group (n=30)		P-value
	Mean	SD	Mean	SD	
T0	96.96	1.63	97.28	0.80	0.33
T1	97.33	0.85	96.92	1.12	0.12
T2	97.25	0.70	97.01	0.99	0.29
T3	97.27	0.70	97.09	0.88	0.38
T4	97.20	0.74	97.22	0.80	0.94
T5	97.30	0.69	97.18	0.80	0.51

There is no statistically significant difference between both groups regarding body temperature measured at forehead (BTF) at various intervals.

Table 5: Comparison of BTA among the groups

	Acetaminophen group (n=30)		Placebo group (n=30)		P-value
	Mean	SD	Mean	SD	
T0	97.6	0.85	97.45	0.90	0.53
T1	97.5	0.85	97.2	0.87	0.18
T2	97.49	0.68	97.28	0.82	0.28
T3	97.46	0.73	97.20	1.09	0.27
T4	97.33	0.74	97.35	0.84	0.91

T5	97.39	0.69	97.45	0.86	0.78

- There is no statistically significant difference between both groups regarding body temperature measured at axilla (BTA) at various intervals.

DISCUSSION

The core body temperature measured at axilla at various intervals had no statistically significant difference between both groups in our study. This is not evaluated in other studies. Hence, further studies are required to validate these results.

In this study, the mean BTF at T0 is 36.08 ºC and the standard deviation of 1.63 in the acetaminophen group. The mean BTF at T0 is 36.26 ºC and the standard deviation of0.80 in the placebo group. These findings are similar with studies done by Kinjo T*et al*.[13] and Shirozu K *et al*.[14] which is statistically insignificant.

In this study, the mean BTF at T3 is 36.26 ºC and the standard deviation of 1.63 in acetaminophen group. The mean BTF at T3 is 36.16 ºCand the standard deviation of0.80 in the placebo group. These findings showed similarity with studies by Rasoli S *et al*.[15] and Gholami A *et al*.[8] which is statistically insignificant.

In our study, shivering scores showed at any period of time during shivering showed less incidence of postoperative shivering in the Acetaminophen group which is statistically significant. These findings are coinciding with studies done by Esmat IM *et al*.[16] and Gholami A *et al*.[8]

In our study, the incidence of severe shivering in the acetaminophen group is 10%, while in the placebo group is 70% which is statistically significant. These findings correlated with studies done by Kinjo T *et al*.[13], Esmat IM *et al*.[16] and Gholami A *et al*.[8] This shows that acetaminophen plays a significant role in lowering the risk of post- operative shivering.

In our study, patients who got acetaminophen had less shivering after surgery than the placebo group (RR= 0.14, 95% CI, 0.01-0.19). This is corresponding to studies done by Kinjo T *et al*.[13], Esmat IM *et al*.[16], and Shirozu K *et al*.[14].

Conclusion

- Perioperative paracetamol administration is effective in reducing incidence and severity of postoperative shivering up to 90 minutes in patients undergoing lower abdominal surgeries under spinal anesthesia compared to a placebo.
- However, further studies are needed to validate these results and also effectiveness of perioperative paracetamol in reducing the shivering up to 10 hours after surgery.

REFERENCES

1. Choi KE, Park B, Moheet AM, Rosen A, Lahiri S, Rosengart A.Systematic Quality Assessment of Published Antishivering Protocols. Anesth Analg 2017; 124: 1539- 1546.
2. Buggy DJ, Crossley AW. Thermoregulation, mild perioperative hypothermia and postanesthetic shivering. Br J Anesth 2000; 84: 615-628.
3. Crossley AW. Six Months of shivering in a district general hospital. Anesthesia 1992; 47: 845-848.
4. Eberhart LHJ, Döderlein F, Eisenhardt G, Kranke P, Sessler DI, Torossian A, *et al*. Independent risk factors for postoperative shivering. Anesth Analg [Internet]. 2005;101(6):1849–57.
5. Henneman E. Organization of the motoneuron pool: The size principle. In: Mountcastle VB, editor. Medical Physiology. 14thed St. Louis: CV Mosby; 1980: 718-741.
6. Klussmann FW, Spaan G, Stelter HJ, Rau B. Synchronization of motor neuron discharges during shivering. Pflügers Arch 1969; 312: R108.
7. Lupandin IV. Regulation of the function of gamma- and alphamotor neurons of antagonist muscles during cold tremor in the cat. Neirofiziologiia 1983; 15: 242-248.
8. Gholami A, Hadavi M. Prophylactic intravenous paracetamol for prevention of shivering after general anesthesia in elective cesarean section. J Obstet Anesth Crit Care [Internet]. 2016 Jul 1;6(2):81.
9. Kranke P, Eberhart LH, Roewer N, Tramèr MR. Pharmacological treatment of postoperative shivering: A quantitative systematic review of randomized controlled trials. Anesth Analg [Internet]. 2002;94(2):453–60.
10. Li X, Zhou M, Xia Q, Li W, Zhang Y. Effect of parecoxib sodium on postoperative shivering: A randomised, double-blind clinical trial. Eur J Anesthesiol. 2014 Apr;31(4):225–30.
11. Sankar-Maharaj S, Chen D, Hariharan S. Postoperative shivering among cannabis users at a public hospital in Trinidad, West Indies. J Perianesth Nurs 2018; 33: 37- 44.
12. Grahn DA, Heller HC. Activity of most rostral ventromedial medulla neurons reflect EEG/EMG pattern changes. Am J Physiol. 1989 Dec;257(6 Pt 2):R1496-505.
13. Kinjo T, Tadokoro T, Tokushige A, Zamami T, Taira S, Ikehara Y, *et al*. Effects of perioperative administration of acetaminophen on postoperative shivering: Arandomized,triple-blind, placebo-controlledtrial.AnesthAnalg.2020Apr;130(4):983–90.
14. Shirozu K, Umehara K, Ikeda M, Kammura Y, Yamaura K. Incidence of postoperative shivering decreased with the use of acetaminophen: a propensity score matching analysis. J Anesth. 2020 Jun;34(3):383–9.
15. Rasoli S, Ansari E, Moslemi F, Ghojazadeh M. The Prophylactic Administration of Intravenous Paracetamol for Control of Shivering During and AfterCesarean Section under Spinal Anesthesia.

Arch Anesth Crit Care [Internet]. 2019 Apr 7;5(2 SE-Research Article(s)).
16. Esmat IM, Mohamed MM, Abdelaal WA, El-Hariri HM, Ashoor TM. Postspinal anesthesia shivering in lower abdominal and lower limb surgeries: a randomized controlled comparison between paracetamol and dexamethasone. BMC Anesthesiol [Internet]. 2021;21(1):262.