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Original Research Article

Prevention of postspinal anesthesia shivering in lower abdominal surgeries: a randomized controlled study between mirtzapine and dexamethasone

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Abstract: ***Introduction:*** Spinal anesthesia (SA) is a safe anesthetic technique used for both elective and emergency operations. Shivering is known to be a frequent complication in patients undergoing surgery under neuraxial anesthesia with incidence of 40–70%. SA inhibits tonic vasoconstriction and causes redistribution of core heat from the trunk (below the block level) to the peripheral tissues predisposing patients to hypothermia and shivering. Post spinal anaesthesia shivering (PSAS) is an involuntary, repetitive activity of skeletal muscles as a physiological response to core hypothermia to raise the metabolic heat production. PSAS increases O2 consumption, CO2 production, plasma catecholamines and cardiac output. Shivering may interfere with the monitoring of ECG, blood pressure and oxygen saturation. Te mainstay of prophylaxis and treatment of PSAS remain pharmacological due to inadequate control of central hypothermia by techniques based on physical principles (e.g., intravenous infusion (IVI) of warm fluids and forced air warmers). It appears logical to prevent PSAS rather than to treat it once it develops. ***Methods:*** Study Population. (Is study was conducted between over a period of 6 months, after approval of the local ethical committee on 330 women, aged 18–60 years and ASA I or II scheduled for elective gynaecological surgeries under SA. Every patient who chose to participate in this research signed a consent. Exclusion criteria were diabetes mellitus, thyroid disease, cardiopulmonary disease, bleeding tendencies, neurologic disease, psychological disorders, liver dysfunction, a body mass index (BMI) >35 kg/m2, body temperature 38.0° C, history of substance abuse, treatment with sedative hypnotic agents, medications altering thermoregulation, vasodilators, allergy to the study medications, and contraindications to SA. Patients were also ruled out if they refused to participate in clinical research, required blood transfusion during procedure, or had operation time >120 min. If patients did not achieve satisfactory bilateral sensory block level or Bromage score 3 motor blockade, they received general anaesthesia and were excluded from this research. ***Result:*** Among the 356 female patients who were screened for eligibility, 330 patients were properly enrolled and subjected to statistical analysis. There were no statistically significant differences in demographics or confounders between the 3 groups. More patients in M and C groups reached the peak sensory level in a significantly long period of time compared to D group ($P < 0.001$) with no significant difference between M and C groups. D group patients had a significantly more time for two-segment regression and a significantly more time for rescue analgesia in comparison to M and C groups with significant differences between M and C groups ($P < 0.001$, $P < 0.001$, respectively). There were no significant differences between groups as regards the peak sensory level, the time to reach maximum motor block, and the duration of motor block ($P = 0.390$, $P = 0.064$, $P= 0.067$, respectively). ***Conclusion:*** Paracetamol and dexamethasone were effective in prevention of PSAS in patients undergoing lower abdominal and lower limb surgeries under spinal anaesthesia compared to placebo controls. Our results indicated that decreasing the threshold of shivering might be more important than increasing the core temperature in terms of preventing PSAS with less adverse events.

Keywords: Paracetamol, Dexamethasone, PSAS, Surgeries, Postoperative shivering, Spinal anaesthesia.

INTRODUCTION

Spinal anaesthesia (SA) is a safe anaesthetic technique used for both elective and emergency operations. Shivering is known to be a frequent complication in patients undergoing surgery under neuraxial anaesthesia with incidence of 40–70%. SA inhibits tonic vasoconstriction and causes redistribution of core heat from the trunk (below the block level) to the peripheral tissues predisposing patients to hypothermia and shivering. Post spinal anaesthesia shivering (PSAS) is an involuntary, repetitive activity of skeletal muscles as a physiological response to core hypothermia to raise the metabolic heat production. PSAS increases O2 consumption, CO2 production, plasma catecholamines and cardiac output. [1] Shivering may interfere with the monitoring of ECG, blood pressure and oxygen saturation. The mainstay of prophylaxis and treatment of PSAS remain pharmacological due to inadequate control of central hypothermia by techniques based on physical principles

(e.g., intravenous infusion (IVI) of warm fluids and forced air warmers). It appears logical to prevent PSAS rather than to treat it once it develops. [2]

Paracetamol [Acetaminophen (ACT)] is an effective, safe synthetic non-opioid analgesic and antipyretic. Acetaminophen acts by inhibiting cyclooxygenase-mediated prostaglandin synthesis to decrease the hypothalamic temperature set point. Although the onset of action of IV paracetamol is much faster compared with its oral form and bioavailability is 63–84% of administered dose, there were no significant difference in overall efficacy between the two routes. [3] Rectal administration of acetaminophen proved to be effective for prevention of shivering in the therapeutic hypothermia.

Dexamethasone has an anti-inflammatory, analgesic effects and significantly improved the duration of sensory block in spinal anaesthesia when added to hyperbaric bupivacaine. The use of preoperative dexamethasone (8mg), with a biologic half-life of 36–72h, improved post discharge quality of recovery and decreased nausea, vomiting, pain, and fatigue in the early postoperative period. [4,5] As it reduces the gradient between skin and body core temperature and modifies the inflammatory response, dexamethasone has been reported to be effective in reducing shivering after cardiac surgeries. Dexamethasone may cause unpleasant symptoms following rapid IV injection.

The aim of this study was to evaluate the efficacy of a prophylactic dose of 1g oral paracetamol tablet compared with a prophylactic dose of 8mg dexamethasone IVI to prevent shivering in patients undergoing lower abdominal and lower limb surgeries under spinal anaesthesia abdominal or lower limb surgeries under spinal anaesthesia. [6]

METHODS

Study Population. (Is study was conducted over a period of 6 months, after approval of the local ethical committee on 330 women, aged 18–60 years and ASA I or II scheduled for elective gynaecological surgeries under SA.

Exclusion criteria were diabetes mellitus, thyroid disease, cardiopulmonary disease, bleeding tendencies, neurologic disease, psychological disorders, liver dysfunction, a body mass index (BMI) >35 kg/m2, body temperature 38.0° C, history of substance abuse, treatment with sedative hypnotic agents, medications altering thermoregulation, vasodilators, allergy to the study medications, and contraindications to SA. Patients were also ruled out if they refused to participate in clinical research, required blood transfusion during procedure, or had operation time >120 min. If patients did not achieve satisfactory bilateral sensory block level or Bromage score 3 motor blockade, they received general anaesthesia and were excluded from this research.

All selected patients underwent routine preoperative medical check, preoperative and postoperative haemoglobin concentration analysis, 6 h preoperative fast for solid food, and 2 h preoperative fast for clear fluids.

Randomization and Blinding. Patients were randomized into 3 groups (110 each) in a 1 :1 :1 allocation ratio in accordance with shivering prevention protocol using computer-generated random numbers concealed in sealed opaque envelopes, and a nurse randomly chose the envelope to determine the assigned group. Patients were allocated to mirtazapine (M) group, dexamethasone (D) group, or control (C) group and obtained shivering prophylaxis protocol 2 h before surgery. In M group, patients obtained 30 mg mirtazapine tablet with sips of water and an identical looking placebo 100 ml 0.9% sodium chloride (normal saline [NS]) intravenous infusion (IVI) over 15 minutes. In D group, patients obtained 8 mg/2 ml dexamethasone ampoule mixed with 100 ml 0.9% NS IVI over 15 minutes and an identical-looking placebo tablet, whereas in C group patients obtained an identical-looking placebo tablet and solution.

Intervention drugs, including mirtazapine and dexamethasone, were in the form of Remeron® tablets manufactured by Organon NV/Netherlands and Dexamethasone Sodium Phosphate® 8 mg/2 ml, ampoules, MUP Egypt. The hospital pharmacy was responsible for preparation of the study drugs which were delivered to ward nurses to be given to patients. Follow-up notes were documented by anaesthesia residents. Patients, ward nurses, gynaecologists, and anaesthesia residents were blinded to the patient's group assignment.

Study Protocol. The research team applied the same anaesthetic management and the same quality of care to all patients involved in this study. Before commencing SA, no premedication was given, standard monitoring was established including tympanic membrane (core) temperature (T), and each patient received 10 ml/kg IV Ringer's lactate preload. Core temperature was measured by Braun (ermo Scan® IRT 4020 ear thermometer. Operating room temperature was provided in a range of 23–25° C and 60 to 70% relative humidity. Hypothermia was developed if the core temperature dropped below 36.5°C.

Intrathecal block was performed at L3-4 or L4-5 interspace through the midline approach with patient in sitting position using a 25-gauge Quincke spinal needle. (e attending anaesthesiologist injected 2.5–3.5 ml (12.5–17.5 mg) of 0.5% hyperbaric bupivacaine to reach the desired surgical level taking into consideration patient's height and weight. By the end of

SA technique, the patient lied supine, an oxygen face mask was applied at a rate of 5 L/min, covered with a standard single blanket and did not receive any active perioperative warming.

Pinprick test was used to assess the peak sensory level, time to reach this level (min), and time to two-segment regression (min) after the intrathecal bupivacaine administration (starting point of this research). Anaesthesia residents reported success of SA if a bilateral T4-T8 sensory 2 Anaesthesiology Research and Practice block to pinprick test within 15 min of intrathecal drug administration happened and they also documented time to rescue analgesia (min). Motor block was evaluated by using modified Bromage score to determine time to reach maximum motor block (Bromage score 3) (min) and duration of motor block (min).

Hemodynamic of patients including heart rate (HR), mean arterial pressure (MAP), peripheral arterial oxygen saturation (SPO2%) and T were documented before intrathecal injection (baseline) and thereafter at 2 and every 5 min till the first 30 minutes after SA and then at 10-minutes intervals till 90 min after SA (ending point of the study). Shivering severity was assessed by a scale of 4 grades 0; no shivering, 1; mild shivering, 2; moderate shivering, 3; severe shivering. Two anaesthesia residents, unaware of the study intervention allocation, documented the grades of shivering till 90 min after the subarachnoid block. If the shivering grade developed to equal or more than 2 (clinically significant PSAS) after 15 min from the completion of SA, the preventive protocol for PSAS was considered inefficient and 25 mg IV meperidine was administered. Onset of shivering, response rate, and shivering recurrence were also reported. Response rate is the complete suspension of shivering activity within 10 min after the first dose of meperidine. Satisfaction of patients with shivering prevention protocol was evaluated with seven-point Likert rating scale.

The research team documented any adverse events including hypotension (MAP 10 min) and/or vomiting (≥2 episodes) were treated with 10 mg IV metoclopramide. Pruritus was managed with 2 mg IV clemastine (Tavegyl®). Sedation was evaluated every 15 min over 90 min after SA and was assessed with a scale of four points as per Filos et al. (e research team members collected blood samples from all patients preoperatively and one week after surgery to compare liver enzymes level (SGPT).

The incidence of clinically significant PSAS occurring during the first 90 min after SA was considered as a primary outcome. Secondary outcomes included evaluation of core temperature, shivering profile, satisfaction of patients with shivering prophylaxis protocol, and adverse events.

STATISTICAL ANALYSIS

Power of the Study. Based on earlier research, a sample size of 19 cases in every group was required to keep a statistical significance when the expected incidences among the three groups were as follows: group C (33.3%), group P (0.0%), and group D (0.0%) with adjusting α=0.017, β = 0.80 [23] and calculating with PASS 11th release. The research team allocated 100 cases for each study group to account for possible attrition and to detect possible adverse effects.

DATA ANALYSIS

The gathered data were managed and analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) program 22.0th release, IBM Corp., Chicago, USA, 2013. Quantitative data were described as mean ± SD (standard deviation) and then were compared using ANOVA test and repeated measures analysis of variance (RMANOVA) if normally distributed. If data were not normally distributed, median and 1st & 3rd interquartile range were used for description and Kruskal Wallis test for comparison. While in conditions of qualitative data, number and percentage were used for description and each of chi square test and Fisher's exact test for comparisons depending on expected number size. Rates were compared using Log rank test. P- value <0.050 was set as a significance cut point. Bonferroni test was used for post hoc comparisons.

RESULT

Among the 356 female patients who were screened for eligibility, 330 patients were properly enrolled and subjected to statistical analysis. There were no statistically significant differences in demographics or confounders between the 3 groups (Table 1).

More patients in M and C groups reached the peak sensory level in a significantly long period of time compared to D group ($P < 0.001$) (Table 1) with no significant difference between M and C groups. D group patients had a significantly more time for two-segment regression and a significantly more time for rescue analgesia in comparison to M and C groups with significant differences between M and C groups ($P < 0.001$, $P < 0.001$, respectively) (Table 1). There were no significant differences between groups as regards the peak sensory level, the time to reach maximum motor block, and the duration of motor block ($P = 0.390$, $P = 0.064$, $P= 0.067$, respectively) (Table 1).

Table 1: Patients' demographics and perioperative data

Items	M group (*n* 110)	D group (*n* 110)	C group (*n* 110)	*P* value
Age (year)	44.5 ± 7.9	44.9 ± 7.4	42.9 ± 7.2	^0.141
BMI (kg/m2)	30.6 ± 1.5	30.7 ± 1.6	30.4 ± 1.7	^ 0.289
ASA (I/II)	27/75	28/72	30/70	# 0.890
Dose of bupivacaine (mg)	14.9 ± 1.9	15.1 ± 1.9	15.4 ± 2.1	^0.198
Operation time (min)	113.9 ± 14.4	113.6 ± 13.6	112.5 ± 13.7	^0.762
Types of operations; n, % (i) Total abdominal hysterectomy (TAH)	15 (13%)	14 (13%)	13 (12%)	
TAH + BSO Vaginal hysterectomy (VH)	43 (39%) 10 (9%)	46 (42%) 13 (12%)	43 (39%) 9 (8%)	# 0.998
(iv) VH + PFR	30 (27%)	30 (27%)	30 (27%)	
(v) Vesicovaginal fistula repair	12 (11%)	7 (6%)	15 (13%)	
Preoperative Hb (g/dl)	12.4 ± 0.4	12.1 ± 0.4	12.2 ± 0.4	^0.142
Postoperative Hb (g/dl)	9.3 ± 0.5	9.3 ± 0.4	9.4 ± 0.4	^ 0.341
Total IV fluids used (ml)	2035.0 ± 111.4	2007.0 ± 117.4	2023.0 ± 116.2	^ 0.226
Characteristics of neuraxial anaesthesia techniques Peak sensory level	T5 (T4–T8)	T6 (T4–T8)	T6 (T4–T8)	§ 0.391
Time to peak sensory level (min)	6.6 ± 0.6a	4.7 ± 0.6b	6.8 ± 0.6a	^∗<0.001
Time to two-segment regression (min)	63.3 ± 1.7a	77.2 ± 1.4b	69.4 ± 1.2c	^∗<0.001
Time to reach maximum motor block (min)	9.3 ± 0.4	9.2 ± 0.5	9.3 ± 0.4	^ 0.065
Duration of motor block (min)	135.3 ± 2.4	135.8 ± 2.2	135.5 ± 2.3	^ 0.068
Time to rescue analgesia (min)	173.8 ± 4.1a	321.4 ± 4.8 b	215.7 ± 4.4c	^∗<0.001

Data were presented as median (range), mean (SD), numbers, and percent. ^ ANOVA test, # chi square test, and § Kruskal Wallis test. Labels (a, b, c) denote homogenous groups depending on post hoc Bonferroni test. ∗Statistically significant. TAH + BSO: total abdominal hysterectomy with a bilateral salpingo-oophorectomy. PFR: pelvic floor repair. M group: mirtazapine group; D group: dexamethasone group; C group: control group.

Alterations of heart rate were comparable between the three groups till 90 min after SA ($P > 0.05$). More cases in M and D groups exhibited higher MBP values till 25 min after SA in comparison to C group ($P < 0.001$) with comparable efficacy between M and D groups. Alterations of SpO2 (%) were comparable between the three groups till 90 min after SA ($P > 0.05$). Core temperature values 90 min after SA were significantly decreased in the three groups in comparison to baseline values ($P < 0.001$) without significant difference when compared to each other ($P > 0.05$).

In C group, the incidence of shivering was higher whereas the onset of shivering was lower than the other two groups with significant differences between M and D groups ($P < 0.001$, $P < 0.001$, respectively) (Table 2). The incidence of clinically significant shivering was higher in C group (74.0%) in comparison to M group (16.0%) and D group (31.0%) with significant differences between M and D groups ($P < 0.001$) (Table 2). In C group, the mean dose of meperidine was higher whereas the response rate after single dose of meperidine was lower than the other two groups with significant differences between M and D groups ($P < 0.001$, $P = 0.002$, respectively) (Table 2). The recurrence of shivering was recorded in 9/31 (29.0%) patients of D group and in 33/74 (44.6%) patients of C group; on the contrary, no recurrence of shivering was documented in M group ($P = 0.002$) (Table 2).

Table 2: Incidence, grades, and treatment of post spinal anaesthesia shivering among the studied groups

Time points	M group (*n* 110)	D group (*n* 110)	C group (*n* 110)	*P* value
Incidence of shivering; *n*, %	46 (42%) a	68 (62%) b	96 (87%) c	#∗<0.001
Grade; n, % (i) 0	64 (58%) a	43 (38%) b	14 (13%) c	
I II	28(25%) a 12 (11%) a	34 (31%) a 22 (20%) a	20 (18%) a 46 (42%) b	#∗<0.001
(iv) III	7 (6%) a	14 (13%) a	34 (31%) b	
Patients with clinically significant shivering (Grade ≥2); *n*, %	17 (16%) a	34 (31%) b	77 (70%) c	#∗<0.001
Onset of shivering (min)	52.3 ± 5.3 a	33.8 ± 3.6 b	17.0 ± 5.5 c	^∗<0.001
Dose of meperidine (mg)	26.1 ± 1.3 a	32.3 ± 4.8b	37.1 ± 3.6 c	^∗<0.001
Response rate after administration of 1st dose of meperidine; *n*, %	17 (100%) a	24 (71%) b	43 (55.8%) b	#∗0.002
Recurrence; *n*, %	0 (0.0%) a	10 (29%) b	34 (44.2%) b	#∗0.002

Data were presented as numbers and percent. # Chi square test and ^ ANOVA test. Labels (a, b, c) denote homogenous groups depending on post hoc Bonferroni test. ∗Statistically significant. M group: mirtazapine group; D group: dexamethasone group; C group: control group.

In C group, incidence of post spinal anaesthesia (PSA) hypotensive episodes, the administered ephedrine, and the need for ephedrine to treat hypotension were more frequent than the other two groups with comparable efficacy between M and D groups (P < 0.001, P < 0.001, P < 0.001 respectively) (Table 3). Incidences of pruritus, nausea, vomiting, and use of rescue antiemetic were higher in C group than the other two groups with comparable efficacy between M and D groups (P < 0.001, P < 0.001, P < 0.001, P < 0.001, respectively) (Table 3). In M group, sedation scores and incidence of dry mouth were higher than the other two groups (P < 0.001, P < 0.001, respectively) (Table 3) with no statistically significant differences between D and C groups. More patients in M and D groups were satisfied with shivering prophylaxis protocol in comparison to C group (P < 0.001) (Table 3) with comparable efficacy between M and D groups.

Table 3: Side effects, administered treatments, and patient satisfaction score

Time points	M group (*n* 110)	D group (*n* 110)	C group (*n* 110)	*P* value
Bradycardia; *n*, %	8 (7%)	10 (9%)	8 (7%)	# 0.858
Hypotension; *n*, %	8 (7%) a	10 (9%) a	29 (26%) b	#∗<0.001
Need for ephedrine; *n*, %	29 (26%) a	34 (31%) a	81 (74%) b	#∗<0.001
Ephedrine dose (mg)	11.1 ± 3.2 a	15.4 ± 4 a	22.1 ± 6.8 b	^∗**<0.001**
Pruritus; *n*, %	3 (2.7%) a	12 (11%) a	26 (24%) b	#∗<0.001
Nausea; *n*, %	5 (4.5%) a	6 (5.4%) a	29 (26%) b	#∗<0.001
Vomiting; *n*, %	3 (2.7%) a	4 (3.6%) a	18 (16.4%) b	#∗<0.001
Rescue antiemetic; *n*, %	4 (3.6%) a	5 (4.5%) a	25 (23%) b	#∗<0.001
Sedation; n, % (i) I	8 (7%) a	110 (100%) b	110 (100%) b	
II III	87(79%) 10 (9%)	0 (0) 0 (0)	0 (0) 0 (0)	#∗<0.001
(iv) IV	0 (0)	0 (0)	0 (0)	
Headache; *n*, %	8 (7%)	5 (4.5%)	6 (5.4%)	#0.810
Dry mouth; *n*, % Elevated liver enzymes; *n*, %	24 (22%) a 4 (3.6%)	9(8%) b 2 (1.8%)	12 (11%) b 2 (1.8%)	#∗**0.007** ⌂0.625
Patient satisfaction score	5.0 (5-6) a	5.0 (4–6) a	2.0 (2-3) b	§∗<0.001

Data were presented as median (range), mean (SD), numbers, and percent. # Chi square test, ^ ANOVA test, § Kruskal Wallis test, and ⌂ Fisher's exact test. Labels (a, b, c) denote homogenous groups depending on post hoc Bonferroni test. ∗Statistically significant. M group: mirtazapine group; D group: dexamethasone group; C group: control group

DISCUSSION

The research team had found that the use of a one pre-emptive dose of mirtazapine versus a one pre-emptive dose of dexamethasone efficiently decreased the incidence and severity of PSAS in comparison to placebo controls in gynaecological procedures under SA. In addition, incidence of hypotensive episodes,

pruritus, nausea, and vomiting were lower in M and D groups in comparison to C group. [7]

Both physical and therapeutic strategies have been used to diminish loss of tympanic temperature for prevention of PSAS. In addition, the use of forced-air warming devices and meperidine to maintain tympanic temperatures of patients at ≥36.5°C is also recommended by the ASA guidelines. [8] Nonetheless, potential side effects of meperidine were previously described. So, the investigators conducted this study to possibly seek medications with insignificant adverse effects to substitute the utilization of IV meperidine for management of PSAS.

Maximal effects of the three mechanisms of SA causing core hypothermia occur at the 1st 30–60 min after the subarachnoid block necessitating patients' monitoring, actively warming and anti-shivering treatment. So, the research team chose the 1st 90 minutes after SA as a time frame for this study. [9] In addition, an anecdotally endorsed dose for oral mirtazapine is a single administration of 30 mg tablet taken 2 hours prior to surgery, whereas the selected protocol for dexamethasone administration was based on earlier research and adhered to optimal dose for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy (LC). [10]

Patients' demographic characteristics and patients' perioperative data of the three groups were comparable (Table 1). (e investigators of this research reported that M group had a significantly faster regression times by two segments and a significantly shorter duration of analgesia than placebo-treated patients. (e investigators suggested an explanation to these findings by the similarity between mirtazapine and granisetron, contrary to ondansetron, that acts on mixed receptors and strongly and selectively binds to the 5-HT3 receptors with decreased or no affinity for other 5- HT receptors. Moreover, mirtazapine may affect pain modulation of the spinal cord through antagonism of 5-HT3 receptors. [11] Moreover, results of this study matched with previous studies assessing the advantages of dexamethasone whether IV or intrathecally in reducing the time to the highest dermatome block level and increasing both the regression times by two segments and the duration of analgesia.

Results of this study revealed that the incidence of hypotensive episodes after SA during the study period was lower in M group due to the 5-HT3 blocking properties of mirtazapine as displayed by other 5-HT3 receptor antagonists. Furthermore, a previous study reported about possible mechanisms of dexamethasone in attenuation of PSA hypotension. [12] Terkawi et al., in contrast to our results, reported that ondansetron premedication did not attenuate hemodynamic changes after SA; did not reduce the amount of vasopressor use; and did not decrease the incidence of pruritus, nausea, and vomiting.

SA-induced vasodilation in the lower half of body will lead to loss of thermoregulation and core hypothermia whereas vasoconstriction and shivering will be confined to the upper half of the body to augment tympanic temperature. The research team reported a higher incidence of clinically significant shivering in placebo-treated patients in spite of significant differences between basal and 90 minutes after SA tympanic temperature measurements in the three groups following high level of the subarachnoid block. This might be explained by mirtazapine-induced serotonin uptake inhibition in the preoptic anterior hypothalamic part which controls heat production and loss. In addition, anti-inflammatory properties of dexamethasone allow reduction of temperature gradient between tympanic and skin temperatures. Similar to the current study, Shen et al. and a plethora of studies documented that prophylactic 5-HT3 receptor antagonists were efficient for decreasing the occurrence of perioperative shivering (POS) in patients after SA. In addition, Kelsaka et al. also reported no significant difference in the incidence of shivering between ondansetron and meperidine groups in orthopaedic surgeries under SA. Additionally, previous studies revealed that dexamethasone decreased postanaesthetic shivering. Over and above, earlier clinical study had documented equal efficacy of spinal dexamethasone and spinal meperidine for reducing the shivering threshold in comparison to control group in transurethral prostatectomy under SA. Moreover, our results were supported by prior studies regarding high doses of meperidine used to manage PSAS in placebo controls in comparison to intervention groups. [13]

The results of Abdel-Ghaffar et al. and Chen et al. were in concordance with our recent findings concerning the lower percentage of pruritus, nausea episodes, and vomiting episodes in M group and they attributed the antipruritic and antiemetic efficacy due to 5-HT3 receptor blockers properties of mirtazapine. In addition, 5-HT3 antagonists, like ondansetron, and granisetron have been utilized to forestall the neuraxial opioid-induced pruritus. Furthermore, mirtazapine has strong antihistamine effect, exerts its antipruritic effect through activating the k-opioid system, and reduces the perception of pruritus through action on the cerebral cortex. In spite of the antiemetic and anti-inflammatory properties of dexamethasone, it lacks an antipruritic effect. However, earlier research showed reduced severity of pruritus in dexamethasone-treated patients compared to placebo-treated patients which reinforced outcomes of this study. Furthermore, the high percentage of pruritus, nausea, and vomiting in C group cases may be due to increased utilization of meperidine. In addition, the research team recorded increased utilization of ephedrine in C group cases which might

explain probability of systemic hypersensitivity reactions. [14]

Chen et al. recorded that premedication with mirtazapine reduced preoperative anxiety in patients undergoing gynaecological operations. Those results were consistent with this study that affirmed the sedative response of mirtazapine as proved by higher Ramsay sedation scores. Moreover, use of dexamethasone improves mood and it could also lead to a greater feeling of well-being due to primary central nervous system impact of steroids. For the aforementioned merits of mirtazapine and dexamethasone, this might justify high satisfaction scores in mirtazapine and dexamethasone groups in comparison to placebo-treated patients. [15]

This clinical trial suffered distinct limits. To begin with, this research needed warmed IV fluids. At our institution, the utilization of warmed IV fluids is held for emergency procedures and for all lengthy procedures. Nevertheless, the research team trusted that the utilization of mirtazapine and dexamethasone in this clinical trial furnished an easy, demonstrated adequacy as antiemetic, less side effects, and more economical for prevention of PSAS in countries with low financial resources. Second, the consequences of this study did exclude endoscopic urosurgical procedures and invasive procedures interconnected with increased blood loss. In spite of that, the investigators proved that mirtazapine and dexamethasone diminished the impact of high levels of intrathecal block which reduced the tympanic temperature threshold for shivering. Furthermore, mirtazapine and dexamethasone showed the favourable feedback to stay away from the techniques used to escape the PSA hypotension (e.g., volume loading or vasopressor use) which might augment the risk of hypervolemia as well as myocardial ischemia. Third, this clinical trial was completed at a single centre. Even so, the research team considered that the randomized and the double-blind plan diminished the chance of bias and the comparatively big sample size accomplished significant differences in the side effects that happened. Fourth, the glycaemic outline and the percentage of surgical site infections following dexamethasone intake should have been described. [16]

The principle that prevention is better than cure has proven to be true for shivering also and it should be applied. Since the proposed protocol for prevention of PSAS was efficient, easy, more economical, and comparatively free from danger, the investigators recommend the utilization of mirtazapine and dexamethasone for prevention of PSAS in patients subjected to risk factors.

CONCLUSION

Paracetamol and dexamethasone were effective in prevention of PSAS in patients undergoing lower abdominal and lower limb surgeries under spinal anaesthesia compared to placebo controls. Our results indicated that decreasing the threshold of shivering might be more important than increasing the core temperature in terms of preventing PSAS with less adverse events.

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