

Randomized Trial

Safety and Efficacy of Dexmedetomidine in Treating Post Spinal Anesthesia Shivering: A Randomized Clinically Controlled Dose-Finding Trial

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Background: The optimum dose of dexmedetomidine for shivering control with the least hemodynamic derangements is still under research.

Objective: To compare the efficacy, hemodynamic and side effects of dexmedetomidine in 3 different doses with those of meperidine for the treatment of shivering in patients undergoing spinal anesthesia for minor elective lower abdominal surgery.

Study Design: Prospective double-blind randomized clinically controlled study.

Setting: University hospital.

Methods: One hundred twenty patients who developed shivering under spinal anesthesia. On shivering, patients were randomly allocated to receive an intravenous 2 mL bolus dose of meperidine 0.4 mg/kg (meperidine group, n = 30), dexmedetomidine 0.5 µg/kg (DEX I group, n = 30), 0.3 µg/kg (DEX II group, n = 30), or 0.2 µg/kg (DEX III group, n = 30). Control of shivering, time taken for cessation of shivering, response rate, recurrence, hemodynamic changes, sedation score, tympanic temperature, and side effects were noted and compared between groups.

Results: The groups were comparable regarding demographic profile, tympanic temperature decline, and shivering onset time ($P > 0.05$). Lower shivering cessation time ($P < 0.001$) and higher response rate ($P < 0.01$) were observed in DEX I and II groups compared with DEX III and meperidine groups, with a nonsignificant difference between DEX I and II groups. Recurrence of shivering activity was higher in DEX III group (36.7%, $P < 0.01$) compared with DEX I (10%), DEX II (6.7%) and meperidine (16.7%) groups. Lower heart rates, systolic and diastolic blood pressure mean values were recorded in DEX I group ($P < 0.05$). Nine patients (30%) in DEX I group were in levels 3 – 5 of sedation ($P < 0.02$) compared with 5 (16.66%), 2 (6.66%), and 4 (13.3) patients in DEX II, DEX III, and meperidine groups, respectively.

Limitations: This study is limited by its small sample size.

Conclusions: Among the 3 doses investigated, dexmedetomidine 0.3 µg/kg effectively treated shivering associated with spinal anesthesia with modest hemodynamic and sedation effects.

Trial Registration: ClinicalTrials.gov Identifier: NCT02382432.

Key words: Dexmedetomidine, hypothermia, shivering, spinal anesthesia

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Shivering is defined as an involuntary, repetitive activity of skeletal muscles as a physiological response to core hypothermia in an attempt to raise the metabolic heat production (1). The reported median incidence of shivering related to neuraxial anesthesia in the control groups of 21 studies is up to 55% (inter quartile range of 40 – 64%) (2). Spinal anesthesia significantly impairs the thermoregulation system by inhibiting tonic vasoconstriction, which plays a significant role in temperature regulation (3). Spinal anesthesia also causes redistribution of core heat from the trunk (below the block level) to the peripheral tissues. These 2 effects predispose patients to hypothermia and shivering (4). Clonidine, meperidine, tramadol, nefopam, and ketamine were the most frequently reported pharmacological interventions and showed a variable degree of efficacy in randomized, double-blinded, placebo-controlled trials (5). Among the pharmacological agents, pethidine (meperidine) has been shown to be one of the most effective treatments (6). Although its mechanism of action is not completely understood, it probably acts directly on the thermoregulatory center or via opioid K receptors (5,7-8). The α -2 receptor agonists are another important class of anti-shivering drugs that, unlike meperidine, produce little respiratory depression. Dexmedetomidine is a highly selective α -2 adrenoceptor agonist with potent effects on the central nervous system (9). Intravenous dexmedetomidine reduces both the vasoconstriction and shivering thresholds (10). Multiple studies have demonstrated the efficacy of dexmedetomidine in prevention of shivering (11). Few clinical trials investigated its efficacy in treatment of established shivering (12). There has been no study regarding the optimal effective dose of dexmedetomidine for treatment of postoperative shivering. Thus, the present study was conducted with the aims of identifying the optimum dose of dexmedetomidine for treatment of shivering associated with the aim of the least hemodynamic derangements. We compared the efficacy, hemodynamic effects, and side effects of dexmedetomidine in 3 doses (0.5, 0.3, and 0.2 μ g/kg) with those of meperidine 0.4 mg/kg for the treatment of shivering in patients undergoing spinal anesthesia for minor elective surgical operations.

METHODS

This prospective randomized double-blind, dose-finding study was approved by the local research ethics committee in the faculty of medicine, Assiut University, Assiut, Egypt, and was registered in Clinical Trials.gov

(Identifier: NCT02382432). After obtaining a written informed consent, patients of both genders aged 18 to 60 years, ASA I or II scheduled for elective minor lower abdominal operations under spinal anesthesia for an anticipated duration of > 60 and < 180 minutes (e.g., inguinal hernioraphy, umbilical hernia repair) who developed shivering during the intra- or postoperative period, were enrolled in the study. Procedures which might require administration of blood or blood products and urological endoscopic operations were excluded. Patients with a body mass index > 30 kg/m², an initial body temperature > 38°C or < 36°C, and those with a history of convulsions, multiple allergies, thyroid disease, Parkinson's disease, dysautonomia, Raynaud's syndrome, hypertension, coronary artery disease, conduction abnormalities or other cardio-respiratory or neuromuscular pathology, middle ear pathology, a known history of alcohol use, treatment with sedative hypnotic agents or vasodilators, or having contraindications to spinal anesthesia, were also excluded.

Using an online research randomizer (<http://www.randomizer.org>), patients who presented with shivering were randomly allocated into 4 groups of 30 patients each to receive meperidine 0.4 mg/kg (Meperidine group), dexmedetomidine 0.5 μ g/kg (DEX I group), dexmedetomidine 0.3 μ g/kg (DEX II group), or dexmedetomidine 0.2 μ g/kg (DEX III group). The assigned drugs were dissolved in 2 mL physiological saline and administered slowly intravenously.

The anesthetic management of the patients was standardized without any premedication. The temperature of the operating room was maintained at 21°C to 22°C (measured by a wall thermometer). Irrigation and intravenous fluids were given with inline warming. All patients were covered with one layer of surgical drapes over the chest, thighs, and calves during the operation and then one cotton blanket over the entire body postoperatively. No other warming device was used and oxygen was administered to all the patients of both groups at a rate of 5 L/min with a face mask. Before performing spinal anesthesia, each patient received 10 mL/kg of lactated Ringer's solution. The infusion rates were then reduced to 6 mL/kg/h. Standard monitoring was established for monitoring non-invasive blood pressure (NIBP), electrocardiograph (ECG), temperature, and peripheral arterial oxygenation (SPO₂%) (Datex-Ohmeda S/5, GE Health Care, Finland). Following the guidelines for asepsis and antisepsis, subarachnoid anesthesia was instituted at either the L3-4 or L4-5 interspaces (midline approach). A volume of 1.5 – 2.5 mL of hyperbaric bupi-

vacaine (Marcaine®, Spinal Heavy 0.5%, Astra Zeneca) was injected using a 25 G Quincke spinal needle to achieve a desirable level in accordance with the surgical procedure. Motor block was assessed using a modified Bromage scale (0 = no motor block; 1 = hip blocked; 2 = hip and knee blocked; 3 = hip, knee, and ankle blocked). Full motor recovery was scored as 0 on the Bromage scale. Sensorial block was assessed by the pinprick test. The levels of motor and sensory blockade were assessed during the intra-operative period.

The presence of shivering was assessed by a blinded observer after the completion of subarachnoid drug injection. Shivering was graded on a scale similar to that validated by Tsai and Chu (13), 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, and 4 = shivering involving the whole body. The incidence and severity of shivering were recorded at 5 minute intervals during the operation and in the recovery room. Only cases that developed shivering of grade > 2 during the peri-operative phase were given treatment on an intention-to-treat basis. According to group assignment, those patients were treated with a single dose of dexmedetomidine 0.5 µg/kg (DEX I group), 0.3 µg/kg (DEX II group), or 0.2 µg/kg (DEX III group), or meperidine 0.4 mg/kg (Meperidine group). The assigned drugs were dissolved in 2 mL physiological saline and administered slowly intravenously over 2 minutes. Following the completion of drug administration, shivering activity was recorded every minute (up to 10 minutes) with any adverse effects or complaints. Shivering control was defined as complete (when post-treatment, the shivering score declined to 0), incomplete (when the scores decreased but did not abolish the shivering completely), and failed (if no change in scores was observed). The shivering onset time (the time in minutes at which shivering started after spinal anesthesia), shivering cessation time (the time in seconds at which complete cessation of shivering behavior occurred), and response rate (number of cases in whom shivering ceased after treatment in 10 minutes) were measured and recorded. Patients who did not respond or in whom recurrence of shivering occurred were treated with a second dose of dexmedetomidine or pethidine in the respective groups.

Tympanic temperature was measured at 15, 30, 60, 90, and 120 minutes after spinal block. A core temperature below 36°C was considered hypothermia. We planned to exclude patients with tympanic temperature

< 35°C, and to actively warm those with tympanic temperatures between 35 – 36 and 36°C. The heart rate, systolic and diastolic blood pressure were continuously monitored and recorded after spinal block before study drug administration (baseline) and at 1, 3, 5, 7, 10, 15, 20, 25, 30, 40, 50, 60 minutes, and in the second, fourth, and sixth hour after study drug injection. Hypotension (defined as a decrease in mean arterial blood pressure > 20% from the baseline or below 60 mmHg) was treated with ephedrine 10 mg intravenous bolus and then with further intravenous infusion of lactated Ringer's solution. Bradycardia (defined as heart rate below 50 bpm) was treated with 0.5 mg atropine intravenously. If patients developed nausea and vomiting, 10 mg metoclopramide was administered. The patient's level of sedation was assessed using an Observer's Assessment of Alertness/Sedation Scale (OAA/SS) (where 5 = responds readily to name spoken in normal tone, 4 = lethargic response to name spoken in normal tone, 3 = responds only after name is spoken loudly and/or repeatedly, 2 = responds only after mild prodding or shaking, 1 = does not respond to mild prodding or shaking). The sedation score was recorded every 10 minutes in the first hour after study drug injection and in the second, fourth, and sixth hour afterwards.

The attending anesthesiologist, surgeon, and patient care giver or data collection personnel were blinded to the patient assignment.

Postoperatively, all patients were monitored, given oxygen via a facemask, and covered with one layer of drapes and one cotton blanket. The post-anesthesia care unit temperature was maintained at 25°C to 26°C and constant humidity (70%). Patients were strictly observed for 6 hours postoperative.

Any adverse effects in the first 24 hours postoperative including hypotension, bradycardia, nausea and vomiting, difficulty in micturition, headache, allergy, and waist and back pain were treated and recorded.

Statistical Analysis

To detect a 20% difference in the response rate among the groups with a minimum response of 50% estimated from initial pilot observations, with 90% power and 5% alpha error (2-tailed), a calculated sample size of 30 cases per group was required. Statistical analysis was performed using SPSS version 21 software (SPSS, Chicago, IL, USA). Data are presented as means ± SD, numbers, frequencies, and percentages.

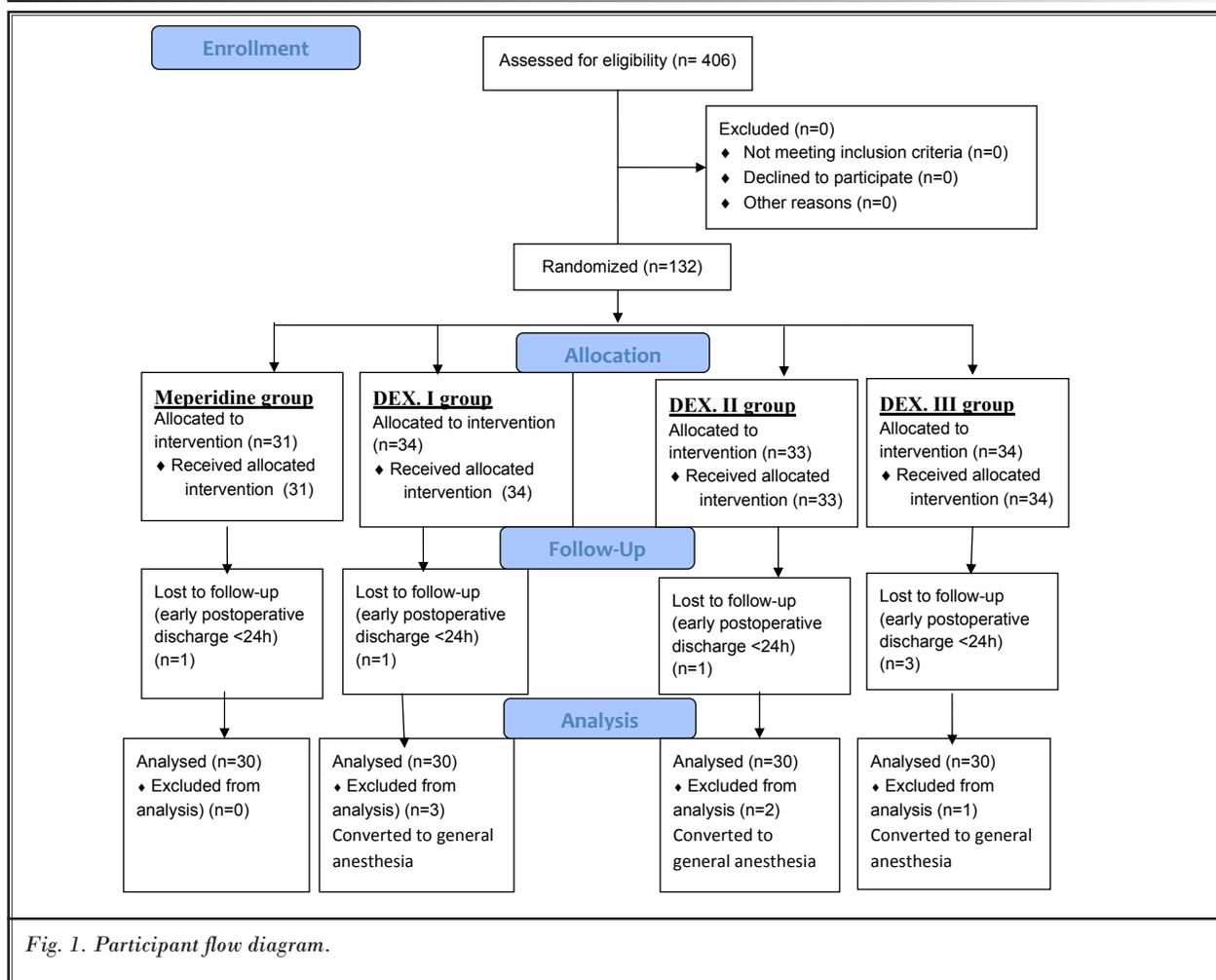
Analysis of variance (ANOVA) followed by post-hoc test were used for comparison of parametric data. The

Kruskal Wallis test was used to compare nonparametric data while the Mann-Whitney test was used to compare differences between 2 groups. The chi-square test was used for comparison between percentages and frequencies. A *P*-value < 0.05 was considered significant.

RESULTS

In total, 406 spinal anesthetics were screened for eligibility to participate in this study; 132 patients (30.76%) developed shivering grade 3 or 4 requiring treatment. Twelve patients were excluded from data analysis due to protocol violation, though all were given treatment. One hundred twenty patients subsequently consented and were enrolled (Fig. 1). These patients were equally distributed in the 4 groups (*n* = 30 per group). The groups were comparable with respect to age, weight, gender, ASA class, duration of surgery, duration of motor block, duration of senso-

rial block, and operation type (Table 1). The tympanic temperatures were similar in the groups (Fig. 2). The tympanic temperatures of the patients were > 36°C and active warming was not required. There were no statistically significant differences for the mean onset times of shivering between groups, which were (24.23 ± 6.81 minutes) in DEX I group, (25.26 ± 6.65 minutes) in DEX II group, (25.00 ± 6.67 minutes) in DEX III group, and (25.13 ± 7.39 minutes) in Meperidine group (*P* = 0.939). The time taken for complete cessation of shivering was significantly lower in the DEX I (96.86 ± 40.68 seconds, *P* < 0.001) and DEX II (96.86 ± 40.68 seconds, *P* < 0.001) groups compared with the DEX III (113.17 ± 22.14 seconds) and Meperidine (129.33 ± 33.80 seconds) groups, with a nonsignificant difference between the DEX I and II groups. The response rate (complete cessation of shivering activity within 10 minutes of one dose of study drug administration) was significantly higher in the DEX



I (96.7%, $P < 0.01$) and DEX II (93.33%, $P < 0.01$) groups compared with the DEX III (76.67%) and Meperidine groups (73.33%), with a nonsignificant difference between the DEX I and II groups. A second dose of study drug administration abolished shivering in patients who exhibited incomplete or failed shivering control in each respective group. The response rate after the second dose was the same for all groups (100%). Recurrence

of shivering activity was significantly higher in the DEX III group (11 patients, 36.7%, $P < 0.01$) compared with the DEX I (3 patients, 10%), DEX II (2 patients, 6.7%), and Meperidine (5 patients, 16.7%) groups (Table 2). Patients in the DEX I and DEX II groups exhibited significant changes in the mean systolic blood pressure compared with the DEX III and Meperidine groups ($P < 0.04$). In the DEX I group, the mean systolic blood pres-

Table 1. Patient's demographics and clinical characteristics.

Patients	Meperidine group N=30	DEX. I group N=30	DEX. II group N=30	DEX. III group N=30	P value
Age (years)	29.86 ± 9.72 (18-50)	30.73 ± 10.26 (19-50)	30.93 ± 9.88	30.96 ± 9.99	0.971ns
Weight (kg)	69.85 ± 8.27 (55-88)	68.34 ± 8.05 (50-90)	70.73 ± 9.88(18 - 50)	71.70 ± 9.99 (20-50)	0.812ns
Gender: M/F	17/13 (56.7%/43.3%)	18/12 (60%/40%)	20/10 (66.7%/33.3%)	19/11 (63.3%/36.7%)	0.197ns
ASA: I/II	27/3 (90%/10%)	27/3 (90%/10%)	28/2 (93.3%/6.7%)	29/1 (96.7%/3.3%)	0.724ns
Duration of surgery (min.).	77.43 ± 26.35 (60-180)	79.73 ± 26.02 (60-174)	81.40 ± 19.71 (61-178)	82.67 ± 20.70 (60-180)	0.305ns
Duration of motor block (min.).	221.53 ± 37.41 (85-452)	215.48 ± 30.25 (90-450)	218.37 ± 29.54 (89-456)	217.81 ± 29.5 (91-457)	0.357ns
Duration of sensory block (min.).	231.59 ± 29.31 (90-280)	238.68 ± 42.58 (90-280)	235.72 ± 39.21 (90-280)	234.71 ± 37.51 (90-280)	0.296ns
Operation type: Inguinal hernioraphy/Umbilical hernia repair.	17/13 (56.7%/43.3%)	18/12 (60%/40%)	20/10 (66.7%/33.3%)	19/11 (63.3%/36.7%)	0.197ns

Data are presented as mean ± SD, range, number and frequency. Significant difference between groups at P . value < 0.05 . ns: No significant difference.

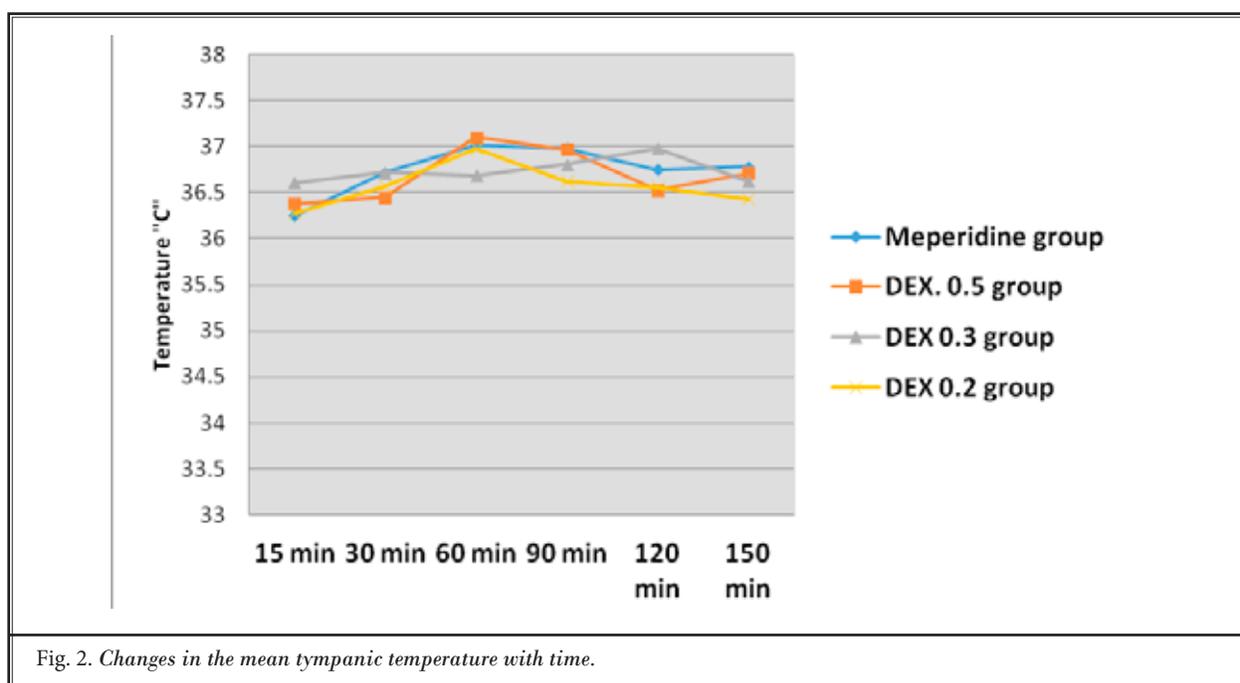


Fig. 2. Changes in the mean tympanic temperature with time.

Table 2. Shivering profile in the studied groups.

	Meperidine group N=30	DEX. I group N=30	DEX. II group N=30	DEX.III group N=30	P Value
Shivering onset time (min.)					
Mean ± SD	25.13 ± 7.39	24.23 ± 6.81	25.26 ± 6.65	25.0 ± 6.67	0.939ns
Range	(14-45)	(13-40)	(14-41)	(14-40)	
Shivering cessation time (sec.)					
Mean ± SD	129.3 ± 33.8	96.9 ± 40.7	99.9 ± 38.8	113.2 ± 22.1	0.001
Range	(80-200)	(40-196)	(46-200)	(80-199)	
Shivering control					
Complete	22 (73.33%)	29 (96.7%)	28 (93.3%)	23(67.67%)	0.01
Incomplete	6 (20%)	1 (3.33%)	2 (6.66%)	7 (23.33%)	
Failed	2 (6.66%)	w ---	--	--	
Response rate after 1st dose (%):	73.33%	96.7%	93.33%	76.67%	0.01
Response rate after 2nd dose (%):	100%	100%	100%	100%	-----
Shivering recurrence:					
Number	5	3	2	11	0.01
Percentage	(16.7%)	(10%)	(6.7%)	(36.7%)	

Data are presented as mean ± SD, range, number and frequency. Significant difference between groups at P value < 0.05. ns: No significant difference.

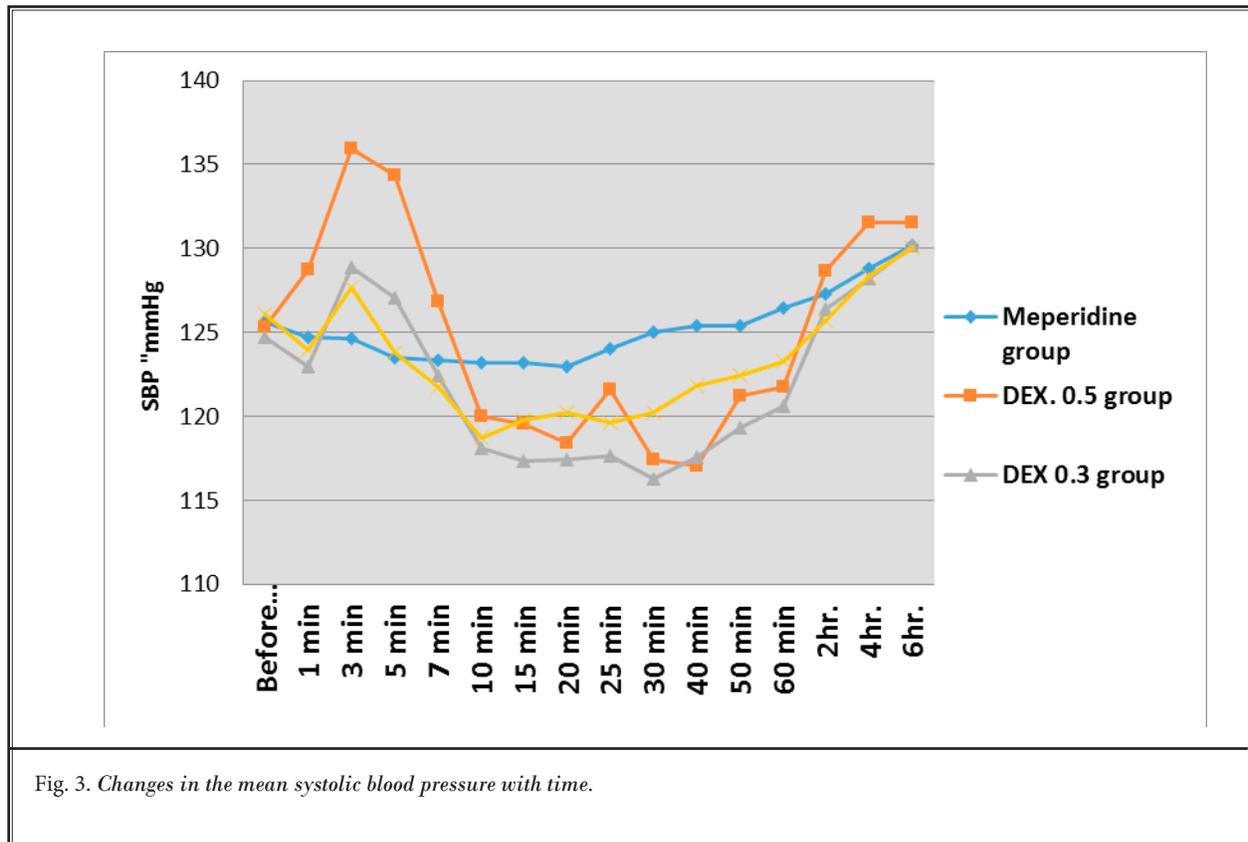


Fig. 3. Changes in the mean systolic blood pressure with time.

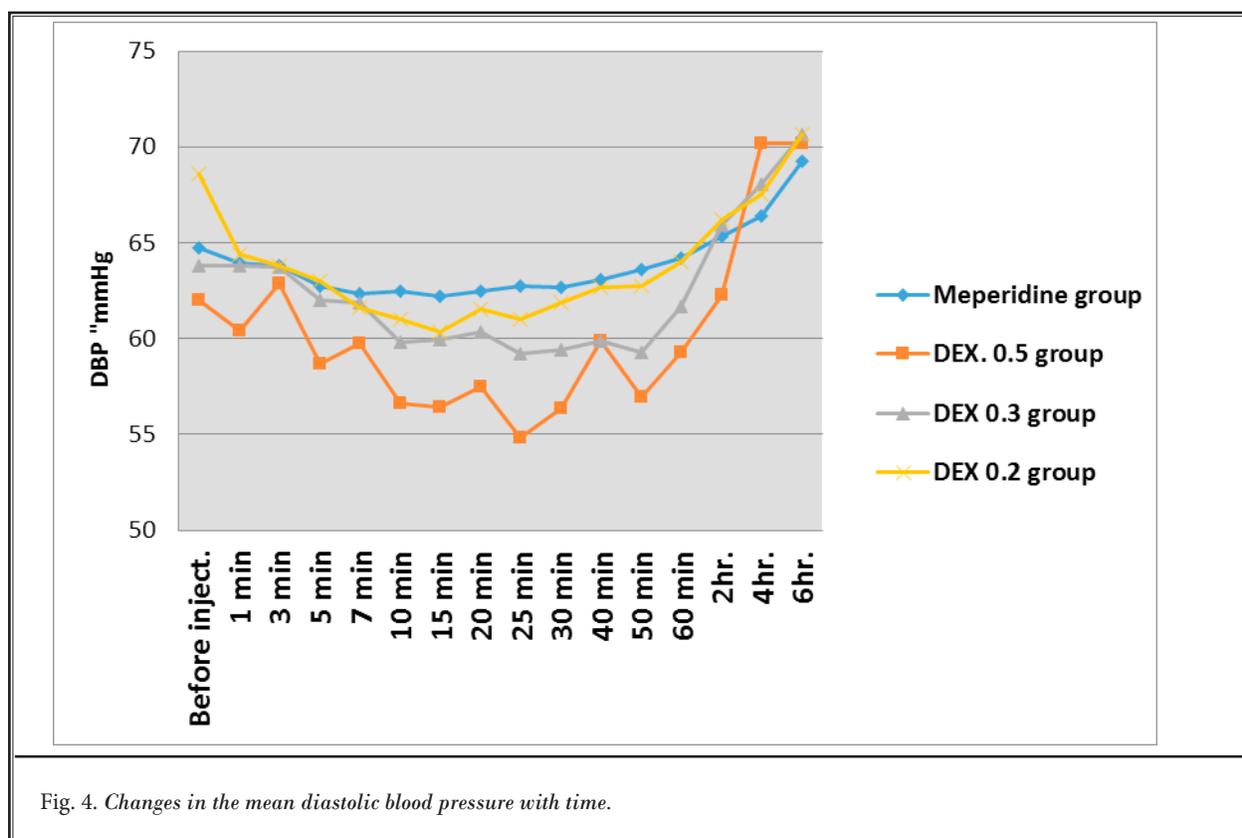


Fig. 4. Changes in the mean diastolic blood pressure with time.

sure values significantly increased at one minute ($P = 0.000$), 3 minutes ($P < 0.04$), and significantly decreased at 25 minutes ($P < 0.03$), 30 minutes ($P < 0.016$), 2 hours ($P < 0.029$), and 4 hours ($P < 0.029$) compared with the baseline. In the DEX II group, the mean systolic blood pressure values significantly decreased at 15 minutes ($P = 0.000$), 20 minutes ($P < 0.04$), 25 minutes ($P < 0.03$), 30 minutes ($P < 0.016$), 40 minutes ($P < 0.029$), 50 minutes ($P < 0.029$), and 60 minutes ($P < 0.029$) compared with the baseline, with a nonsignificant difference between the DEX I and II groups. No significant differences were observed in the mean systolic blood pressure in the DEX III or Meperidine groups, compared with the baseline (Fig. 3). Patients in the DEX I group exhibited significant changes in the mean diastolic blood pressure compared with other study groups ($P < 0.003$). Compared with the baseline, the mean diastolic blood pressure values in the DEX I group significantly decreased at 20 minutes ($P < 0.03$), 25 minutes ($P = 0.000$), 30 minutes ($P < 0.002$), and 50 minutes ($P < 0.003$), and significantly increased in 2 hours ($P = 0.000$) and 4 hours ($P = 0.000$) after injection of dexmedetomidine. No significant changes were observed in the mean diastolic blood pressure in the

DEX II, DEX III or Meperidine groups groups, compared with the baseline (Fig. 4). Intergroup comparison of the mean heart rate value revealed a highly significant difference between groups from 3 minutes until 6 hours after study drug injection ($P < 0.001$). The lowest mean heart rate values were observed in the DEX I group which reached a statistical significance at one minute ($P < 0.05$) and 3 minutes ($P < 0.01$) after injection of dexmedetomidine, compared with the baseline (Fig. 5). In the Meperidine group, significant increases in heart rate were observed from 20 minutes until 6 hours after the injection of Meperidine compared with the baseline ($P = 0.000$). There were no significant differences between the DEX I and II groups. There were no statistical differences between the groups in the peripheral arterial oxygen saturation at any time point (data not represented). Nine patients (30%) in the DEX I group were in levels 3 – 5 of sedation ($P < 0.02$) compared with 5 (16.66%), 2 (6.66%), and 4 (13.3) patients in the DEX II, DEX III, and Meperidine groups, respectively. Intergroup comparison for sedation score revealed significant difference at 50 minutes ($P < 0.01$), 60 minutes ($P < 0.01$), and 2 hours ($P < 0.01$) after study drug ad-

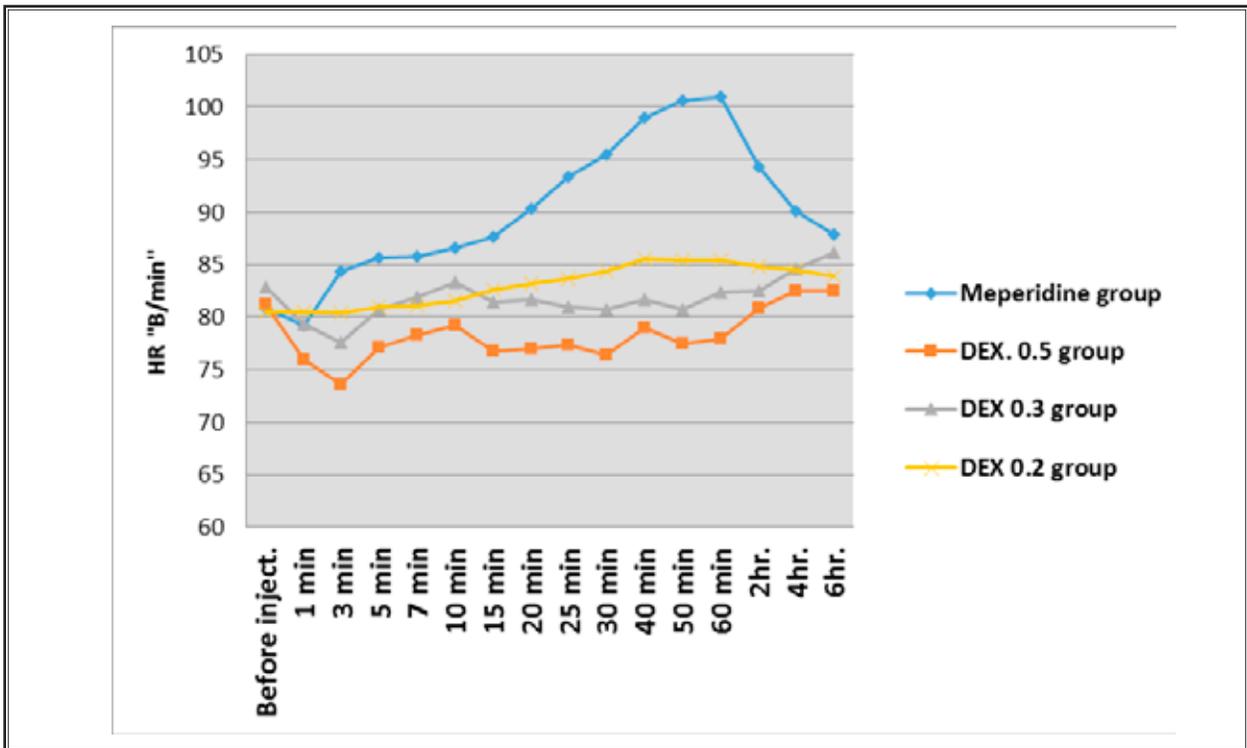


Fig. 5. Changes in the mean heart rate with time.

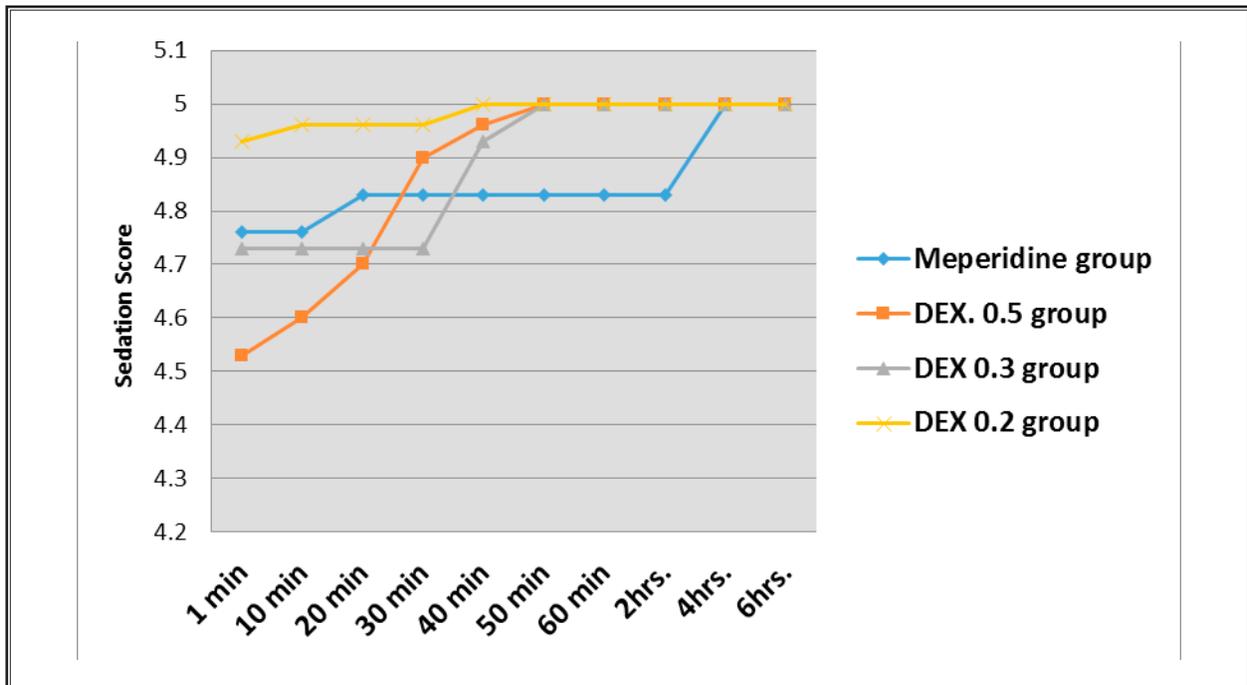


Fig. 6. Changes in the mean sedation score with time.

Table 3. Intra-operative and postoperative adverse events.

	Meperidine group N=30	DEX I group N=30	DEX II group N=30	DEXIII group N=30	P Value
Hypotension	4(13.3 %)	10(33.3%)	4(13.3%)	3(10%)	0.03
Hypertension	--	1(3.3%)	--	---	----
Bradycardia	---	2 (6.66%)	--	---	----
Tachycardia	1(3.33%)	----	----	---	
Sedation	4(13.3)	9 (30%)	5(16.66%)	2(6.66%)	0.02
Nausea	5(16.66%)	3 (10%)	2(6.66%)	2(6.66%)	0.271 ns
Vomiting	3(10%)	1(3.33%)	--	--	0.351 ns
Headache	1(3.3%)	---	---	---	-----

Data are presented as number and frequency.

Significant difference between groups at P value < 0.05 .

ns: No significant difference.

ministration, with a nonsignificant difference in other time points (Fig. 6). No patient in the study presented with sedation score < 3 . Ten (30.33%, $P < 0.03$) patients in the DEX I group compared with 4 (13.3%), 3 (10%), and 4 (13.3 %) patients in the DEX II, DEX III, and Meperidine groups, were presented with hypotension and were treated with ephedrine 10 mg i.v. Two patients in the DEX I group developed bradycardia and were treated with 0.5 mg atropine intravenously. Episodes of oxygen desaturation or respiratory depression were not detected in any patient during the study. There were no statistically significant differences for the incidences of other adverse events between groups (Table 3).

Discussion

This study evaluated the effect of intravenous dexmedetomidine in the treatment of shivering after spinal anesthesia in 3 different doses (0.5, 0.3, and 0.2 $\mu\text{g}/\text{kg}$), in comparison with intravenous meperidine 0.4 mg/kg. Among the 3 doses investigated, dexmedetomidine 0.3 $\mu\text{g}/\text{kg}$ effectively treated shivering associated with spinal anesthesia with modest hemodynamic and sedation effects. The neurotransmitter pathways involved in shivering are complex and involve opioids, α -2 adrenergic, serotonergic, and anti-cholinergic receptors. Drugs acting on these systems are utilized in the prevention or treatment of this condition (1). The anti-shivering effect of dexmedetomidine has not been adequately investigated. Like clonidine, dexmedetomidine is associated with a lower rate of shivering. Intravenous infusion of dexmedetomidine reduced the vasoconstriction threshold and the shivering threshold. It did not change the sweating threshold. Dexmedetomidine decreased the concentration-response curves

for vasoconstriction and shivering in a linear fashion (10). Therefore, with dexmedetomidine, thermoregulatory responses were inhibited within a wider range of temperatures. Our results showed the superiority of dexmedetomidine 0.5 and 0.3 $\mu\text{g}/\text{kg}$ over dexmedetomidine 0.2 $\mu\text{g}/\text{kg}$ and meperidine in the treatment of shivering for the following reasons: an early onset of action; a higher rate of cessation of shivering; and lesser recurrence of shivering, with a nonsignificant difference between dexmedetomidine 0.5 and 0.3 $\mu\text{g}/\text{kg}$. Dexmedetomidine 0.2 $\mu\text{g}/\text{kg}$ was as effective as pethidine {meperidine?} in treating shivering, however, a higher shivering recurrence rate (36.6%) disables this dose from clinical application as a single anti-shivering medication. Dexmedetomidine displays specific and selective α -2 adrenoceptor agonism in the brain and spinal cord. The responses to activation of these receptors include decreased sympathetic tone with attenuation of the neuro-endocrine and hemodynamic responses to anesthesia and surgery. Thus, dexmedetomidine can mediate both the beneficial and unwanted effects of shivering provoked by hypothermia, such as increased catecholamine concentrations, oxygen consumption, blood pressure, and heart rates (14-16). The hemodynamic effects of dexmedetomidine are biphasic. When it is administered intravenously it causes hypotension and bradycardia until central sympathomimetic effect is achieved and then it causes moderate decreases in mean arterial pressure and heart rate (17,18). In accordance, patients who received 0.5 $\mu\text{g}/\text{kg}$ showed significant alteration in systolic and diastolic blood pressures and heart rate with frequent surges and declines and frequent administration of vasopressors. The least change in heart rate, and systolic and diastolic blood pressure

if any was recorded was with dexmedetomidine 0.2 µg/kg. In this study, the hemodynamic instability recorded in the DEX groups is not uncommon and was treated with fluid infusion, vasopressors, and atropine. The highest dose of dexmedetomidine investigated in this study (0.5 µg/kg) effectively controlled shivering but with controllable hemodynamic instability and sedation. Dexmedetomidine 0.3 µg/kg effectively treated shivering with moderate effect on hemodynamics. Dexmedetomidine is used for prevention of shivering in a dose of 1 µg/kg, a dose that is suspected to produce more sedation and hemodynamic derangement (11). In this study, more patients developed sedation with dexmedetomidine 0.5 µg/kg than other groups ($P < 0.02$). The quality and duration of sedation was different between DEX groups and meperidine. Patients in DEX groups who developed sedation were easily aroused and the sedation was of shorter duration than in Meperidine group patients. The sedative effect of dexmedetomidine is characterized by being short term and easily arousable (arousable sedation). Other clinically available sedatives failed to produce such sedation. A European phase III trial stated that even complex tasks, such as communication by pen and paper, are possible under dexmedetomidine primary therapy (19). One of the main objectives in using sedative agents is that the drug should not cause respiratory depression. In previous studies, it has been shown that α_2 -adrenergic agonists cause no or minimal respiratory depression (20,21). In accordance, none of our patients had respiratory depression during the operation or in the PACU. The reported median incidence of shivering related to neuraxial anesthesia is up to 55% (inter quartile range of 40 – 64%) (2). Risk factors associated

with shivering include type and duration of anesthesia, surgical procedure, level of sensory blockade, age, and temperature of the operating room and infusion fluids (22). The lower incidence of shivering (30.76%) reported in this study may be due to difference in the associated risk factors and the use of warmed irrigation and intravenous fluids. There are some limitations in our study; the sample population consisted of adult patients who were relatively healthy undergoing an elective procedure of minimal invasiveness with no blood loss or major fluid shift. It needs to be determined whether the present findings can be generalized to other operations associated with increased blood loss and in patients presented with cardiovascular disease or instability. As the dictum says, "prevention is better than cure," it holds true for shivering also and it should be practiced. However, since the treatment of established shivering is efficacious, simple, inexpensive, and relatively safe, and since prevention is only efficacious if the baseline risk is very high, we recommend the "wait and see" strategy. We conclude that dexmedetomidine 0.3 µg/kg effectively treated shivering associated with spinal anesthesia with modest hemodynamic and sedation effects. We therefore recommend dexmedetomidine 0.3 µg/kg as a good choice for treating shivering in patients undergoing inguinal hernioraphy or umbilical hernia repair under spinal anesthesia. Further studies are needed to confirm our findings in more invasive operations and in patients with cardiovascular instability.

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