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Dexmedetomidine infusion prevents postoperative shivering in patients undergoing gynecologic laparoscopic surgery

Semra KARAMAN[1,*], İlkben GÜNÜŞEN[1], Mustafa Arda CEYLAN[1], Yücel KARAMAN[2], Esra Nur ÇETİN[1], Abdurrahim DERBENT[1], Ahmet Mete ERGENOĞLU[3]

[1]Department of Anesthesiology and Reanimation, Faculty of Medicine, Ege University, İzmir, Turkey
[2]Department of Anesthesiology and Reanimation, Tepecik Teaching Hospital, İzmir, Turkey
[3]Department of Obstetrics and Gynecology, Faculty of Medicine, Ege University, İzmir, Turkey

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Aim: This placebo-controlled, randomized study was performed to evaluate the efficacy of dexmedetomidine in preventing postoperative shivering.

Materials and methods: Sixty patients undergoing gynecologic laparoscopic surgery were assigned randomly to 2 groups to be administered either dexmedetomidine as a loading of 1 μg kg^{-1} for 10 min followed by a maintenance infusion of 0.5 μg kg^{-1} h^{-1} (Group D, n = 30), or a normal saline infusion (Group S, n = 30).

Results: Postoperative shivering was observed in 14 patients in Group S and in 3 patients in Group D (P = 0.001). The sedation scores were higher in the dexmedetomidine group than in the saline group (P < 0.05). Postoperative pain scores were higher in the saline group for the first 40 min (P < 0.05). Perioperative tympanic temperatures were not different between the groups.

Conclusion: Intraoperative dexmedetomidine infusion reduces postoperative shivering in patients undergoing gynecologic laparoscopy.

Key words: Dexmedetomidine, gynecologic laparoscopy, postoperative shivering

1. Introduction

Postoperative shivering occurs in up to 60% of patients recovering from general anesthesia (1). Patients report that shivering is remarkably uncomfortable, and some even find the accompanying cold sensation worse than surgical pain. Moreover, shivering may aggravate postoperative pain simply by stretching surgical incisions. Shivering also occasionally impedes monitoring techniques and increases intraocular and intracranial pressures (2).

As shivering is a response to hypothermia, body temperature should normally be maintained within the range of 36.5–37.5 °C (3). A major factor contributing to intraoperative hypothermia is radiant heat loss from the exposure of skin surfaces and abdominal viscera to the ambient environment. Other factors include the use of ambient irrigation solution in the peritoneal cavity, ambient intravenous (IV) fluid, and ventilation with dry anesthetic gases. The mechanism of heat loss during laparoscopy is different from that during open surgery. Laparoscopic operations eliminate the exposure of abdominal viscera to the ambient environment but expose the peritoneal surface to large volumes of ambient CO_2 gas during pneumoperitoneum (4,5). Thus, patients undergoing laparoscopy in particular are at risk of intraoperative hypothermia.

Various drugs, including pethidine, other opioids (alfentanil, pentazocine, fentanyl, sufentanil, or buprenorphine), doxapram, clonidine, and ketanserin, have all been reported to be effective in suppressing postoperative shivering (6,7). Although many drugs are used to treat postoperative shivering, the search for an ideal drug is still ongoing.

Dexmedetomidine, an alpha-2 agonist, is a new drug used for analgesia and sedation either in perioperative settings or in intensive care units (8,9). In previous studies, a prophylactic single dose of dexmedetomidine was generally found to be effective for shivering, but there are a few studies demonstrating the effect of dexmedetomidine via infusion in the intraoperative period on shivering after gynecologic laparoscopy (10,11).

The aim of this placebo-controlled, randomized study was to evaluate the efficacy of intraoperative

* Correspondence: semra.karaman@ege.edu.tr

dexmedetomidine infusion on postoperative shivering after gynecologic laparoscopy under general anesthesia.

2. Materials and methods

This prospective, randomized, double-blind, placebo-controlled study was approved by the local ethics committee. Informed consent was obtained from all patients. Sixty patients with American Society of Anesthesiologists (ASA) physical status I or II, between the ages of 20 to 50 years and undergoing elective gynecologic laparoscopy, were included in the study. Patients with hyperthyroidism, cardiopulmonary or respiratory disease, a psychological disorder, or an initial body temperature of >37.5 °C or <36.5 °C were excluded from the study.

None of the patients were premedicated. In both groups, general anesthesia was induced with propofol 2.5 mg kg^{-1} and fentanyl 1 μg kg^{-1}, followed by the administration of rocuronium (0.6 mg kg^{-1}) to facilitate endotracheal intubation. General anesthesia was then maintained with sevoflurane (2 ± 0.5% end-tidal oxygen) in a 50% air–oxygen mixture. Bispectral index (BIS) values were maintained between 40 and 60. If a BIS value of >60 1 μg kg^{-1} was observed, fentanyl was administered. Ventilation was mechanically controlled to maintain an end-tidal carbon dioxide pressure tension of 30–35 mmHg. The patients were covered with surgical drapes during anesthesia but were not actively heated. The temperature of the operating rooms was kept between 20 and 23 °C.

Participants were randomized into 1 of 2 study groups, using a computer-generated random number table, as Group D or Group S. After endotracheal intubation, Group D received a loading dose of dexmedetomidine of 1 μg kg^{-1} over 10 min, followed by an infusion of 0.5 μg kg^{-1} h^{-1}. Group S received the same amount of 0.9% saline infusion. The drugs were prepared in coded syringes by an anesthesiologist who was not involved in the anesthetic or postoperative management of the patient. The infusions were stopped at the beginning of the closure of the fascia, and then 1 g of paracetamol (Perfalgan, 100 mL, Bristol Myers Squibb) and 1 mg kg^{-1} of tramadol (Grünenthal GmbH) were administered by IV infusion to all patients.

Tympanic temperatures (Braun®) and hemodynamic data for all patients were recorded before and after induction of anesthesia; after intubation; at 15, 30, and 60 min during the operation; and just before and after extubation (Datex-Ohmeda®, Helsinki, Finland). The patients who needed an additional dose of fentanyl, and to whom atropine or ephedrine were administered intraoperatively due to bradycardia (<45 bpm) and hypotension, were recorded.

At the end of surgery, residual neuromuscular blockade was antagonized with IV neostigmine at 0.04 mg kg^{-1} and atropine at 0.02 mg kg^{-1}, and the patients were extubated. Extubation time (from termination of sevoflurane application until extubation), the duration of anesthesia, and the duration of surgery were noted.

In the recovery room, all patients received oxygen via a face mask and were covered with a cotton blanket and monitored. The shivering, pain, and sedation scores were assessed by an investigator in charge of the postanesthesia care unit (PACU) who was not aware of the administered drug. Postoperative shivering, pain, and sedation scores were recorded every 10 min during the first hour. The intensity of postoperative shivering was graded using a 5-point scale between 0 and 4, similar to the one validated by Sagir et al. (12): 0 = no shivering; 1 = piloerection, 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. Postoperative pain was graded on a visual analogue scale (VAS) with 0 mm = no pain, 100 mm = very severe pain. Postoperative sedation was graded as: 1 = alert, 2 = alert but drowsy, 3 = responds to voice, 4 = responds to gentle tactile stimulation, 5 = responds to vigorous tactile stimulation, 6 = not able to be aroused (10). The patients who had a pain score of greater than 40 mm received 1 mg kg^{-1} of intramuscular diclofenac sodium, and the patients with shivering grades of more than 2 received 0.5 mg kg^{-1} of IV meperidine.

2.1. Statistical analysis

Statistical analysis was performed using SPSS 15.0 (SPSS Inc., Chicago, IL). The incidence of postanesthetic shivering was used as the main end-point for statistical analysis. Based on previously published data (10), a sample size of 27 patients per group was sufficient to detect a reduction in postoperative shivering of at least 30% when compared with the control by using Fisher's exact test with an α risk set at 5% and the β risk at 20%.

Results were expressed with an absolute number (n), a percentage (%), or mean ± standard deviation (SD). Differences in age, body weight, duration of surgery, duration of anesthesia, extubation time, and the effects of treatment in all parameters of the 2 groups (tympanic temperatures, mean arterial pressures [MAPs], heart rates [HRs]) were tested using the Student t-test. The frequency distributions of ASA physical status; fentanyl, ephedrine, and atropine administration; shivering and the severity of shivering; degree of sedation; and drug side effects were tested statistically using the chi-square test and Mann–Whitney U test. Data within groups were analyzed using repeated-measures analysis of variance followed by post hoc Bonferroni correction testing. A P-value of less than 0.05 was considered to be significant.

3. Results

Patient characteristics, duration of surgery, and anesthesia were similar in both groups (Table 1).

Extubation time was longer in the dexmedetomidine group than in the placebo group ($P < 0.05$). There were significant differences within the groups regarding intraoperative hemodynamic parameters when compared with the preoperative values. Hypotension developed in 2 patients in Group D but in none in the placebo group. These patients were successfully treated with 5 mg of ephedrine. MAPs were lower in the dexmedetomidine group, especially after induction of anesthesia, at 60 min, and before extubation. Mean HRs were lower in the dexmedetomidine group after onset of the infusion at all measuring times except for 15 min. Significantly more patients in the dexmedetomidine group needed atropine to treat intraoperative bradycardia than in the placebo group ($P > 0.05$) (Table 1). None of the patients in the dexmedetomidine group were given fentanyl during the operation, whereas 5 patients in the placebo group needed intraoperative fentanyl (Table 1). The total dexmedetomidine and fentanyl consumption in Group D was 98.6 ± 20.1 μg and 77.1 ± 28.5 μg, respectively, while in Group S, fentanyl consumption was 64.5 ± 10.8 μg. Postoperatively, MAP and HR were lower in the dexmedetomidine group at all measuring times.

The tympanic temperatures of both groups showed a statistically significant reduction at the end of the operation when compared with the baseline values ($P < 0.05$). There were no statistically significant differences between groups in the intraoperative and postoperative values (Figure).

Postoperative shivering was observed in 14 patients in the placebo group (46.6%) and in 3 patients in the dexmedetomidine group (10%) ($P = 0.001$). The intensity of shivering was lower in the dexmedetomidine group than in the placebo group ($P > 0.05$), and grade 4 shivering was not noted in any of the patients in the dexmedetomidine group (Table 2).

Table 1. Patient characteristics and perioperative data (mean ± SD, n, %).

	Group S (n = 30)	Group D (n = 30)
Age (years)	31.9 ± 4.7	32.33 ± 6.2
Weight (kg)	65.87 ± 9.9	64.5 ± 10.86
ASA grade (I / II)	19 / 11	21 / 9
Duration of surgery (min)	65.83 ± 11.75	62.33 ± 19.90
Duration of anesthesia (min)	74.67 ± 11.13	71.17 ± 18.36
Extubation time (min)	5.2 ± 1.34	7.63 ± 1.62*
Operation room temperature (°C)	21.63 ± 1.03	21.93 ± 1.18
PACU temperature (°C)	24.97 ± 0.89	24.6 ± 0.81
Patient receiving atropine (n) / %	5 / 16.6	11 / 36.6
Patient receiving ephedrine (n) / %	0	2 / 6.6
Patient receiving fentanyl (n) / %	5 / 16.6	0

* $P < 0.05$ (between the groups).

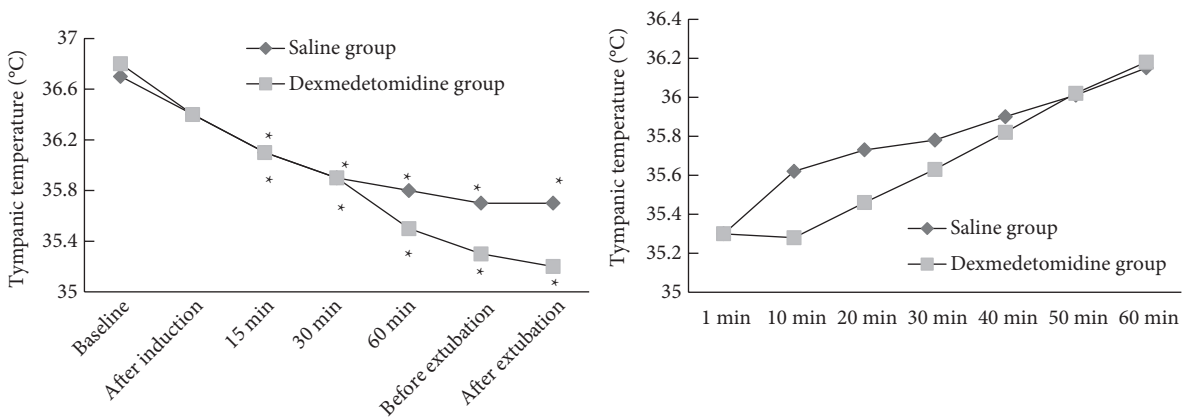

Figure. Mean intraoperative (left) and postoperative (right) tympanic temperatures. *$P < 0.05$ compared to baseline values

Table 2. Postoperative shivering scores [median (minimum–maximum)].

Time (min)	Group S (n = 30)	Group D (n = 30)
0	1.5 (0–4)	0 (0–3)*
10	1.5 (0–4)	0 (0–3)*
20	1 (0–4)	0 (0–3)*
30	0.5 (0–4)	0 (0–3)*
40	0 (0–2)	0 (0–2)
50	0 (0–2)	0 (0–2)
60	0 (0–0)	0 (0–0)

*P < 0.05 (between the groups).

Sedation scores were lower than 3 in all patients. However, sedation scores were significantly higher at all times in the dexmedetomidine group than in the placebo group (P < 0.05) (Table 3).

Pain scores were higher in the saline group during the first 40 min (P < 0.05). Moreover, the time to first analgesic requirement was shorter in the placebo group (10.3 ± 5.7 vs. 37.8 ± 5.7 min; P < 0.05).

4. Discussion

In the present study, 14 of 30 patients (46.6%) in the placebo group suffered from postoperative shivering. We found that intraoperative infusion of dexmedetomidine significantly reduced the frequency and severity of postanesthetic shivering with respect to placebo in patients undergoing gynecologic laparoscopy under general anesthesia.

The α2-receptor agonists can also be used for shivering. They are effective in treating established postanesthetic shivering and exert their effects by vasoconstriction and reducing the thresholds for shivering (13).

Core hypothermia and vasoconstriction often occur before postanesthetic shivering, although that is not always the case. Furthermore, intraoperative hypothermia is a common event during laparoscopic surgery because the contact of carbon dioxide (CO_2), which is usually delivered at room temperature (20–21 °C) and at relatively low humidity, with the peritoneal surface can cause hypothermia (12,14,15). The risk of intraoperative hypothermia is increased especially when the duration of the laparoscopic operation is long (>3 h), resulting from the higher volume of CO_2 instilled during the procedure. Similar to the study done by Elvan et al. (11), baseline

Table 3. Postoperative sedations scores [median (minimum–maximum)].

Time (min)	Group S (n = 30)	Group D (n = 30)
0	1 (0–2)	2 (0–2)*
10	1 (0–2)	2 (0–2)*
20	1 (0–2)	1 (0–2)*
30	0 (0–2)	1 (0–2)*
40	0 (0–2)	1 (0–2)*
50	0 (0–2)	1 (0–2)*
60	0 (0–2)	0 (0–2)

* P < 0.05 (between the groups).

core temperature in the present study began to decrease after 10 min, reaching a drop of 1.3° C below the baseline temperature at 60 min. However, there were no statistically significant differences between the groups. In the postoperative period, temperatures started to rise toward baseline values, but the difference between the groups did not reach the level of significance. Postanesthetic shivering could be induced by mild perioperative hypothermia.

Tramadol has been found to be effective in treating postanesthetic shivering (16). According to core temperature measurements, only 20% of the patients in the dexmedetomidine group experienced postanesthetic shivering after an abdominal hysterectomy when dexmedetomidine was infused at a rate of 0.4 $\mu g\,kg^{-1}h^{-1}$ (10). In the present study, we found 10% lower postanesthetic shivering in the dexmedetomidine group. We attributed this difference to tramadol being administered at the end of surgery for postoperative analgesia and, possibly, to tramadol and dexmedetomidine acting synergically (17). In our study, tympanic temperature measurements were comparable between the 2 groups, while Elvan et al. (11) found them to be lower in dexmedetomidine groups. Those authors attributed this to dexmedetomidine reducing the core temperature. Differences in the types of surgical procedures and postoperative analgesia could also be the sources of discrepancies in results.

Similar to findings of other studies in the literature, dexmedetomidine alone caused negligible sedation and did not depress respiration markedly (18). Respiratory depression was not encountered in any of the patients while in the recovery room, although extubation time was longer in the dexmedetomidine group. Even though the sedative effects of dexmedetomidine might have contributed to the alleviation of shivering, we believe that the proven effect of dexmedetomidine in the prevention of shivering is by the reducing of vasoconstriction and the shivering threshold centrally.

Horn et al. (19) argued that nonthermoregulatory shivering was facilitated by postoperative surgical pain. Numerous researchers demonstrated the analgesic effects of dexmedetomidine. The analgesic effect of dexmedetomidine appears to be mediated by both supraspinal and spinal mechanisms, with the α2-adrenoceptors in the locus ceruleus (a supraspinal site) and dorsal horn of the spinal cord being involved in this activity (20,21). Sitilci et al. (22) argued that patients could achieve better postoperative comfort and the need for tramadol would be lower if dexmedetomidine was infused continuously during a surgical procedure. Similarly, in a placebo-controlled trial, Venn et al. (23) reported that dexmedetomidine decreased the need for rescue sedation and analgesia significantly for up to 24 h after the operation. Gurbet et al. (20) reported that effective postoperative analgesia and reduction in requirement for postoperative morphine with consequent reduction in the incidence of adverse effects could be achieved by continuous IV administration of dexmedetomidine during abdominal surgery. In the present study, significantly higher VAS scores in the dexmedetomidine group were found than in the placebo group within the first 40 min, associated with the high frequency of shivering in the placebo group.

Compared to the placebo group, MAP and HR values measured during and after the surgery were significantly lower in the dexmedetomidine group, and these hemodynamic findings were reported in other studies, as well (20,24). Use of α2-receptor agonists for prevention of postanesthesia shivering can be complicated by their principal pharmacological effects, namely hypotension and bradycardia (25), but none of the patients who received dexmedetomidine in the present study experienced clinically significant bradycardia or required correction of hemodynamics.

In conclusion, the results of this study indicated that intraoperative dexmedetomidine infusion rendered a significant reduction in the frequency and severity of postanesthetic shivering while causing minimal sedation. Intraoperative dexmedetomidine infusion, especially during laparoscopic procedures, is an alternative worth considering in alleviation of postoperative shivering, as well as in analgesia and sedation.

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