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Effects of remifentanil and dexmedetomidine on the mother's awareness and neonatal Apgar scores in caesarean section under general anaesthesia

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Abstract

Objective: This study aimed to compare the effects of remifentanil and dexmedetomidine on awareness during the induction of general anaesthesia.

Material and Methods: Ninety patients scheduled for elective caesarean section under general anaesthesia were included and randomly divided into three anaesthesia groups: 2 mg/kg propofol (control group); 2 mg/kg propofol and 1 μg/kg dexmedetomidine (dexmedetomidine group); and 2 mg/kg propofol and 1 μg/kg remifentanil (remifentanil group). All patients received routine monitoring, and Apgar scores at 1 and 5 minutes were recorded. The bispectral index and the isolated forearm technique were used to determine the depth of anaesthesia.

Results: Bispectral index values at skin and uterine incisions and at delivery were similar among the groups. The number of patients who responded positively to the isolated arm technique during the induction period was also similar. One-minute Apgar scores in the control group were significantly lower and 5-minute Apgar scores significantly higher than those in the other groups.

Conclusion: The effects of remifentanil and dexmedetomidine added to propofol on maternal awareness, neonatal Apgar scores, and bispectral index values were similar compared with propofol alone. However, it was observed that remifentanil controlled the haemodynamic responses to sympathetic stimuli in a better manner than dexmedetomidine.

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General anaesthesia, awareness, caesarean section, remifentanil, dexmedetomidine, propofol, heart rate, blood pressure

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Background

Pregnant women who are scheduled for elective caesarean section are operated on under general anaesthesia. The most appropriate anaesthetic method should be chosen in terms of the pregnant woman's preference, and according to clinical and laboratory findings and the experience of the anaesthetist. A previous study that analysed pregnant women retrospectively for 10 years reported that there was an increase in the rate of regional anaesthesia in Turkey.[1] The rates of general anaesthesia, spinal anaesthesia, combined spinal-epidural anaesthesia, and epidural anaesthesia were 45%, 45%, 6.6%, and 2.8%, respectively. During general anaesthesia, the incidence of being awake has been reported as 0.1%–1%.[2–5] The frequency of the reported incidence of psychological symptoms in patients experiencing awareness ranges from 33% to 69%.[6,7] Patients are at high risk of awareness during cardiac, trauma, and caesarean surgeries.[2,8,9]

Almost all opioid analgesics and sedatives can easily pass through the placenta and affect the foetus. Therefore, the use of lower doses of anaesthetic agents during induction of anaesthesia in pregnancies creates a high-risk group for intraoperative awareness.[10,11]

Awareness can be in the form of hearing voices, feeling paralysis, developing anxiety, intubation, and painful remembrance. General anaesthesia, which aims to make the body insensitive to painful stimuli, should be sufficiently deep. Clinical symptoms associated with sympathetic activation[12] and end-tidal volatile anaesthetic concentration[13] are not sufficient to assess the depth of anaesthesia and intraoperative awareness. Although various studies have shown that electroencephalography (EEG)-based monitors reduce the risk of awareness in measuring the depth of anaesthesia, it only reflects cortical activity.[14] Monitoring the depth of anaesthesia during the operation is important for producing solutions to this problem.

This study investigated the effects of remifentanil and dexmedetomidine added to propofol on intraoperative awareness in the induction of general anaesthesia in caesarean section.

Materials and methods

This study was conducted in 90 patients with American Society of Anaesthesiologists I or II classification, who had an indication for elective caesarean section. The patients provided informed written consent and institutional ethics committee approval was obtained. Patients with severe cardiovascular disease, renal and liver failure, advanced asthma and chronic obstructive pulmonary disease, and antipsychotic, antihypertensive, and beta-blocker drug use were excluded.

Patients were taken to the operation room and their echocardiogram, blood pressure, heart rate, and peripheral oxygen saturation values were monitored (KMA 900, Petaş Profesyonel Elektronik San ve

Tic A.Ş, Ankara, Turkey). Infusion of lactated Ringer's solution was started by establishing peripheral vascular access on the back of the right hand with an 18 G cannula. Monitoring of the anaesthetic depth was performed with bispectral index monitoring (BIS XP monitor, Model A-2000TM; Aspect Medical System, Newton, MA, USA). BIS values of 40–60 were accepted as adequate surgical anaesthetic depth, and the values were recorded. A sphygmomanometer cuff was mounted to the right arm before induction. Before applying a neuromuscular blocker, the motor response was suppressed by inflating the sphygmomanometer cuff to 250 mmHg of pressure to evaluate Tunstall's isolated forearm technique.[15] Following induction, the instruction of "if you hear it, press my hand and leave it" was provided to the patients three times with a 1-minute interval. The answers were evaluated as positive or negative. Any positive answer to three instructions was recorded as "positive". The sphygmomanometer cuff was deflated after the evaluations.

Patients were randomly divided into three groups by the sealed envelope method. A total of 0.9% NaCl in the propofol (control) group (n = 30), 1 μg/kg remifentanil in the remifentanil group (n = 30), and 1 μg/kg dexmedetomidine in the dexmedetomidine group (n = 30) were administered intravenously within 10 minutes before induction of anaesthesia. Induction of anaesthesia was achieved with 2 mg/kg propofol and 0.6 mg/kg rocuronium in all of the groups. Endotracheal intubation was followed by volume-controlled mechanical ventilation with 50% oxygen and 50% air + 1% sevoflurane, with the end-tidal carbon dioxide concentration setting of 35–40 mmHg. Anaesthesia was administered at 2 μg/kg fentanyl and sevoflurane and 50% oxygen and 50% air. BIS values remained at 40–60 after delivery of the neonate.

Table 1. Brice questionnaire form

1- What is the last thing you remember before you slept?
2- What is the first thing you remember when you woke up?
3- Do you remember anything between sleeping and waking up?
4- Did you dream of anything during the sleep period of your operation?

While the fascia and subcutaneous area were being closed, anaesthesia with 20 mL of levobupivacaine 0.25% was administered, and ventilation with 100% oxygen was provided. After the patients were treated with 0.01 mg/kg atropine and 0.03 mg/kg neostigmine, extubation was performed after checking that spontaneous breathing was sufficient. The patients were questioned about recalling perioperative events using the Brice Questionnaire[16] (Table 1) 24 hours after the operation.

Mean, standard deviation, frequency and ratio values are shown. Distribution of the variables was tested by the Kolmogorov–Smirnov test. Homogeneity of variance of the variables was tested. For analysis of parametric data, the Tukey and Tamhane tests were used in ANOVA sub-analyses. The Mann–Whitney U-test was used in Kruskal–Wallis subanalyses in the analysis of nonparametric data. The chi-square test was used for analysis of proportional data. IBM SPSS Statistics, Version 19.0 (IBM Corp., Armonk, NY, USA) was used in the analyses. Analyses were made at 95% confidence interval. A p-value <0.05 was considered as statistically significant.

Results

A total of 90 pregnant women with a term pregnancy who were aged from 18–42 years of age were included in the study. Mean age, height, and weight of the patients

were not significantly different among the groups (Table 2).

Mean arterial pressure in the remifentanil group was significantly lower than that in the dexmedetomidine and control groups at the time of induction and intubation (all $p < 0.05$) (Table 3). Mean heart rate in the dexmedetomidine and remifentanil groups was significantly lower than that in the control group during induction, intubation, skin incision, and uterine incision (all $p < 0.001$) (Table 4).

Table 2. Demographic data

	Control group (n = 30)	Remifentanil group (n =30)	Dexmedetomidine group (n = 30)	p
Age (years)	29.6 ± 4.7	29.7 ± 6.3	29.2 ± 6.8	0.136
Height (cm)	61.1 ± 6.4	162.1 ± 5.8	162.1 ± 5.9	0.773
Weight (kg)	73.7 ± 14.1	80.5 ± 8.6	80.0 ± 11.6	0.051

Values are presented as the mean ± standard deviation.

Table 3. Mean arterial pressure in the three groups (mmHg)

	Control group	Remifentanil group	Dexmedetomidine group	p
Induction	100 ± 14	87 ± 10*	96 ± 8	<0.001
Intubation	110 ± 17	78 ± 9*	103 ± 13	<0.001
Skin incision	115 ± 21	99 ± 10*	106 ± 11	<0.001
Uterine incision	102 ± 17	97 ± 9*	106 ± 9	0.016
Delivery	98 ± 21	101 ± 8	99 ± 20	0.764
Post-fentanyl	84 ± 14	81 ± 9	89 ± 11	0.057
Uterine closure	78 ± 12	85 ± 10	83 ± 12	0.066
Skin closure	98 ± 22	86 ± 9	89 ± 12	0.016
Extubation	106 ± 17	104 ± 10	103 ± 10	0.242

*$p < 0.05$ compared with the control and dexmedetomidine groups.
Values are presented as the mean ± standard deviation.

Table 4. Heartbeat in the three groups (beats per minute)

	Control group	Remifentanil group	Dexmedetomidine group	p
Induction	94 ± 15	76 ± 10*	70 ± 7*	<0.001
Intubation	115 ± 15	83 ± 13*	84 ± 10*	<0.001
Skin incision	113 ± 16	96 ± 16*	89 ± 17*	<0.001
Uterine incision	103 ± 13	91 ± 14*	85 ± 11*	<0.001
Delivery	98 ± 13	95 ± 15	86 ± 12**	0.003
Post-fentanyl	86 ± 10	81 ± 10	76 ± 9**	0.001
Uterine closure	85 ± 9	81 ± 10	76 ± 10**	0.006
Skin closure	99 ± 11	83 ± 9*	81 ± 9*	<0.001
Extubation	102 ± 11	106 ± 9	96 ± 12**	0.003

*$p < 0.05$ compared with the control group, **$p < 0.05$ compared with the control and remifentanil groups.
Values are presented as the mean ± standard deviation.

There was no significant difference in mean BIS index values at skin incision, uterine incision, and delivery among the groups. The mean BIS index value in the control group was significantly higher at induction and intubation than that in the dexmedetomidine and remifentanil groups (all $p < 0.05$) (Figure 1).

One-minute Apgar scores in the control group were significantly lower than those in the remifentanil and dexmedetomidine groups (both $p < 0.05$). Five-minute Apgar scores in the dexmedetomidine group were significantly higher than those in the remifentanil and control groups (both $p < 0.05$) (Figure 2).

The isolated forearm technique positivity rates among the groups were similar ($p > 0.05$) (Figure 3). None of the patients was able to recall the perioperative events at the questionnaire conducted at 24 hours postoperatively.

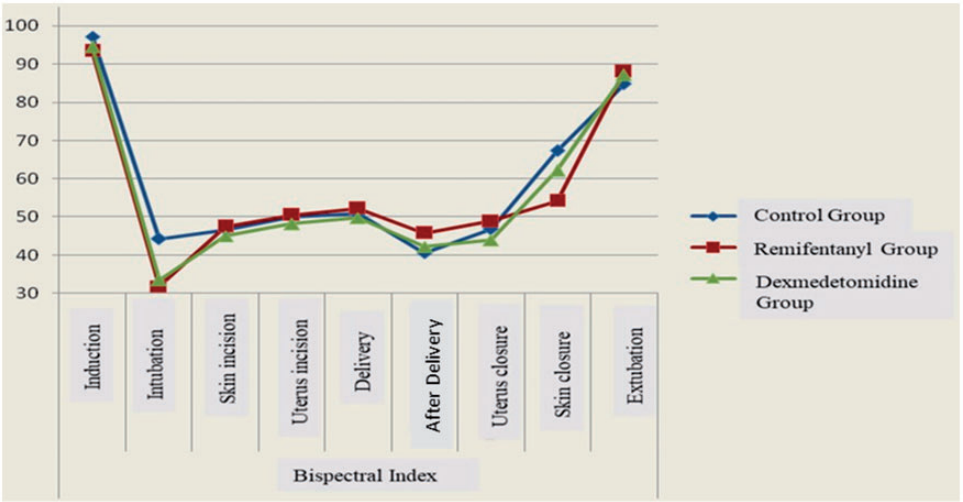

Figure 1. Bispectral index values of the groups (mean ± SD).

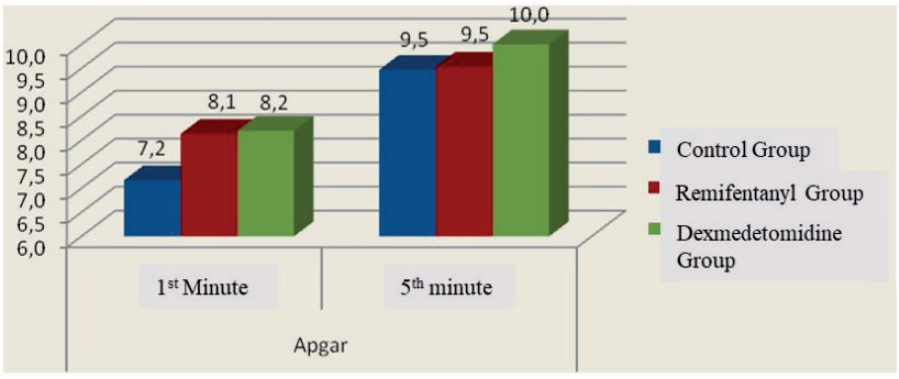

Figure 2. Apgar score values at 1 and 5 minutes in the groups.

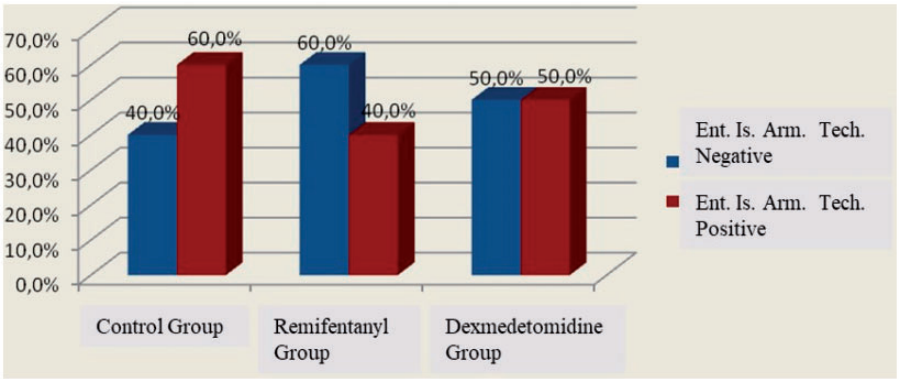

Figure 3. Negative and positive rates of the isolated forearm technique (n, %). Ent. Is. Arm. Tech. = Isolated forearm technique.

Discussion

In our study, the incidence of awareness was similar among the groups. However, BIS values in the dexmedetomidine and remifentanil groups were significantly lower at induction and intubation of anaesthesia than those in the control group.

While the probable awareness rate during general anaesthesia is approximately 1/19600, it is 1/670[17] during caesarean section. Therefore, high-risk anaesthesia techniques, as well as high-risk patients, need to be investigated for awareness during surgery. Therefore, we studied caesarean section as a high-risk surgical group to examine awareness. Intraoperative awareness is more frequent than postoperative recall. However, a previous study showed that 66% of awareness was observed in patients who received the isolated forearm technique before the operation.[18] Furthermore, remembrance was observed postoperatively in one quarter of these patients.

Cerebral monitoring, such as cerebral status monitors, entropy, auditory evoked potential, and the BIS are used to determine the depth of anaesthesia. Titration of the hypnotic component of anaesthesia using the BIS has widespread application in current clinical practice in terms of reducing the dose of anaesthetic to be administered and shortening the length of stay in the hospital. Co-administration of drugs may limit the traumatic effect of intraoperative awareness.

One of the most important expectations in the obstetric application of anaesthesia is the protection of the newborn from depressant medications while the mother is sleeping at a sufficient depth. To reduce depression of the newborn to the lowest level, anaesthesia is maintained at a superficial level causing the problem of awareness in the mother, who is under the influence of a myorelaxant. Ghoneim et al.[19] reported that the most frequent reason for intraoperative awareness was superficial anaesthesia.

Monitoring of the BIS and isolated forearm technique were used in our study to examine the effects of dexmedetomidine or remifentanil applied on the depth of anaesthesia and awareness. Although BIS values remained within target values in all of the patients, the incidence of intraoperative awareness in the control group was high, even though there was no significant difference.

Hypnosis and amnesia cannot always be guaranteed, even though monitoring ofend-tidal volatile anaesthetic concentrations

is a method that is used to remove awareness.[20,21] Haemodynamic parameters are not reliable when examining the depth of anaesthesia. Although physiological changes (tachycardia, hypertension) can reflect poor anaesthesia, a harmful stimulus response cannot be predicted using hypovolemic or beta-adrenergic blockers. However, tachycardia and hypertension due to sympathetic activation may occur even at a depth of adequate anaesthesia. Muscle relaxant use can complicate the physiological effects of anaesthesia. Although EEG reflects the effects of general anaesthesia in brain monitoring, it is not practical for intraoperative monitoring.[22]

Recent studies have reported that BIS monitoring reduces the risk of awareness, while in other studies, more awareness was experienced or BIS monitoring did not show any superiority to other monitoring methods.[20,23–26] Avidan et al.[21] compared end-tidal anaesthetic gas concentrations and BIS monitoring in a consecutive series of 2000 patients. The incidence of volatile anaesthetic gas consumption and awareness was similar among the groups. Awareness occurred in the periods when the BIS value was higher than 60. Therefore, the authors concluded that BIS monitoring would not cause a false sense of confidence. In our study, the positive rate of the isolated forearm technique was 60% in the control group, 40% in the remifentanil group, and 50% in the dexmedetomidine group in the induction period in which all patients had a BIS < 60. Hadavi et al.[27] reported that none of the patients remembered an event related to surgery at 24 hours postoperatively using a questionnaire, although 20% of the pregnancies had a BIS > 60. In our study, a BIS > 60 was recorded in 18% of the patients, especially in the skin closure period. Additionally, none of the patients remembered an event related to surgery at 24 hours postoperatively, although the response to the isolated forearm technique was positive in approximately half of the patients. To maintain haemodynamic responses in women undergoing caesarean section in whom general anaesthesia is applied, short-acting opioids, such as alfentanil and remifentanil, can be used.[28–31] These opioids can also be used in pregnant women with hypertension and cardiac disease[32,33] in case paediatric support is provided against the risk of respiratory depression in the neonate. Li et al.[34] observed the effects of remifentanil and dexmedetomidine on maternal haemodynamics and neonatal results using the BIS in elective caesarean delivery. Badawy et al.[35] investigated the effects of remifentanil and dexmedetomidine on haemodynamics in adverse preeclampsia and neonatal outcomes in preeclamptic adult patients. Nair et al.[36] examined the available literature to determine possible indications for caesarean section during labour and non-obstetric surgery. Aguilar-Montiel et al.[37] used remifentanil and dexmedetomidine as an alternative to regional analgesia at birth and investigated their effects.

In our study, although there were significant differences in the Apgar score among the groups, respiratory depression requiring airway support was not detected in any of the neonates. We are unable to explain this difference in Apgar scores in terms of the pharmacodynamics of drugs used.

Conclusion

The effects of remifentanil and dexmedetomidine added to propofol on awareness of mother, BIS values, and neonatal APGAR scores are similar compared with propofol alone in caesarean sections. However, remifentanil controls the haemodynamic responses to sympathetic stimuli in a better manner than does dexmedetomidine.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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