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COMPARISON OF THE EFFECTS OF ANESTHESIA TECHNIQUE AND MATERNAL WARMING ON NEONATAL BODY TEMPERATURE IN CESAREAN SECTION OPERATIONS: A RETROSPECTIVE STUDY

SEZARYEN OPERASYONLARINDA UYGULANAN ANESTEZİ TEKNİĞİ VE MATERNAL ISITMANIN YENİDOĞAN VÜCUT SICAKLIĞINA ETKİLERİNİN KARŞILAŞTIRILMASI: RETROSPEKTİF ÇALIŞMA

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ABSTRACT

Objective: Both general and spinal anesthesia are preferred methods in cesarean section operations. Inadequate thermoregulation mechanisms of newborns and changes in maternal body temperature caused by anesthetic approaches adversely affect the newborn. Our study aimed to retrospectively compare the effects of different anesthetic techniques and maternal warming on neonatal body temperature in cesarean section operations.

Method: Our study was performed retrospectively on the data of 112 American Society of Anesthesiologists(ASA) I-II-III patients who underwent cesarean section after ethics committee approval. General anesthesia was defined as Group G1 (n:28) heated with a hot air blower system and Group G2 (n:28) without heating. Spinal anesthesia was defined as Group S1 (n:28) heated with a hot air blower system and Group S2 (n:28) without heating. Demographic data, number, and week of pregnancy were recorded. Apical heart peak (AHP), non-invasive blood pressure (BP) [systolic blood pressure (SBP), diastolic blood pressure (DBP)], peripheral capillary oxygen saturation (SpO_2), and body temperatures at baseline, at 5, 15, and 20 min and at the time the baby left the womb were recorded. Newborns were recorded at 0 and 1 minute. APGAR scores of the newborn at 1 and 5 minutes were recorded. Patients with chills, shivering, nausea, and vomiting were recorded in all groups.

Results: Infant temperature and APGAR scores were significantly higher in the groups receiving spinal anesthesia(Group S1+S2) than in the groups receiving general anesthesia (Group G1+G2), respectively ($p<0.05$). Maternal temperature averages were statistically significantly higher in Groups G1 and S1 than in Groups G2 and S2, respectively ($p<0.05$).

Conclusions: Maternal warming and spinal anesthesia increase maternal and neonatal body temperature and APGAR scores. Therefore, maternal warming and spinal anesthesia techniques are recommended for pregnant women.

Keywords: Neonatal hypothermia, cesarean section, general anesthesia-spinal anesthesia, maternal warming, APGAR score

ÖZ

Amaç: Sezaryen operasyonlarında genel ya da spinal anestezi uygulamasının her ikisi de tercih edilen yöntemlerdir. Yenidoğanların termoregülasyon mekanizmalarının yetersizliği ve anestezik yaklaşımların maternal vücut ısısında oluşturduğu değişimler yenidoğanı olumsuz etkilemektedir. Çalışmamızın amacı; sezaryen operasyonlarında uygulanan farklı anestezi teknikleri ve maternal ısıtmanın yenidoğan vücut sıcaklığına etkilerini retrospektif olarak karşılaştırmaktır.

Yöntem: Çalışmamız etik kurul onayı alındıktan sonra sezeryan operasyonu geçiren Amerikan Anesteziyoloji Derneği'nin fiziksel durum sınıflaması (ASA) I-II-III olan 112 hastanın verileri üzerinden retrospektif olarak yapıldı. Genel anestezi uygulanan sıcak hava üflemeli sistem ile ısıtılan Grup G1 (n:28), ısıtma uygulanmayan Grup G2 (n:28) olarak tanımlandı. Spinal anestezi uygulanan sıcak hava üflemeli sitem ile ısıtılan Grup S1 (n:28), ısıtma uygulanmayan Grup S2 (n:28) olarak tanımlandı. Demografik veriler, gebelik sayısı ve haftası kaydedildi. Hastaların kalp tepe atımları (KTA), non-invaziv kan basıncı [sistolik kan basıncı, diyastolik kan basıncı], periferik oksijen saturasyonu (SpO_2) ve vücut sıcaklıklarının başlangıç, 5. ,15. , 20. dk ve bebeğin anne karnından çıktığı andaki değerleri kayıt edildi. Yenidoğanın 0. dk ve 1. dakikada kaydedildi. Yenidoğanın 1. ve 5. dakikadaki APGAR skorları kaydedildi. Tüm gruplarda üşüme, titreme, bulantı, kusma görülen hastalar kaydedildi.

Bulgular: Bebek sıcaklığı ve APGAR skorları spinal anestezi yapılan(Grup S1+S2) gruplarda genel anestezi alan(Grup G1+G2) gruplardan sırasıyla anlamlı yüksek bulundu ($p<0,05$). Anne sıcaklık ortalamları Grup G1 ve S1 de sırasıyla G2 ve S2 istatiksel olarak anlamlı yüksek bulundu ($p<0,05$).

Sonuç: Maternal ısıtma uygulaması ve spinal anestezi anne ve yenidoğan vücut sıcaklığını ve yenidoğanın APGAR skorunu arttırmaktadır. Bu nedenle gebelerde maternal ısıtma ve spinal anestezi tekniği tercih edilmesi önerilir.

Anahtar Kelimler: Yenidoğan hipotermisi, sezeryan, genel anestezi-spinal anestezi, maternal ısıtma, APGAR skoru

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Introduction

Perioperative hypothermia is a decrease in body temperature below 36°C from the first hour before anesthesia to the first 24 hours after anesthesia.[1] Hypothermia develops as a result of disruption of the thermoregulation mechanism due to factors such as anesthesia and premedication drugs, antiseptic solutions, low ambient temperature, wet surgical sterile drapes on the patient, cold intravenous fluids, use of non-humidified gases and exposure of tissues.[1,2] Hypothermia is observed with a frequency of 50-90% in the perioperative period.[3] As a result of hypothermia, complications such as prolonged duration of action of anesthetic drugs, increased recovery time after anesthesia, increased surgical wound infection, coagulopathy, respiratory and cardiovascular system depression, and increased hospital stay may occur.[4]

Cesarean delivery has increased in many industrialized countries in recent years for various reasons. General or spinal anesthesia is the preferred method for cesarean section. Both methods have different advantages and disadvantages.[5,6]

During general anesthesia, anesthetic agents cause hypothermia by inhibiting central thermoregulation by affecting hypothalamic functions, whereas neuraxial anesthesia causes hypothermia by causing vasodilation and subsequent heat redistribution in the internal organs.[2]

Considering the inadequacy of the thermoregulation mechanisms of newborns and the changes in maternal body temperature caused by all anesthetic approaches, it is very important to ensure maternal normothermia to protect the newborn from hypothermia and its adverse effects.[7] Various methods can be applied to prevent perioperative hypothermia. Hot air fans, radiant heaters, and resistance blankets warm the patient from the outside and reduce heat distribution from the center to the periphery.[4,8] Not enough studies show the effects of active heating techniques on maternal and neonatal body temperature during cesarean section.[9]

Our study aimed to retrospectively compare the effects of different anesthesia techniques and maternal warming on neonatal body temperature in cesarean section operations.

Methods

Our study was conducted retrospectively on the data of 112 patients who underwent cesarean section operation in the gynecology and obstetrics clinic between January 1 and May 1, 2017, after approval (approval dated 13/06/2017 and numbered 1576) was obtained from the Ethics Committee of Health Sciences University Şişli Hamidiye Etfal Training and Research Hospital. All procedures were performed following the ethical standards specified in the Declaration of Helsinki (2008).

The data of American Society of Anesthesiologists (ASA)I-II-III patients, for whom complete data were available by reviewing anesthesia documents and neonatal unit records, were included. ASA IV patients, patients under 18 years of age, patients with neuropsychiatric diseases, and patients with substance abuse were excluded from the study.

The patients whose data were analyzed were divided into four groups. Of the 56 patients who underwent general anesthesia for cesarean section, 28 patients who were heated with a hot air blower system were defined as Group G, and 28 patients who were not heated were defined as Group G2. Of the 56 patients who underwent spinal anesthesia for cesarean section, 28 patients who were heated with a hot air blower system were defined as Group S1, and 28 patients who were not heated were defined as Group S2.

- *Group G1 (n:28) General anesthesia / heated with a blown heater
- *Group G2 (n:28) General anesthesia / no heating
- *Group S1 (n:28) Spinal anesthesia / heated with a blown heater
- *Group S2 (n:28) Spinal anesthesia / no heating

Demographic data such as age, weight, height, body mass index (BMI), body mass index (BMI), ASA, the number of weeks of pregnancy, and gestational week of the patient were recorded from the preanesthetic evaluation document. All patients were operated in the same operating room, and the ambient temperature was kept constant at 24°C. All patients underwent standard monitoring with electrocardiogram (ECG), non-invasive blood pressure (BP) [systolic blood pressure (SBP), diastolic blood pressure (DBP)] and peripheral capillary oxygen saturation (SpO_2) after admission to the operating room. All patients in Group G1 and Group S1 were warmed with a warm air blower system (Bair Hugger™ brand heating device) from the beginning.

The patient's body temperature was measured with a laser thermometer (Medix® brand). Intravenous hydration was started with a 20-gauge angiocath.

After preoxygenation, anesthesia induction was performed with 2 mg/kg propofol and 0.6 mg/kg rocuronium, and orotracheal intubation was performed in Group G1 and Group G2 patients under general anesthesia. Sevoflurane with 50% oxygen and 50% air mixture was used to maintain anesthesia. Fentanyl 1 mcg/kg was administered intravenously after the baby's exit from the womb. Spinal anesthesia was performed with 2.1 cc bupivacaine hydrochloride (Marcain® Spinal 0.5% Heavy) after cerebrospinal fluid (CSF) flow was observed by entering the L3-4 spinal space with a 25-gauge Quinckle spinal needle after skin disinfection in the sitting position in Group S1 and Group S2.

In all groups, apical heart peak (AHP), BP (SBP and DBP), SpO_2, and body temperature values were recorded at baseline and 5 minutes, 15 minutes, and 20 minutes afterward. In all groups, the body temperature of the newborn babies was measured and recorded with a laser thermometer by a neonatologist at the time of emergence from the mother's womb and 1 minute thereafter. In all groups, a neonatologist evaluated and

recorded APGAR scores of newborn babies at the 1st and 5th minute.

Patients with chills, shivering, nausea, and vomiting as complications in all groups were recorded. Ephedrine requirements of patients who underwent spinal anesthesia were recorded.

The patients who underwent general anesthesia were administered neuromuscular blockade antagonization with 0.01 mg/kg atropine and 0.03 mg/kg neostigmine at the end of the operation when spontaneous respiration occurred after anesthesia maintenance was terminated. After spontaneous respiration was adequate and airway reflexes were complete, they were extubated and sent to the ward.

Patients who underwent spinal anesthesia were followed up at the end of the operation until the motor and sensory blockade ended and sent to the ward.

Statistical Analysis

SPSS program (Version 22, SPSS Inc., Chicago, IL, USA) was used for calculations. Descriptive statistics were given as numbers and percentages for categorical variables and mean, standard deviation, minimum, maximum, and median for numerical variables. Since the numerical variables did not fulfill the normal distribution condition, two independent group comparisons were made using the Mann-Whitney U test. The ratio of categorical variables between groups was tested by Chi-Square Analysis. The statistical alpha significance level was accepted as $p<0.05$.

Results

The data of 112 patients who underwent cesarean section in the Gynecology and Obstetrics Clinic were retrospectively analyzed. There was no statistically significant difference between the age, gestational week, number of pregnancies, and ASA distribution of the groups. BMI was statistically significantly higher in Group G2 compared to Group G1 ($p<0.05$). Mean height was statistically significantly higher in Group S1 than in Group S2 ($p<0.05$). The mean weight was statistically significantly higher in Group S1 than in Group G1 ($p<0.05$) (Table 1).

There was no statistically significant difference in systolic arterial pressure between general and spinal patient groups at all times ($p>0.05$). Mean SBP was statistically significant at all times in Group G1 compared to Group S1 ($p<0.05$). In Group G2, it was statistically significantly higher than Group S2 at 0 and 5 minutes. ($p<0.05$) (Table 2).

The mean diastolic arterial pressure was found to be statistically significantly higher in Group G1 compared to Group S1 at 20 minutes ($p<0.05$).

There was no statistically significant difference between Group G1 and Group G2, Group S1, and Group S2 patient groups at all times in maternal peak heart rate. The mean AHP was found to be statistically significantly higher in Group G1 at 5 minutes compared to Group S1 ($p<0.05$). In Group G2, it was statistically significantly higher than Group S2 at 0 and 5 minutes ($p<0.05$).

Table 1. Demographic Data of Patients

	Group G1	**Group G2**		**Group S1**	**Group S2**		**G1 vs. S1**	**G2 vs. S2**
	mean ± SD	mean ± SD	p	mean ± SD	mean ± SD	p	p	p
Age (years)	28.4±5.9	28.4±6.7	0.967	26.6±6.4	26.7±5.7	0.948	0.176	0.398
Weight (kg)	74.4±7.8	77.6±7.6	0.119	80.3±8.9	75.1±13.8	0.098	0.008*	0.129
Height (cm)	167.9±6.6	166.7±5.6	0.495	170.4±4	164.3±7.7	0.002*	0.148	0.162
BMİ (kg/m^2)	26.4±2.4	28.0±3.2	0.044*	27.6±2.9	27.8±4.7	0.474	0.112	0.328
Gestational week	38.7±1.1	38.8±1.1	0.701	39.0±0.9	39.0±0.7	0.701	0.334	0.797
Number of Pregnancies	2.2±0.8	2.6±1.1	0.256	2.1±0.8	2.2±1.2	0.877	0.485	0.194
ASA	1.64±0.56	1.57±0.57	0.614	1.43±0.63	1.43±0.57	0.877	0.111	0.313

*p<0.05

BMİ: Body mass index, ASA: American Society of Anesthesiologists, SD: Standard deviation

kg: kilogram, cm: centimetre

Table 2. Systolic Blood Pressure Values

	Grup G1	**Grup G2**		**Grup S1**	**Grup S2**		**G1 vs. S1**	**G2 vs. S2**
	mean ± SD	mean ± SD	p	mean ± SD	mean ± SD	p	p	p
SBP (mmHg) 0. min	120.4±14.4	118.8±14.8	0.604	112.6±12.3	109.1±18.2	0.095	0.026*	0.015*
SBP (mmHg) 5. min	119.9±13.2	115.1±13.1	0.158	111.1±11.1	107.6±16.8	0.124	0.009*	0.043*
SBP (mmHg) X. min	117.8±11.3	113.9±12.3	0.146	110.4±11.1	107.4±14.5	0.139	0.019*	0.054
SBP (mmHg) 15. min	117.4±10.6	112.8±11.6	0.194	110.3±12.2	108.5±12.8	0.640	0.035*	0.146
SBP (mmHg) 20. min	117.3±10.8	111.9±10.5	0.155	110.6±12.1	109.3±13.1	0.543	0.046*	0.285

*p<0.05

X. min : Maternal systolic blood pressure values at the time the baby leaves the womb

SBP: Systolic blood pressure, min: minutes, SD: Standard deviation

There was no statistically significant difference in mean SpO_2 between all patient groups at all times.

Mean maternal temperature was significantly higher in the heated groups (Group G1, Group S1) compared to the unheated groups (Group G2, Group S2) (p<0.05) (Table 3).

There was a significant difference in the mean infant temperatures and APGAR scores at all times in the heated patient groups. Mean infant temperatures and APGAR scores were statistically significantly higher in Group G1 and Group S1 than in Group G2 and Group S2, respectively (p<0.05).

In the unheated groups, the mean APGAR scores of Group S2 were statistically significantly higher than Group G2 (p<0.05) (Table 4).

Patients did not need ephedrine in any of the groups. Chills and shivering rates were significantly higher in the non-heated groups (Group G2 and Group S2) than in the heated groups (Group G1 and Group S1) (p<0.05). Nausea and vomiting were significantly higher in Group S2 compared to Group G2 (p<0.05) (Table 5).

Table 3. Maternal Temperature Values

	Group G1	**Group G2**		**Group S1**	**Group S2**		**G1 vs. S1**	**G2 vs. S2**
	mean ± SD	mean ± SD	p	mean ± SD	mean ± SD	p	p	p
Maternal temperature(°C) 0. min	36.7±0.2	36.4±0.1	<0.001*	36.7±0.1	36.4±0.1	<0.001*	0.521	0.089
Maternal temperature (°C) 5. min	36.7±0.1	36.4±0.1	<0.001*	36.7±0.1	36.4±0.1	<0.001*	0.622	0.099
Maternal temperature(°C) X. min	36.7±0.1	36.4±0.1	<0.001*	36.7±0.1	36.4±0.1	<0.001*	0.327	0.993
Maternal temperature(°C) 15. min	36.7±0.1	36.4±0.1	<0.001*	36.8±0.2	36.4±0.1	<0.001*	0.056	0.729
Maternal temperature(°C) 20. min	36.7±0.1	36.4±0.1	<0.001*	36.7±0.1	36.4±0.1	<0.001*	0.123	0.171

*p<0.05

X. min: Maternal temperature at the time the baby leaves the womb, SD: Standard deviation, min: minutes

Table 4. Infant Temperature and APGAR score

	Group G1	**Group G2**		**Group S1**	**Group S2**		**G1 vs. S1**	**G2 vs. S2**
	mean ± SD	mean ± SD	p	mean ± SD	mean ± SD	p	p	p
Infant Temperature(°C) 0. min	36.6±0.1	36.4±0.1	<0.001*	36.7±0.1	36.4±0.1	<0.001*	0.001*	0.670
Infant Temperature(°C) 1. min	36.6±0.1	36.4±0.1	<0.001*	36.7±0.1	36.4±0.1	<0.001*	0.001*	0.622
APGAR Score 1. min	8.71±0.66	7.46±0.51	<0.001*	9.46±0.58	8.04±0.74	<0.001*	<0.001*	0.003*
APGAR Score 5. min	9.29±0.71	8.14±0.52	<0.001*	9.82±0.39	8.82±0.67	<0.001*	0.002*	<0.001*

*p<0.05

min: minutes

Table 5. Complications

	Group G1		**Group G2**			**Group S1**		**Group S2**			**G1 vs. S1**	**G2 vs. S2**
	n	%	n	%	p	n	%	n	%	p	p	p
Used Ephedrine	0	0.0	0	0.0	-	0	0.0	0	0.0	-	-	-
Chills	0	0.0	15	53.6	<0.001*	0	0.0	24	85.7	<0.001*	-	0.009*
Shivering	0	0.0	11	39.3	<0.001*	0	0.0	19	67.9	<0.001*	-	0.032*
Nausea	0	0.0	3	10.7	0.236	5	17.9	12	42.9	0.080	0.051	0.007*
Vomiting	0	0.0	3	10.7	0.236	5	17.9	12	42.9	0.080	0.051	0.007*

*p<0.05

n: Number of patients, %: Percentage

Discussion

Both general anesthesia and regional anesthesia techniques affect the thermoregulation mechanism in different ways and cause perioperative hypothermia. The temperature drop during anesthesia develops with the redistribution of central heat to peripheral tissues.[10] The preferred method of anesthesia is not the only factor affecting the occurrence of perioperative hypothermia. The size and duration of the surgical procedure, ambient temperature, and the amount of fluids used are other factors that may cause hypothermia.[11,12] It is thought that monitoring pregnant women at 24°C room temperature and the fact that cesarean section operations are not very long-lasting surgical procedures relatively reduce the incidence of hypothermia.[13] In our study, the ambient temperature of the operation room was kept constant at 24°C.

There are no European or American national recommendations for the use of perioperative warming in women undergoing cesarean section.[14] Although

several studies investigate active warming during cesarean section, there is no consensus that it improves maternal and neonatal outcomes.[15] In a study conducted by Bernardis et al. in pregnant women undergoing spinal anesthesia during cesarean section, it was shown that active warming for thirty minutes starting before the procedure reduced the development of hypothermia.[16] According to a meta-analysis including twelve patients, Munday J et al. stated that intravenous fluid warming must be applied during cesarean section.[17] They also stated that opioids used during spinal anesthesia rather than spinal anesthesia constitute a risk factor for hypothermia. In a study conducted by Cobb B. et al. on pregnant women undergoing cesarean section with spinal anesthesia, it was shown that the combined use of blown and intravenous fluid warmers was insufficient to prevent hypothermia and shivering.[18] Butwick AJ et al. also showed that active heating did not reduce hypothermia and shivering in pregnant women who underwent spinal anesthesia.[19] It is known that prevention of surgical wound infection, myocardial ischemia, coagulopathy, and blood loss is important in general and regional anesthesia.

Fetal temperature is usually one degree higher than maternal temperature and is directly related to maternal temperature. Neonatal hypothermia is more likely to be seen in cesarean operations where maternal contact is kept shorter than normal delivery.[20] Negishi C et al. determined temperature gradients by measuring tympanic membrane and skin surface temperature in eleven pregnant women who underwent epidural anesthesia and showed that epidural anesthesia disrupted thermoregulation control in pregnant women and increased the central-peripheral temperature gradient.[21] There are a limited number of studies showing the effects of different anesthesia techniques used during cesarean section on neonatal body temperature. Yentur EA et al. investigated the effects of epidural and general anesthesia on neonatal body temperature, APGAR scores, and fetal blood gases in 63 pregnant women undergoing cesarean section. The body temperature (37.4°C) of the babies born in the epidural anesthesia group was lower than the general anesthesia group. They attributed this low level to the length of the procedure and the large amount of intravenous fluid used in the epidural group. However, APGAR scores at one minute in newborns were found to be higher.[22] Horn EP et al. emphasized that hypothermia was less common in pregnant women who underwent spinal anesthesia and in infants born from them.[23] There are conflicting data on APGAR scores of babies born to mothers who underwent different anesthesia techniques. Sendağ F et al. found similar APGAR scores in newborns born to pregnant women who underwent epidural and general anesthesia.[24] However, in one of the similar studies, APGAR scores of babies born to mothers who underwent general and epidural anesthesia were found to be lower. The other study showed no difference between the APGAR scores of babies born to mothers who underwent general and spinal anesthesia.[25,26] According to a meta-analysis including 13 studies in which Sultan P et al. evaluated the effects of maternal warming during cesarean section on the maternal and newborn, it was shown that maternal warming with a hot air blower or an intravenous liquid heater reduced the incidence of maternal hypothermia and shivering and improved APGAR scores and umbilical blood gas pH in the newborn.[27] In the study conducted by Hoefnagel et al., there was no significant difference in the neonatal APGAR values of patients who underwent regional anesthesia with or without active heating.[28] Our study found no difference between maternal temperature measurements in both groups. In the general and spinal anesthesia groups in which maternal heating was performed, the body temperatures of the newborns (36.6°C) were higher than in the non-heated groups. Neonatal temperature (36.7°C) was higher in the spinal anesthesia and maternal warming group. Hypothermia was not observed in any of the mothers and newborn babies. APGAR scores were higher in newborn babies in the spinal anesthesia and warming group, but none had an APGAR score below seven. This may be explained by keeping the ambient temperature constant. In addition, in spinal anesthesia, the heat reduction is limited to the lower extremities, and the emergence time of the baby is faster.

In a study by Topal et al., maternal hypothermia and shivering were found to be significantly lower in the heated patient group of patients undergoing cesarean section compared to the control group.[29] The findings were similar in our study.

The incidence of nausea and vomiting was not found to be different in patients who underwent heating compared to those who did not. Nausea and vomiting were more frequent in the group of patients who underwent spinal anesthesia and were not heated. We think that this is due to the sympathetic blockade in spinal anesthesia.

In our study, systolic blood pressure arterial values were lower in the spinal anesthesia group, as expected in neuraxial blocks, and there was no significant difference between diastolic blood pressure arterial and peak heart rate measurements. None of the patients had hypotension requiring ephedrine administration. Although the primary aim of our study was not to evaluate hemodynamic changes, no hemodynamic differences were found between patients with and without heating.

The limitations of our study are the experience of a single center and the retrospective nature of the study. In addition, the small number of patients in the study can be said to be another limitation.

Maternal warming and spinal anesthesia increase maternal and neonatal body temperature and neonatal APGAR score. Therefore, maternal warming and spinal anesthesia techniques are recommended for pregnant women.

Description

Presented as an oral presentation at 52nd Congress of the Turkish Society of Anaesthesiology and Reanimation, November 07-11, 2018 at Sueno Deluxe Hotel, Belek Antalya.

Compliance with Ethical Standards

The study protocol was approved by Ethics Committee of Health Sciences University Şişli Hamidiye Etfal Training and Research Hospital. (approval dated 13/06/2017 and numbered 1576)

Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contribution

KU, ASÇ, HŞT: Consept; KU, ASÇ, HŞT: Design; KU, ASÇ, HŞT, EFG: Data Collection and Processing; KU, ASÇ, EFG: Analysis and Interpretation; KU, ASÇ, EFG: Literature Search; KU, ASÇ, HŞT: Writing, Reviewing and Editing. All the authors read and approved the final manuscript.

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