Effect of Anesthesia Techniques on Pain Severity, Hemodynamic Changes, and Patients' Satisfaction in Elective Cesarean Section

Abdollah Jafarzadeh^{1,2}, Maryam Hadavi^{2,3}, Gholamhossein Hasanshahi^{2,4}, Mohsen Rezaeian⁵, Reza Vazirinejad⁶, Fariba Aminzadeh⁷, Ali Sarkoohi⁸

¹ Department of Immunology, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran

² Molecular Medicine Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

³ Department of Anesthesiology, School of Paramedical, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

⁴ Department of Immunology, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

⁵ Department of Epidemiology and Biostatistics, School of Medicine, Occupational Environmental Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

⁶ Department of Social Medicine, Social Determinants of Health Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran ⁷ Department of Gynecology and Obstetrics, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

⁸ Department of Anesthesiology, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Received: 11 Feb. 2019; Accepted: 28 Jun. 2019

Abstract- The severity of postoperative pain and hemodynamic changes during and post-cesarean section have a direct effect on the neonatal and maternal condition. This study aimed to compare pain severity, hemodynamic changes, and patient satisfaction following two anesthesia techniques in elective cesarean section. In this blinded study, 60 women who were candidate for cesarean section were allocated into two equal groups of general anesthesia (GA) and spinal anesthesia (SA). Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and O₂ Saturation at pre cesarean (T0), the uterine incision time (T1), end of surgery (T2), 6h (T3), 12h (T4), and 24 hours post-cesarean (T5) were measured. A Visual Analog Scale assessed post-cesarean pain, 6, 12, and 24 hours post-cesarean. Gender, birth weight, first- and fifth-minutes' apgar score was recorded in the checklists. The VAS score was significantly higher in the GA group at 6h, 12h, and 24 hours post-cesarean (P=0.017, respectively). SBP and DBP at T1 in the GA group were significantly higher than in the S.A group (P<0.001). The heart rate at T0 and T1 in the GA group was lower than the SA group (P=0.001, P=0.045 respectively). The difference between the apgar scores of the two groups was not significant. SA for cesarean section was associated with lower postoperative pain, systolic and diastolic blood pressure. However, the two groups had no significant difference in terms of patients' satisfaction and apgar scores.

© 2019 Tehran University of Medical Sciences. All rights reserved. *Acta Med Iran* 2019;57(7):424-429.

Keywords: Pain; Hemodynamic changes; Spinal anesthesia; General anesthesia; Cesarean section; Patient satisfaction

Introduction

Cesarean Section is the most common surgical procedure for pregnant women (1). The increasing incidence of cesarean sections in the world is a reminder of the importance of anesthesia and its various techniques in obstetrics and Gynecology (2,3). General anesthesia (GA) has some benefits such as lower incidence of hypotension, controlled ventilation, and rapid induction, but diffusion of anesthetic drugs from the placenta, respiratory aspiration, failure in tracheal intubation, postoperative nausea, and vomiting have been reported as complications of this technique (4-6). The usage of regional anesthesia (RA) for cesarean section has been increased to reduce these maternal and fetal problems (7,8). Among RA techniques, spinal anesthesia is more widely used because of the simplicity of performing and its cost-effectiveness (9). However, complications such as failure to accessing the subarachnoid space in first attempt, insufficiency of

Corresponding Author: M. Hadavi

Department of Anesthesiology, School of Paramedical, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Tel: +9834258397, Fax: +9834258397, E-mail address: hadavimaryam@yahoo.com

anesthesia level (10), nausea and vomiting, needle phobia, fear of permanent paralysis, asystole, postoperative headache (11), hypotension and hypotension induced neonatal depression have been reported (12,13).

Postoperative pain is an important factor affecting the hemodynamic status, patient satisfaction, and onset of breastfeeding. Nesek-Adam *et al.*, evaluated postoperative pain in 40 patients undergoing peripheral vascular surgery and concluded that SA is preferable to GA (14). Sharaf *et al.*, reported that SA was associated with a higher rate of postoperative pain relief after laparoscopic cholecystectomy than GA. They mentioned this was due to the addition of fentanyl to a local anesthetic agent during an intrathecal injection (15).

Naghibi *et al.*, showed no significant difference between the SA and GA groups for postoperative pain scores at 6, 12 and 24 hours after the lower abdominal surgery (16). Many reports have shown RA and GA have the same index in terms of neonatal health (17-20), but today RA techniques are used more often in cesarean section (21). The present study was designed to compare patient satisfaction, postoperative pain severity, and hemodynamic changes following use of SA versus GA in elective cesarean section.

Materials and Methods

The Ethics Committee of the Rafsanjan University of Medical Sciences has approved the protocol for this randomized, blinded prospective study. Sixty women who were candidate for cesarean section in Niknafs hospital (Rafsanjan, southeastern Iran) were randomly allocated to GA (n=30) and SA (n=30) groups. The inclusion criteria were the American Society of Anesthesiologists physical status (ASA) I-II, single, and uncomplicated pregnancy. Exclusion criteria included co-existing diseases such as hypertension, diabetes, cardiovascular disease, medication taking, smoking, alcohol and opium addiction. To remove confounding variables, the gynecologist and the anesthesiologist were considered the same in all procedures.

The information such as age, weight, gravidity, history of cesarean section, indication of cesarean, gestational age, and duration of surgery were recorded. Systolic blood pressure (SBP) and diastolic blood pressure (DBP), heart rate (HR), and oxygen saturation of arterial blood (O₂sat) before the cesarean (T0), at the uterine incision time (T1), end of surgery (T2), 6 (T3), 12 (T4) and 24 hours (T5) post-cesarean were measured in both groups. Birth weight, neonatal gender, first and fifth minutes Apgar score was recorded too.

In the SA group, all patients received 500 ml Ringer solution. The electrocardiogram (ECG), noninvasive blood pressure (NIBP), heart rate (HR), and peripheral oxygen saturation (SpO₂) were monitored. After explaining the procedure, the SA was performed in sitting position using a 25G spinal needle (Quincke Needle, Japan) and 2.5 ml Marcaine 0.5% (AstraZeneca, Sweden) in the lumbar 3-4 interspace (22). Then the patient was placed in the trendelenburg position, and the required anesthesia level was induced (T4-T6). Blood pressure, HR, and SpO₂ were recorded immediately after SA and every 5 minutes thereafter.

GA was induced by 4-6 mg/kg sodium pentothal and 1-1.5 mg/kg succinylcholine. After tracheal intubation (tube No. 7) and cuff inflation, oxygen and nitrous oxide were administrated (each one 50%) (23). Muscle relaxation induced by 0.2-0.3 mg/kg atracurium. In order to increase the depth of GA, 1-2 μ g/kg fentanyl was given after clamping the umbilical cord and disconnecting the mother and newborn.

The protocol for post-cesarean pain relief was similar. Patients in both groups received 50 mg pethidine I.M 4 h after the surgery, and two hours later, diclofenac sodium suppository was prescribed and repeated every 6 hours three times.

Postoperative pain was measured using the Visual Analog Scale (VAS) 6, 12, and 24 hours post-cesarean. In this method, the patient's pain intensity is measured using a graded ruler (0 to 10 cm), which the zero number represents the absence of pain, and the number 10 indicates the most severe pain. In the present study, scores ≤ 2 , 3-6 and 7-10 were considered as painless, moderate, and severe pain, respectively (24). All patients were asked about the first post-cesarean day satisfaction. Data were analyzed using SPSS software version 20. To compare the results, independent t-test, Chi-square, one-way ANOVA, and Fisher exact test were used. *P*<0.05 was considered as significant.

Results

The mean \pm SD of participants' age was 32.52 \pm 4.69 years. Most of the participants were in the 31-35 years age group. The demographic characteristics of the participants in the GA and SA groups were compared in table 1. Results show that there was no significant difference between the two groups in terms of demographic variables, and the groups were matched with each other.

In 94.1% of cases, the cause of cesarean section was repeated cesarean, which Chi-square test showed no

significant difference between two groups (P=0.595). In the SA group, 13 neonates (43.3%) and in the GA group, 12 neonates (42%) were female. Fisher's exact test did not show a significant difference between these two groups. The mean±SD apgar score of neonates in the SA

in the 1st and 5th minute was 8.97 ± 0.18 and 10.00 ± 0.00 , and in the GA group, 8.90 ± 0.31 and 10.00 ± 0.00 respectively (*P*>0.05). The mean±SD neonatal weight in the SA group was 3278.78±425.08 g and in the GA group 3312.76±402.42 g (*P*>0.05).

 Table 1. The demographic characteristics of the participants and duration of surgery in the general and spinal anesthesia groups

Seneral and Spinal anesties Broups					
Variable	Spinal Anesthesia group Mean±SD	General Anesthesia group Mean±SD	Р		
				Age (year)	32.06±5.06
Weight (Kg)	81.97±8.23	85.10±12.80	0.265		
Gestational age (week)	38.77±0.57	38.97±0.49	0.150		
Gravidity (Number)	2.37±0.61	2.57±0.73	0.255		
Previous CS (Number)	1.20±0.48	1.33±0.48	0.288		
Duration of surgery (Minute)	37.67±5.83	35.67±8.07	0.276		
Independent t test					

Independent t-test

The mean±SD VAS score in 6h, 12h, and 24 hours after surgery in the SA group were 5.87±2.16, 5.17±2.07, 3.43±1.96, and in the GA group, 7.10±1.56, 6.70±1.62, and 4.70±2.02, respectively. The independent t-test showed a significant difference between the two groups, meaning that the VAS score was significantly higher in the GA group (P=0.014, P=0.002, P=0.017, respectively). The ANOVA test revealed a significant difference in trend of changes in VAS score at different times in both groups (P<0.001). VAS scores in SA and GA groups were significantly reduced at 24 hours, postcesarean section compared to 12 hours (P=0.002 and P < 0.001, respectively) and 6 hours post-cesarean section (<0.001). In the GA group, the VAS score 12 hours, post-cesarean was significantly lower than the 6 hours post-cesarean. However, in the SA group, this decrease was not significant. In figure 1, pain severity 6, 12 and 24 hours, post-cesarean was compared between the groups. There were no cases of mild pain in the GA group.

SBP and DBP, HR, and O₂sat in the two groups at

preoperative (T0), the uterine incision time (T1), end of surgery (T2), 6 (T3), 12 (T4) and 24h post-cesarean (T5) were compared in Table 2.

Independent T-tests showed SBP and DBP at T1 for the GA group was significantly higher compared to the SA group. However, the heart rate at T0 and T1 in the GA group was lower. In addition, the increase in SBP and DBP at T1 in the GA group was significant in comparison with T0.

In the SA group, 36.8% and in the GA group, 35.3% had a history of cesarean section. The previous cesarean section anesthesia method was similar to the current cesarean section in 80% of participants. They were satisfied with the method of anesthesia and consciously selected anesthesia in the current cesarean section. Of the remaining 20%, the anesthesia method in the current cesarean section. One participant in each group stated that it was more satisfied with the previous cesarean section anesthesia method.

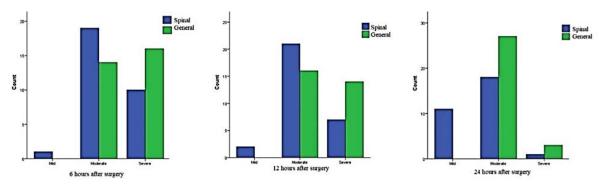


Figure 1. Comparison of pain intensity of 6, 12, and 24 hours, post-cesarean in S.A and G.A groups

⁴²⁶ Acta Medica Iranica, Vol. 57, No. 7 (2019)

	oxygen saturation in the two groups.				
		Spinal Anesthesia group General Anesthesia group	Р		
		Mean±SD	Mean±SD	-	
SBP(mmHg)	TO	126.13±17.11	121.17±4.89	0.132	
	T1	112.53 ± 19.20	135.97±23.20	< 0.001*	
	T2	109.17 ± 13.17	114.00 ± 7.12	0.082	
	Т3	$109.10{\pm}10.02$	111.83±9.33	0.279	
	T4	108.47±9.75	109.93±7.64	0.519	
	Т5	111.17 ± 12.84	108.20±9.77	0.318	
DBP(mmHg)	TO	79.73±12.87	74.80±6.99	0.070	
	T1	66.60±15.86	82.73±13.34	< 0.001 *	
	Т2	67.80±9.76	69.00±8.24	0.609	
	Т3	64.27±8.56	65.33±6.42	0.587	
	T4	64.80±5.59	65.98±4.63	0.376	
	Т5	66.93±7.48	67.80±5.91	0.620	
HR(bpm)	TO	100.00±13.92	90.20±8.03	0.001 *	
	T1	98.03±18.76	89.07±14.88	0.045 *	
	Т2	88.77±14.14	83.23±7.29	0.062	
	Т3	80.53±9.19	77.17±6.43	0.106	
	T4	73.23±6.09	72.43±6.21	0.616	
	Т5	77.53±9.29	80.10±5.50	0.198	
O2Sat	TO	97.47±1.52	98.40±1.52	0.021	
	T1	97.80±1.73	97.37±3.38	0.534	
	T2	97.37±1.38	97.17±0.70	0.481	
	Т3	97.10±0.99	96.90±0.48	0.326	
	T4	96.73±0.98	97.00±0.58	0.206	
	Т5	96.77±0.93	97.00±0.64	0.265	

Table 2. Systolic blood pressure, diastolic blood pressure, heart rate, and arterial oxygen saturation in the two groups.

Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), oxygen saturation (O2Sat). Preoperative (T0), uterine incision time (T1), end of cesarean (T2), 6h post-cesarean (T3), 12h post-cesarean (T4) and 24h post-cesarean (T5). *=significant between two groups.

Discussion

In this study, patient satisfaction, pain severity, and hemodynamic changes following SA versus GA in the elective cesarean section were compared. In 94.1% of cases, the cause of cesarean delivery was repeated cesarean. Cesarean section is performed for various reasons such as higher maternal age, maternal obesity, and fetal distress (25) and is related to several factors such as socioeconomic factors, physician's preference, and fear of physical injury, high age of mothers in the first delivery and the determination of the specific baby's birth date. In Qarekhani and Sadatian (2009) study, the most common cause of cesarean delivery was a previous cesarean section (26), which is in accordance with the present study. Encouraging women to vaginal delivery after cesarean delivery (VBAC) is the best way to reduce the frequency of repeat cesarean section (27).

In the present study, the mean \pm SD of VAS score in the GA group at 6, 12, and 24 hours post-cesarean were significantly higher than the SA group. However, in Havas *et al.*, study, there was no significant difference between the severity of pain at 6, 12, and 24 hours postsurgery in the cesarean section with GA and SA (28). It should be noted that in the Havas et al., study, IV patient-controlled analgesia (PCA) with pethidine was used for postoperative analgesia. This method has a significant role in pain reduction and no significant difference in pain severity in the two groups.

Based on the ANOVA test, intragroup difference in VAS score was significant at different times in both groups. This means that during the time, the intensity of pain was significantly reduced. In the SA and GA groups, VAS scores 24 hours post-cesarean compared with 12 and 6 hours post-cesarean were significantly reduced. Immune system reactions are well known in reduction of inflammation caused by tissue damage and postoperative pain intensity. For example, Interleukin 6 is a major pro-inflammatory cytokine that is released very early in response to tissue damage. Hong and colleagues stated that interleukin 6; one-hour postsurgery was detectable in the blood and peaked at 4 to 6 hours later (29). Herroeder et al., also reported a maximum plasma IL-6 level between 4 and 6 hours post-surgery (30). Some studies have shown that plasma levels of interleukin 10 increase after major surgery (31,32). Interleukin 10 is a cytokine with potent antiinflammatory properties (33) that suppresses the expression of inflammatory cytokines such as interleukin 6 (34). The main function of interleukin 10 is

to reduce immune responses and limit tissue damage. One of the major causes of significant decrease in pain intensity over time may be related to the release of antiinflammatory cytokines and inhibition of inflammatory cytokines. In addition, less post-cesarean pain in the spinal anesthesia group allow patients to start walking earlier. Gastrointestinal tract function is improved by walking therefore, constipation, abdominal distension, and pain will be reduced.

The present study showed pain severity in the GA group was significantly higher compared to the SA group at 24 hours, post-cesarean, however, did not lead to a significant difference in the mean±SD of SBP, DBP, HR, and O2Sat between the two groups. Therefore, none of these techniques might be preferred regarding post-cesarean hemodynamic status.

The results of the present study showed that SBP and DBP were significantly higher in the GA group than the SA group at the uterine incision time. Sympathetic nerve blockade caused by spinal anesthesia leads to reduction of peripheral vascular resistance and blood pressure decreases. The increase in SBP and DBP at T1 in the GA group was significant compared to T0. Stimulation of proprioceptors during laryngoscopy in GA induces impulse dependent increases of SBP and DBP.

In the present study, there was a significant difference between the groups in terms of SBP at the uterine incision time. However, there was no significant difference in the first minute apgar score in two anesthesia methods. In a review study done by Kim *et al.*, 46 clinical trials were studied to compare the effects of GA, SA, epidural anesthesia, and spinal-epidural anesthesia during cesarean section. In their study, there were significant differences in first minute apgar score between SA versus GA (35). In Martin *et al.*, study, neonates who born underwent GA had significantly lower first and five-minute Apgar scores. In their research, emergency cesarean section was also studied, while in the present study only elective cesarean section was examined. This may lead to differences in results.

In our study, the heart rate at T0 and T1 in the GA group was lower than the SA group. Considering that the average of SBP in the SA group at these times was less than the GA group, the higher heart rate in the SA group maybe was a defensive reaction to compensate for the drop in blood pressure.

The major limitation of this study included: the severity of pain in two groups was not compared immediately after surgery because, in this period, the general anesthetic agents affected the patients, and the use of VAS criteria was not possible.

The findings of this study showed that spinal anesthesia in comparison to general anesthesia is associated with lower pain intensity, lower systolic and diastolic blood pressure in the post-cesarean period. However, these two methods did not differ significantly in terms of apgar scores and patient satisfaction. Spinal anesthesia improved postoperative conditions of patients due to decreasing pain and need for analgesia.

Acknowledgments

Authors of the present study warmly appreciate the Rafsanjan University of Medical Sciences for financial supports.

References

- Cunningham F, Leveno K, Bloom S, Spong CY, Dashe J. Williams Obstetrics, 24e: Mcgraw-hill; 2014.
- Yeoh SB, Leong SB, Heng AST. Anaesthesia for lowersegment caesarean section: Changing perspectives. Indian J Anaesth 2010;54:409-14.
- 3. Niino Y. The increasing cesarean rate globally and what we can do about it. Biosci Trends 2011;5:139-50.
- Chestnut DH, Wong CA, Tsen LC, Kee WDN, Beilin Y, Mhyre J. Chestnut's obstetric anesthesia: principles and practice: Elsevier Health Sciences; 2014.
- 5. Kee WN. Confidential enquiries into maternal deaths: 50 years of closing the loop. Br J Anaesth 2005;94:413-6.
- 6. Emmett R, Cyna A, Andrew M, Simmons S. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. The Cochrane Library. 2002.
- Wong C. General anesthesia is unacceptable for elective cesarean section. Int J Obstet Anesth 2010;19:209-12.
- Abdollahpour A, Azadi R, Bandari R, Mirmohammadkhani M. Effects of adding midazolam and sufentanil to intrathecal bupivacaine on analgesia quality and postoperative complications in elective cesarean section. Anesth Pain Med 2015;5: e23565.
- Bucklin BA, Hawkins JL, Anderson JR, Ullrich FA. Obstetric Anesthesia Workforce SurveyTwenty-year Update. Anesthesiology 2005;103:645-53.
- Gori F, Pasqualucci A, Corradetti F, Milli M, Peduto V. Maternal and neonatal outcome after cesarean section: the impact of anesthesia. J Matern Fetal Neonatal Med 2007;20:53-7.
- Van de Velde M, Schepers R, Berends N, Vandermeersch E, De Buck F. Ten years of experience with accidental dural puncture and post-dural puncture headache in a tertiary obstetric anaesthesia department. Int J Obstet Anesth 2008;17:329-35.

- Fathi M, Imani F, Joudi M, Goodarzi V. Comparison between the effects of ringers lactate and hydroxyethyl starch on hemodynamic parameters after spinal anesthesia: A Randomized clinical trial. Anesth Pain Med 2013;2:127-33.
- Alimian M, Mohseni M, Safaeian R, Faiz SHR, Majedi MA. Comparison of hydroxyethyl starch 6% and crystalloids for preloading in elective caesarean section under spinal anesthesia. Med Arch 2014;68:279-81.
- Nesek Adam V, Rasic Z, Schwarz D, Grizelj-Stojcic E, Rasic D, Krstonijevic Z, et al. The effect of spinal versus general anesthesia on postoperative pain and analgesic requirements in patients undergoing peripheral vascular surgery. Coll Antropol 2012;36:1301-5.
- 15. Sharaf A, Burki AM, Mahboob S, Bano R. Comparison of postoperative pain relief following use of spinal anesthesia versus general anesthesia for patients undergoing laparoscopic cholecystectomy. Anaesthesia, Pain & Intensive Care 2018;22.
- Naghibi K, Saryazdi H, Kashefi P, Rohani F. The comparison of spinal anesthesia with general anesthesia on the postoperative pain scores and analgesic requirements after elective lower abdominal surgery: A randomized, double-blinded study. J Res Med Sci 2013;18:543-8.
- 17. Richardson MG. Regional anesthesia for obstetrics. Anesthesiol Clin North Am 2000;18:383-406.
- Mattingly JE, D'Alessio J, Ramanathan J. Effects of obstetric analgesics and anesthetics on the neonate. Pediatric Drugs 2003;5:615-27.
- Littleford J. Effects on the fetus and newborn of maternal analgesia and anesthesia: a review. Can J Anaesth 2004;51:586-609.
- Kavak ZN, Başgül A, Ceyhan N. Short-term outcome of newborn infants: spinal versus general anesthesia for elective cesarean section: A prospective randomized study. Eur J Obstet Gynecol Reprod Biol 2001;100:50-4.
- Ghazi A, Raja Y. Combined low-dose spinal-epidural anaesthesia versus single-shot spinal anaesthesia for elective caesarean delivery. Int J Obstet Anesth 2007;16:90-1.
- Cyna, A. M, Andrew, M, Emmett, R. S, Middleton, P, Simmons, S. W. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. Cochrane Database Syst Rev. 2006; 18: CD002251.
- 23. RD. M. Miller's anesthesia. Philadelphia: Elsevier, 2015.
- 24. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual analog scale for pain (vas pain),

numeric rating scale for pain (nrs pain), mcgill pain questionnaire (mpq), short-form mcgill pain questionnaire (sf-mpq), chronic pain grade scale (cpgs), short form-36 bodily pain scale (sf-36 bps), and measure of intermittent and constant osteoarthritis pain (icoap). Arthritis Care Res 2011;63: 240-52.

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, et al. Obstetrícia de Williams. Brasil: McGraw Hill, 2016.
- 26. Qarekhani P, Sadatian A. Principals of obstetrics & gynecology. Tehran: Noore-Danesh. 2009;248.
- Darvishi E, Mortazavi S, Nedjat S, Holakouie Naieni K. Experiences of women and gynecologists on the choice of delivery method: A qualitative research. J Health Sys Res. 2012;8:59-68.
- Havas F, Orhan Sungur M, Yenigün Y, Karadeniz M, Kilic M, Özkan Seyhan T. Spinal anesthesia for elective cesarean section is associated with shorter hospital stay compared to general anesthesia. Agri 2013;25:55-63.
- Hong J-Y, Lim KT. Effect of preemptive epidural analgesia on cytokine response and postoperative pain in laparoscopic radical hysterectomy for cervical cancer. Reg Anesth Pain Med 2008;33:44-51.
- Herroeder S, Pecher S, Schönherr ME, Kaulitz G, Hahnenkamp K, Friess H, et al. Systemic lidocaine shortens length of hospital stay after colorectal surgery: a double-blinded, randomized, placebo-controlled trial. Ann Surg 2007;246:192-200.
- 31. Weis F, Beiras-Fernandez A, Schelling G, Briegel J, Lang P, Hauer D, et al. Stress doses of hydrocortisone in highrisk patients undergoing cardiac surgery: effects on interleukin-6 to interleukin-10 ratio and early outcome. Crit Care Med 2009;37:1685-90.
- 32. Simsek E, Karapinar K, Bugra O, Ulus AT, Sarigul A. Effects of albumin and synthetic polypeptide-coated oxygenators on IL-1, IL-2, IL-6, and IL-10 in open heart surgery. Asian J Surg 2014;37:93-9.
- 33. Mosser DM, Zhang X. Interleukin-10: new perspectives on an old cytokine. Immunol Rev 2008;226:205-18.
- Sun X, Wang D, Yu H, Hu L. Serial cytokine levels during wound healing in rabbit maxillary sinus mucosa. Acta Otolaryngol 2010;130:607-13.
- 35. Kim WH, Hur M, Park S-K, Yoo S, Lim T, Yoon HK, et al. Comparison between general, spinal, epidural, and combined spinal-epidural anesthesia for caesarean delivery: a network meta-analysis. Int J Obstet Anesth 2019;37:5-15.