Research Article

A comparative study of bupivacaine versus bupivacaine-lidocaine soaked gel-foam in caesarean section wounds

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Abstract

Background: One of the major challenge in the immediate post-operative period after Caesarean section, is to avoid excessive pain and postoperative nausea and vomiting because both compromise the mother–child relation. **Aims** To evaluate and compare the use of subcutaneous gelfoam soaked with either of bupivacaine 0.25% or a mixture of lidocaine 2% and bupivacaine .025% for postoperative analgesia after elective CS under GA. **Materials and Methods:** A total 105 parturient (ASA) physical status II who underwent elective CS under GA were randomly allocated into Group C**:** received gel-foam soaked with 20 ml of 0.9% normal saline, Group B: the gel-foam soaked with 20 ml bupivacaine 0.25% or Group BL: the gel-foam seoaked with a mixture of 10ml bupivacaine 0.25% and 10 ml lidocaine2%. Peri and postoperative haemodynamics, VAPS at 1, 2, 4, 8, 12, 18 and 24 hours, number of patients needed analgesia, 1st analgesic request, total analgesic requirements over 1st 24 hours and side effects (such as nausea and vomiting) and wound healing were recorded. **Results:** More heamodynamic stability in the treated groups almost the times of postoperative follow up. VASP was significantly lower in B and BL groups in comparison to group C at 1, 2, 8, 12& 24 hrs, The only detected difference between B and BL groups was significantly lower VAPS at 1hr in BL group but it reversed to be in B group at 4 hrs (i.e. earlier onset of analgesia in BL group but more intense in B group at 2 & 4hrs). The time to 1st analgesic request was significantly longer and number of patients who needed analgesia and the total postoperative 24h analgesics consumption was significantly lower in group B and group BL when compared to the control group with no significant difference between B and BL. Significantly higher incidence of postoperative nausea and vomiting in group C with more anti-emetics consumption in comparison to B and BL groups, however, there were no complications regarding the wound healing or the surgical site. **Conclusion:** Placement of spongostan soaked with bupivacaine or with a mixture of lidocaine 2% and bupivacaine 0.25% on half of the dosage subcutaneously in wound of caesarean section was safe, and effective in providing more haemodynamic stability and postoperative analgesia

Keywords: bupivacaine, lidocaine, spongostan, postoperative analgesia

Introduction

Childbirth is a vital enjoy in a woman's life, taken the many millions of births each year, the occurrence of postpartum pain that interferes with the day by day activities in even a small percentage of women will have a big socioeconomic impact[(1)].

Disruption in the woman's mobilization and care of her baby due to postoperative pain is another negative aspect of cesarean delivery[(2)]

Presently, opioids are commonly used for relief of postoperative pain after caesarean section, either by using intrathecal administration prior to section or postoperative parenteral administration[(3)]**.** But the opioid usage is associated with many unwanted side effects such as nausea, drowsiness and vomiting[(4)]**.** There-after, there are needs for alternative analgesics to reduce the consumption of opioids[(5)]**.**

Because surgical pain originates from the surgical wound, a rational technique to perioperative pain treatment has been directed towards the use of local anesthetic infiltration on the site of surgery, as this technique is effective, with minimal side effects, inexpe-nsive and without need for expertise[(6)].

Local anesthetics (LA) can be injected via catheters placed in surgical wounds to offer post-operative analgesia by both single shoot and continuous infiltration. However, the usage of local anesthetic wound infiltration for post-operative pain relief has conflicting reports and different views towards this issue[7].

Absorbable gelatin powder, spongostan, is a hemostatic material for local application that can be used in surgical approaches with venous hemorrhages and exudation in situations where conventional homeostasis is difficult. In addition to its hemostatic effect, spongostan can be used as a drug reservoir and might offer sustained release of some drugs[8]. It adheres to bleeding sites and, because of its uniform porosity, absorbs more or less 45 times its weight. When implanted in the tissues, it could be absorbed over a period of two weeks[9]

Aim of the work

To assess and compare the use of subcutaneous gelfoam soaked with either 20ml bupivacaine 0.25% or a mixture of 10 ml lidocaine 2% and 10ml bupivacaine 0.25% for postoperative analgesia after caesarean section and its impact on haemodynamics. With primary endpoint the first analgesic request and the total post-operative analgesic consumption. and secondary endpoints were incidence of any side effects and Wound healing.

Methodology

After institutional approval and informed consents obtained from all patients, this prospective, double-blind, randomized, placebo-controlled study was carried out at the department of anesthesia and intensive care in El-Minia University Hospital of gynecology and obstetrics during the period from August 2015 till July 2016 on a total 105 women, aged 18-35y, (ASA) physical status II who under-went elective caesarean section under general anesthesia due to medical conditions (e.g. coagulopathy) or refusal of the patient to regional anesthesia. Parturients with allergy to any of the used medications, previous pelvic surgery or chronic pelvic pain, opioid addiction, psychiatric disorders, inability to understand VAS or previous complicated caesarean section were excluded.

On enrollment into the study, the participants were randomly allocated into three groups of 35 patients each using computer generated table and randomization sequence was concealed in sealed envelopes assignment held by an assistant who also prepared the studied medications used but not involved in the clinical management or data collection. The protocol was opened after the study had been completed. Control group (C group) treated with gel-foam soaked with 20 ml of 0.9% normal saline, bupivacaine group (B group) the gel-foam soaked with 20 ml bupivacaine 0.25% and bupivacaine – lidocane Group (BL group) treated with gel-foam soaked with a mixture of 10ml bupivacaine 0.25% and 10 ml lidocaine2%.

Anesthetic manegment: -

All patients received preoperative evaluation and physical examination and were instructed on how to use a 10cm VAS diagram for measurement of their postoperative pain. On arrival to the operative room, arterial blood pressure, ECG, and pulse oximetry monitors (Mindray monitor, model: IMEC12- China) were applied. The basal hemodynamic were recorded and then intraoperatively at 5, 15, 35, 45 min. and postoperatively at 10, 30 mins, 1, 2, 4, 8, 12, 18 and 24 hrs.

An intravenous 20 G cannula was inserted and the patients received 5 ml/kg of 0.9% saline and were pre-oxygenated with 100% oxygen via a well fitted mask for 3 minutes or 4- 5 vital capacity breaths.

The patient was positioned in a supine position with left lateral tilt. Induction of anesthesia was carried out after the patient was catheterized, abdominal skin decontaminated, draped and the surgical team was scrubbed.

A standardized anesthesia protocol was used in the form of thiopental at 5 mg/kg, succinyl-choline at 1.5 mg/kg for tracheal intubation with cricoid pressure was applied until endotracheal intubation was confirmed and the cuff of the tube was inflated. Anesthesia was then maintained with isoflurane in oxygen and non-depolarizing muscle relaxant recuro-nium of 0.6 mg/kg after the return of spontaneous

breathing with mechanical ventilation started. Surgery performed in all cases with pfannenstiel incision. After delivery of the baby and umbilical cord clamping, 20 IU of oxytocin diluted in 1000 ml of 0.9% saline, fentanyl 1μg.kg and prophylactic antibiotics were administered intravenously with reversal of the left lateral tilt position of the surgical table.

Near the end of surgery, gel-foam (Curamedical B.V. The Netherlands, Amesterdam) was prepared by an assistance under complete aseptic condition, removing the sterile compressed sponge from its packaging, cutting it into desired sizes convenient to the wound size then immersed in sterile saline and then withdrawn, squeezed between gloved fingers to expel air bubbles. Also the studied medications, either 0.9% normal saline (Otsuka Ateco Pharma, Egypt), bupivacaine 0.25% (MYLAN S.A.S., France) or lidocaine2% (Grand Pharma, Egypt) were prepared in similar sterile coded syringes and supplied to the surgeon before skin closure in a double blinded fashion (neither the patient nor the investigator or the surgeon was aware of the group assignment) to place the gel-foam in the wound subcutaneously and inject the prepared medications into it, then close the incision.

Figure (1): Gel foam before unpackaging

Reversal of residual neuromuscular blockade was done by using appropriate doses of neostigmine and atropine during the skin closure and after spontaneous respiration returned.

Postoperatively, all patients received routine postoperative care and postoperative pain was assessed at 1, 2, 4, 8, 12, 18 and 24 hrs by visual analogue pain scale score (VAPS) which consists of a straight line with the endpoints defining extreme limits such as 'no pain at all' and 'pain as bad as it could be , if it was ≥4, ketorolac 30mg IV was given at 6 hours intervals at least with a maximum dose of 120mg/day, if the analgesia was not adequate intravenous fentanyl at 1mic/kg was given. The time of 1st analgesic request (time elapsed from the end of surgery until the first patient's request for analgesia or if VAPS ≥ 4), number of patients needed analgesia and total analgesic requirement over 1st 24 hrs was calculated. Also the patients were followed up for any side effects e.g. allergic reactions, toxicity, pruritus, nausea and vomiting and wound healing.

Statistical analysis

The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 20. Descriptive statistics were done for Parametric quantitative data by mean, SD and min& max. of the range, and for non-parametric quantitative data by median and IQ range, while done for categorical data by number and percentage. One Way ANOVA test used for parametric quantitative data between 3 groups followed by Post Hoc Tukey correction between each 2 groups, and for non-parametric quantitative data between the 3 groups using

Kruskal Wallis test followed by Mann Whitney test between each 2 groups.

Within each group, paired sample t test used for parametric quantitative data and Wilcoxon signed rank test. for qualitative data. The level of significance was taken at (P value < 0.05).

Sample size calculation: The number of patients required in each group was determined after a power calculation according to data obtained from pilot study. Pilot which reported a mean total Fentanyl consumption of 70 *mic* with SD of 18.71 in group I, and reported a mean total Fentanyl consumption of 60 *mic* with standard deviation of 20.31 in group II, and reported a mean total fentanyl consumption of 56 *mic* with standard deviation of 22.74 in group III**.** A sample size of 105 patients was determined to provide 80% power for one way ANOVA test at the level of 5% significance using G Power 3.1 9.2 software.

Results

This study detected the three groups were comparable as regard the age, weight and operative time. Table (1)

Table (1): Demographic data in the studied groups (data presented as mean ±SD or %)

Variable	Group C (n=35)	Group B (n=35)	Group BL (n=35)	P value
Age (Y) Range Mean ± SD	(19-35) 26.51±4.05	(19-38) 26.8±4.83	(19-38) 27.22±4.83	0.807
Weight (Kg) Range Mean ± SD	(80-105) 91.77±5.93	(68-125) 88.45±15.26	(70-120) 87.57±13.79	0.329
Operative time (mins) Range Mean ± SD	(41-45) 42.4±1.39	(40-45) 43.65±4.26	(42-45) 43.05±4.53	0.368

NO significant difference among the study groups (p>0.05)

Regarding hemodynamics, preoperatively, there was no statistically significant difference between the studied groups. Postoperatively, significant rise in HR & MAP was recorded in C group in comparison to the baseline. Significantly lower readings were recorded in HR at all-time points and MAP up to 2 hrs in B & BL groups when compared to C group with no significant difference was detected between each other. fig (2) and table (2)

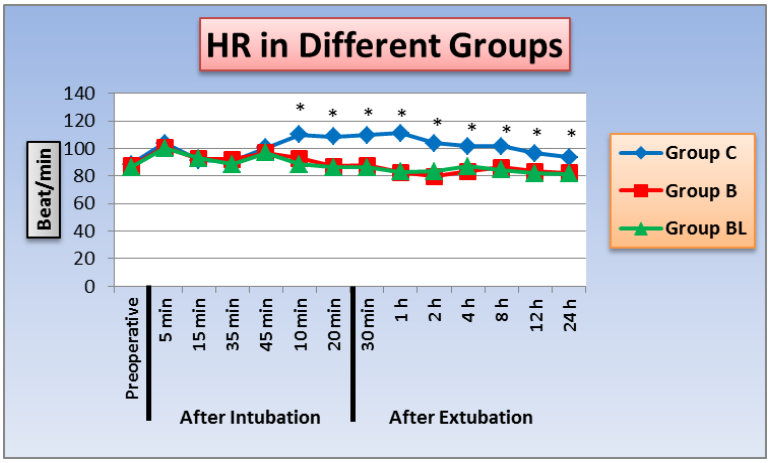

Figure (2): The changes in the mean heart rate (HR) in the studied groups (beat/min).

Table (2): Changes in the mean arterial blood pressure (MAP) (mmHg) in the studied groups (data presented as mean±SD)

Time	Group C (n=35)	Group B (n=35)	Group BL (n=35)	P value
Preoperative				
Range	(76.67-103.33)	(73.33-116.67)	(73.33-106.67)	0.516
Mean ± SD	91.28±5.66	92.52±11.25	93.85±10.09	
After intubation				
5 min	#	#	#	
Range	(86.67-116.67)	(86.67-126.67)	(76.67-126.67)	0.190
Mean ± SD	102.09±7.18	106.04±10.89	106.38±13.53	
15 min				
Range	(73.33-106.67)	(70-118.33)	(70-118.33)	0.447
Mean ± SD	89.73±9.7	92.42±14.42	93.38±12.66	
35 min			#	
Range	(76.67-103.33)	(60-116.67)	(70-106.67)	0.813
Mean ± SD	88.66±7.01	88.95±15.11	87.33±9.99	
45 min	#			
Range	(86.67-116.67)	(60-126.67)	(60-120)	0.244
Mean ± SD	101.71±5.96	97.76±16.59	96.28±16.36	
After extubation				
10 min	#		#	
Range	(86.67-116.67)	(70-116.67)	(70-110)	**< 0.001***
Mean ± SD	99.9±6.83	89.09±12.7+	86.9±13.01±	
30 min	#		#	
Range	(88.33-113.33)	(70-108.33)	(70-106.67)	**< 0.001***
Mean ± SD	101.9±5.54	89.71±11.46+	85.85±11.38±	
1h	#	#	#	
Range	(83.33-116.67)	(70-106.67)	(70-103.33)	**< 0.001***
Mean ± SD	99.33±7.78	88.19±11.11+	85.42±9.43±	
2h	#	#	#	
Range	(76.67-113.33)	(70-105)	(73.33-96.67)	**< 0.001***
Mean ± SD	95.38±8.79	85.42±9.378+	84.81±9.13±	
4h		#		
Range	(80-106.67)	(73.33-106.67)	(73.33-116.67)	0.330
Mean ± SD	91.95±6.74	88.28±10.317	90.81±13.34	
8h			#	
Range	(73.33-113.33)	(70-116.67)	(70-106.67)	0.213
Mean ± SD	94.28±9.02	90.7±12.525	90.23±9.47	
12h			#	
Range	(73.33-103.33)	(73.33-106.67)	(73.33-103.33)	0.633
Mean ± SD	89.33±7.25	89.71±9.847	87.85±8.41	
24h		#	#	
Range	(73.33-96.67)	(70-106.67)	(73.33-96.67)	0.504
Mean ± SD	85.71±6.88	88.04±9.697	86.81±8.13	

*: Significant difference between 3 groups at p value < 0.05 #: Significant difference with in group at + Significant 05 + Significant difference of C vs B ± Significant difference of C vs BL

The postoperative VASP score was significantly lower in group B and BL in comparison to group C at all time-points, The only detected difference between B and BL groups was significantly lower VAPS at 1hr in BL group but it reversed to be in B group at 4 hrs (i.e. earlier onset of analgesia in BL group but more intense in B group) table (3) Consequently, significantly longer time to 1st analgesic request in group B (4.81±3.65, P -value 0.001) and group BL (4.33±1.94, P- value 0.001) when compared to the control group (1±0) with significantly lower number of patients who needed analgesia & total amount of postoperative 24h analgesics requirement Fig. (3) table (4)

Table (3): Postoperative Visual Analogue Pain Scale (VAPS) (Data presented as median ± IQ range)

Time	Group C (n=35)	Group B (n=35)	Group BL (n=35)	P value
1h Median IQR	6 6-7	3 (3-3)+ ♦	3 (2-3)±	**<0.001***
2h Median IQR	# 4 (4-5)	# 2 (2-3) +	# 2 (2-3))±	**<0.001***
4h Median IQR	# 5 (4-5)	3 (3-3) + ♦	# 4 (3-5)	**<0.001***
8h Median IQR	# 5 (5-7)	4 (4-5) +	5 (4-5))±	**0.005***
12h Median IQR	# 4 (4-5)	# 4 (3-4)+	# 4 (3-4))±	**<0.001***
18h Median IQR	# 3 (3-4)	3 (3-3)+	3 (2-3))±	**<0.001***
24h Median IQR	# 3 (3-3)	2 (2-2)+	# 2 (2-2))±	**<0.001***

*: Significant difference between 3 groups at p value < 0.05 +Significant difference of C vs B ± Significant difference of C vs BL ♦ Significant difference of B vsBL #: Significant difference with in group at p value < 0.05

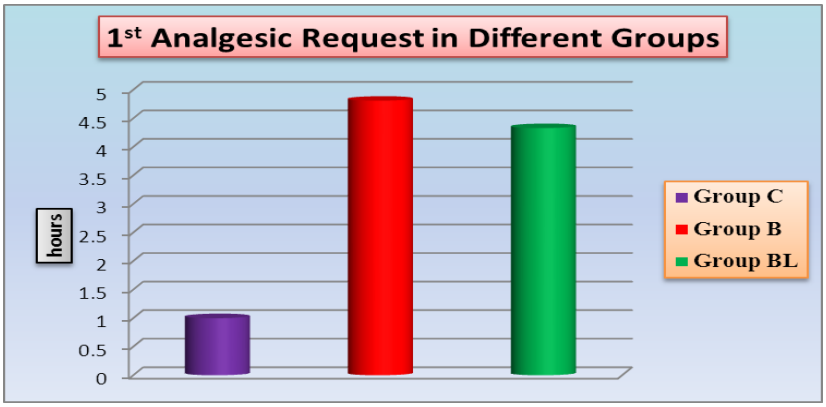

Figure (3): 1st analgesic request (hrs) among the groups

Significant higher incidence of postoperative nausea and vomiting was detected in the control group with more consumption of anti-emetics in comparison to B and BL groups, but no complications regarding wound healing or the surgical site were recorded. table. (4).

Table (4) Number of patients required analgesia, Total analgesic &antiemetic consumption (data presented as no. and percentage, mean ± SD)

Variable	Group C (n=35)	Group B (n=35)	Group BL (n=35)	P value
Analgesic request				
No	**0(0%)**	**24(67.6%)**	**17(48.6%)**	**<0.001***
Yes	**35(100%)**	**11(32.4%)+**	**18(51.4%)±**	
Total amount of fentanyl (µg/person)				
Range	(50-100)	(35-90)	(35-100)	**<0.001***
Mean ± SD	90±10	49.44±15.32+	62.72±23.59±	
Total amount of ketorolac (mg/person)				
Range	(90-120)	(30-90)	(60-90)	**<0.001***
Mean ± SD	96±12.17	63.33±10.02+	78±16.43±	
Antiemetic request				
Yes	74.3%	88.6%	91.4%	**<0.001***
No	25.7%	11.4%	8.6%	

*: Significant difference between 3 groups at p value < 0.05 + Significant difference of C vs B ± Significant difference of C vs BL

Discussion

The proof of the benefits of a single dose of local anesthetic in the cesarean wound is restricted and contradictory. In 2010, Nguyen et al.,[10] observed that bupivacaine infiltration in the surgical site decreased the amount of rescue morphine consumption post CS in women operated under general anesthesia.

For CSs under GA, bupivacaine-soaked sponges appear relatively cost-effective, easy to perform, feasible even in less-resourced regions, with a better side effect profile than other options. From this concept, and due to raising of the number of patients requiring general anesthesia either by their well or those who are contraindicated to regional anesthesia, this study, attempted to evaluate and compare the analgesic effect of bupivacaine and a mixture of lidocaine with bupivacaine (to combine the rapid onset of lidocaine and long duration of bupivacaine) when gelfoam soaked with either of them and placed subcutaneously in surgical wound as an attempt and an easy way to reduce patients opioid requirement with a corresponding reduction in opioid-related side effects.

Our results detected that the studied drugs produced more hemodynamic stability, rapid onset of analgesia, delaying the time of first analgesic request, decreasing the total amount of postoperative analgesics with less incidence of nausea and vomiting in comparison to the control group. The use of bupivacaine was superior in producing more intense analgesia with delayed time of first analgesic request than in the group of lidocain and bupivacaine mixture although the later showed a more rapid onset of analgesia, otherwise no significant difference detected between these two groups. This was obvious in comparing B group with BL group, the visual analogue pain score was significantly lower in group BL at 1hr postoperatively. However, the picture is reversed at 2 & 4 hrs postoperatively where it was significantly lower in group B in comparison to group BL. This is can be explained by the rapid onset of lidocaine which hasten the onset of analgesia in group BL and long

duration of bupivacaine which intense the analgesia in group B that received a larger volume of bupivacaine. These beneficial effects can be explained by that spongostan can act as a drug reservoir and can offer sustained release of the used LA. It could provide a higher drug concentration in the cesarean section wound and prolonged drug effect that permits women to feel more relaxed and comfortable.

In agreement with the results of the present study, simvali et al.,[9] who found that pain scores and cumulative analgesic consumption were lower in bupivacain group compared to the control group during the first eight hours after surgery.

Also Kafali et al..,[11] found that the pain score of bupivacaine-soaked spongostan group and postpartum total analgesic were lower than in control group treated with local lignocaine infiltration and it was statistically significant at all-time intervals during the first 24 hours.

On contrary, Gamli et al.,[12] who studied the efficacy of local application of gelfoam soaked with bupivacaine and the use of parenteral opioid at the site of iliac graft operations in controlling postoperative pain, and found no significant difference between groups in VAS scores although narcotic dosage were significantly less in the group B at 24 and 48 hours.

Side effects and complications are important to be recorded and analyzed whenever a new technique is adopted in clinical practice. In the current research, significantly lower incidence of nausea and vomiting was found in bupivacaine and bupivacaine-lidocaine groups in comparison to the control group, and no complications were recoded related to the surgical wound.

Agree with our results, Simvali et al[9] who stated in their study that the frequency of postoperative nausea, vomiting and antiemetic drug requirement have been lower in lower in the study group and rates of wound erythema and infection were low and similar between groups on the second and ninth postoperative. Also Sielaff et al.,[13] investigated the feasibility, efficacy and safety of a unique gelatin-based sponge as a hemostat in thyroid surgery and confirmed that it had excellent safety and haemostatic efficacy.

Limitations of the current study were that Peak plasma concentration, plasma half-life, and total clearance of the used doses of the studied drugs were not investigated. Also there was some shortage in the data concerning the long term follow up and if any chronic pain occurred after caesarean section due to the short hospital stay and economic factors.

References

1. Bijl, R. C., Freeman, L. M., Weijenborg, P. T., Middeldorp, J. M., Dahan, A., & van Dorp, E. L. A retrospective study on persistent pain after childbirth in the Netherlands. Journal of pain research, 2016; 9:1.
2. Allen VM, O'Connell CM, Liston RM and Baskett TF. Maternal morbidity associated with cesarean delivery without labor compared with spontaneous onset of labor at term. Obstet Gynecol 2003;102:477-82.
3. McDonnell, N. J., Keating, M. L., Muchatuta, N. A., Pavy, T. J. G., & Paech, M. J. Analgesia after caesarean delivery. Anaesthesia and intensive care 2009; 37:539-51.
4. Hegmann KT, Weiss MS, Bowden K, Branco F , DuBrueler K. Opioids for Treatment of Acute, Subacute, Chronic, and Postoperative Pain. J Occup Environ Med 2014;56:143-59.
5. White PF. The changing role of non-opioid analgesic techniques in the management of postoperative pain. Anesth Analg 2005; 101:5-22.
6. Kehlet H, and Kristensen BB. Local anesthetics in the surgical wound – is the pendulum swinging towards increased use? Reg Anesth Pain Med 2009;34:389–90.
7. Moiniche S and Dahl JB. Wound catheters for post-operative pain management: overture or finale? Acta Anaesthesiol Scand 2011;55:775-77.
8. Gerald A. Update on hemostasis: neuro-surgery Surgery 2007; 142:55–6
9. Simavli S, Kaygusuz I, Kinay T, Baylan AA and Kafali H. Bupivacaine-soaked absorbable gelatin sponges in caesarean section wounds: effect on postoperative

pain, analgesic requirement and haemodynamic profile. International journal of obstetric anesthesia 2014;23:302-08.
10. Nguyen NK, Landais A, Barbaryan A. Analgesic efficacy of Pfannenstiel incision infiltration with ropivacaine 7.5 mg/ml for caesarean section. Anesthesiol Res Pract 2010;1-7. doi:10.1155/2010/542375.
11. Kafali H, Iltemur Duvan C, Gozdemir E, Simavli S, Ozturk Turhan N. Placement of bupivacaine-soaked Spongostan in episiotomy bed is effective treatment modality for episiotomy associated pain. J Minim Invasive Gynecol 2008;15:719–22.
12. Gamli, M., Dalgic, A., Ornek, D., Horasanli, E., Kilci, O. & Dikmen, B. Evaluation of the efficacy of bupivacaine soaked in Gelfoam® at the iliac crest bone graft site. Brazilian Journal of Anesthesiology 2012;62:811-819.
13. Sielaff M, Hermanns M, Uhlig R, Abou-Ghazale´ Tand Steinmuller T. Early experience with a novel gelatine-based sponge for local haemostasis in thyroid surgery. In Vivo 2014;28:255–8.