# **PRODUCT INVESTIGATIONS**

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MEDICAL SCIENCE

MONITOR

Use of Gelatin Sponge Affects Postoperative Morbidity In Cesarean Section Patients

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Background:	This study aimed to determine the effects of use of a local hemostatic gelatin sponge (GS) on postoperative morbidity in patients undergoing cesarean section (CS).
Material/Methods:	The records of 318 patients who underwent CS surgery were retrospectively evaluated. Group 1 consisted of
	59 patients with gelatin sponge (GS) applied, and Group 2 consisted of 259 patients with no GS applied. The
	groups were compared for time to the first flatus, nausea and vomiting, requirement for anti-emetic drugs, de-
	velopment of postoperative ileus, and the length of hospitalization.
Results:	The patients in Group 1 and Group 2 were statistically similar in mean age, gravida, parity, and body mass in-
	dex (BMI) (p=0.352, p=0.275, p=0.458, and p=0.814, respectively). No significant difference was determined in
	the number of patients with nausea, vomiting, anti-emetic drug use, febrile morbidity, and postoperative ileus
	( $p=0.063$ , $p=0.436$ , $p=328$ , $p=0.632$ , and $p=0.179$ , respectively). Time to the first flatus and length of hospital-
	ization were significantly longer in Group 2 (p<0.001 and p<0.001, respectively).
Conclusions:	Delay in recovery of bowel motility may be due to the local hypersensitivity reaction caused by GS and/or dis-
conclusions.	location of this local hemostat. Women who receive gelatin sponge treatment during CS should be monitored
	closely for the recovery of postoperative intestinal motility.
MeSH Keywords:	Cesarean Section • Gelatin Sponge, Absorbable • Postoperative Complications
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### Background

Surgical hemorrhage is associated with increased morbidity and mortality. Approximately 30% of bleeding originates in the surgical area. The duration of hospitalization is 2- to 2.5fold longer in patients who undergo blood transfusions due to heavy surgical bleeding [1,2].

In case surgical bleeding cannot be controlled with cauterization, ligation, or other conventional hemostasis methods, local hemostats can be used [3,4]. Local hemostats include gelatin sponges, oxidized cellulose, Ostene, microfibrillar collagen, thrombin, thrombin with gelatin, fibrin sealants, platelet sealants, polyethylene glycol hydrogels, cyanoacrylates, glutaraldehyde cross-linked albumin, fibrin dressings, chitin dressings, chitosan dressings, and mineral zeolite dressings [5].

Gelatin sponge is an absorbable medical dressing applied to the bleeding surface in order to provide hemostasis. This dressing is an off-white, water-insoluble, non-elastic, flexible material obtained from pig skin or cowhide. Gelatin sponge is capable of absorbing large amounts of blood and other fluids. It also provides a mechanical matrix which aids in the initiation of clotting. After clotting is initiated, thromboplastin is secreted from thrombocytes and the gelatin sponge provides a scaffold for clotting. Gelatin sponge has been frequently and effectively used in anorectal operations, neurosurgery, nasal bleeding, and urological interventions [6,7]. The present study aimed to determine the effects of gelatin sponge on postoperative morbidity of women undergoing cesarean section.

### **Material and Methods**

The present study was approved by the Ethics Committee and Institutional Review Board of Pazarcik State Hospital, where it was conducted.

### Study design and patients

This was a retrospective review of 333 women who consecutively underwent their first cesarean section between March 2009 and December 2015. Exclusion criteria were cesarean hysterectomy, surgical management of severe postpartum hemorrhage, perioperative hyperalimentation, previous bowel surgery-with the exception of appendectomy, bowel obstruction, history of inflammatory bowel disease, chemotherapy within the previous week, previous abdominal or pelvic radiation, postoperative endotracheal or naso/orotracheal intubation, and postoperative admission to the intensive care unit.

After 15 women were excluded, the remaining 318 women were allocated into 2 groups. Group 1 included 59 women

in whom gelatin sponge (Spongostan®; Ferrosan, Soe-borg, Copenhagen, Denmark) was applied during cesarean section. Group 2 included 259 women in whom gelatin sponge was not applied during cesarean section.

Data related to age, gravidity, parity, body mass index, presence of adhesions, bowel packing, duration of hospitalization, use of anti-emetic drugs, and postoperative characteristics were acquired from the medical files.

### Delivery by cesarean section

In all patients, delivery by cesarean section was performed using the Joel-Cohen and Stark technique. After the abdomen was accessed via a Pfannenstiel incision, bladder dissection was made and the infant was delivered with a transverse incision through the lower segment of the uterus. The uterine incision was closed as a continuous single layer. Bleeding was brought under control with additional sutures and/or electrocauterization. Despite this, gelatin sponge was applied in cases of minimal but persistent bleeding. Then, the rectus muscle fascia was closed continuously. In cases where the subcutaneous distance was more than 2 cm, the subcutaneous fascia was uncovered and sutured.

### Postoperative follow-up

Visits were made by the surgeons twice a day. The patient was questioned regarding nausea and vomiting, abdominal pain, and other complaints. In the first postoperative 24 hours, vital signs were recorded by nurses every hour and at 6-hour intervals thereafter.

Patients were asked to inform nurses when flatus was first passed postoperatively, as this has been shown to be an indicator of the return of bowel motility [8,9]. During postoperative monitoring, patients were permitted to drink water and fruit juice after the 12<sup>th</sup> hour.

In patients who had not passed flatus in the first 24 hours, abdominal auscultation was performed. Only the intake of fluids was permitted until the passage of first flatus in patients who had bowel sounds. In patients with hypoactive bowel sounds or no bowel sounds, oral intake was stopped and an abdominal X-ray was obtained in a standing position. Patients with an observable air-fluid level on radiography were determined to have ileus. A nasogastric tube was applied to patients found to have ileus and those with excessive nausea, vomiting, and/ or abdominal distension. Nasogastric tubes were not applied in any patients without these complaints. In patients with terminated oral intake, 2000 ml of 5% dextrose and 1000 ml of Ringer lactate solution were administered intravenously over 24 hours. No medications (including enema) or tactile stimuli were applied to any patients with delayed passage of flatus.

#### Table 1. Patient demographic and operative characteristics.

	Group 1 (n=59)	Group 2 (n=259)	P-value
Gravida	2.17±0.41	2.62±0.24	0.352
Parity	1.45±0.23	1.53±0.32	0.275
Age, years	25.74 <u>±</u> 6.37	27.92±5.51	0.458
BMI (kg/m²)	28.02±3.68	27.95 <u>+</u> 4.75	0.814

Values are expressed as mean ± standard deviation.

 Table 2. Indications for primary cesarean section.

Indications	Group	o 1 (n=59)	Group	2 (n=259)	P-value
Malpresentation	19	(32.2%)	87	(33.5%)	0.110
Fetal distress	13	(22.0%)	61	(23.6%)	0.463
Failure of induction of labour with oxytocin	8	(13.6%)	37	(14.3%)	0.318
Obstructed labour	11	(18.6%)	33	(12.6%)	0.082
Multiple pregnancy	4	(6.8%)	26	(10.0%)	0.229
Antepartum hemorrhage	3	(5.1%)	10	(3.9%)	0.573
Cord prolapse	1	(1.7%)	3	(1.1%)	0.965
Preeclampsia	0	(0.0%)	2	(1.0%)	0.920

The criteria for hospital discharge included stable vital signs, unassisted ambulation, solid food tolerance without vomiting, normal urination, and the absence of other postoperative complications.

### Statistical analysis

Collected data were analyzed using Statistical Package for Social Sciences version 20.0 software (SPSS IBM Inc., Armonk, NY). Continuous variables are expressed as mean  $\pm$  standard deviation, and categorical variables are denoted as numbers or percentages, as appropriate. The distributions of variables were tested with the Kolmogorov-Smirnov test. The Student's t-test and Mann-Whitney U test were used for statistical comparisons. Two-tailed p-values <0.05 were considered statistically significant.

### Results

Table 1 displays the demographic characteristics of the study cohort. The women who received gelatin sponge during cesarean section and the women who did not receive gelatin sponge had statistically similar age, gravidity, parity, and body mass index (BMI) (p=0.352, p=0.275, p=0.458, and p=0.814, respectively).

The indications for the first cesarean section are shown in Table 2. The gelatin sponge group and the control group were statistically similar in indications for cesarean delivery. The most frequently encountered indication in both groups was malpresentation, followed by fetal distress and failure of induction of labor.

Table 3 demonstrates the postoperative complications of the study cohort. When compared to the women who did not receive gelatin sponge, the women who received gelatin sponge during cesarean delivery had a significantly longer time to first flatus and significantly longer hospitalization (p<0.001 and p<0.001, respectively). The women who received gelatin sponge during cesarean section and the women who did not receive gelatin sponge were statistically similar with respect to nausea, vomiting, anti-emetic drug use, febrile morbidity, and postoperative ileus (p=0.063, p=0.436, p=328, p=0.632, and p=0.179, respectively).

## Discussion

Local hemostats offer an alternative method for the hemostasis of bleedings originating from venous plexuses and capillaries [10]. Gelatin sponge, which is derived from porcine dermal gelatin, has been used for local hemostasis since 1945 [11]. By reducing intraoperative blood loss, local hemostats reduce

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Table 3. Study results.
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	Group 1 (n=59)	Group 2 (n=259)	P-value
Time to first flatus (hrs)	29.14±6.75	13.46±5.40	<0.001*
Length of hospital stay (hrs)	48.64±11.78	31.27±13.42	<0.001*
Nausea	10 (16.9%)	21 (8.1%)	0.063
Vomiting	6 (10.1%)	16 (6.2%)	0.436
Antiemetic medication	7 (14.3%)	18 (6.9%)	0.328
Febrile morbidity	3 (5.1%)	8 (3.3%)	0.632
Postoperative ileus	3 (5.1%)	3 (1.4%)	0.179

Values are expressed as numbers (%) except for time to first flatus and length of hospital stay, which are expressed as mean  $\pm$  standard deviation. \* p<0.05 was accepted to be statistically significant.

the use of systemic hemostats, shorten the time required to achieve hemostasis, decrease the need for transfusion and its associated risks, and shorten the duration of surgical operations and hospital stay [12,13].

The use of gelatin sponge may cause various adverse effects, including acute or chronic hypersensitivity reactions, granuloma formation, foreign body reactions, or brain/spinal cord pressure. Moreover, gelatin sponge may act as a focus for infections. In the efficiency and safety studies performed during the licensing process for use of gelatin sponge, a definitive relationship with at least 1 adverse effect, such as pyrexia, tachycardia, asthenia, or peripheral edema, was reported in 83% of subjects [14].

The absorption time of gelatin sponge may vary depending on the size and location of placement, but is generally considered to be approximately 5 weeks [14]. However, in a study conducted on rats, this period was shown to extend to up to 120 days [15]. Even if total absorption is expected within this period, the smallest amount of gelatin sponge required for hemostasis should be used to minimize adverse effects [12,16,17].

The absorption mechanism of gelatin sponge has yet to be fully elucidated. However, it has been reported that an inflammatory response is evoked around the hemostat until it is completely absorbed [12]. Hajosch et al. [18] hypothesized that the hemostatic performance of gelatin sponge may be linked to enhanced implantation of fibrinogen on the nanorough material surface of the local hemostat. In a study by Barbolt et al. [19], gelatin sponge was placed in a subdural area in rabbits and absorption was determined to have been via granulomatous inflammation. It has been presumed that the inflammatory process related to the absorption of gelatin sponge may be associated with postoperative morbidity. To the best of our knowledge, this is the first study to assess the effects of gelatin sponge use on postoperative morbidity of women who deliver by cesarean section. It has been previously reported that the use of local hemostats may shorten the duration of hospitalization [4,12,13]. In the present study, the length of hospital stay was significantly longer in the women who received gelatin sponge during cesarean section. This significant difference can be attributed to the significantly longer time taken for the first flatus to pass. Although not statistically significant, the rate of patients with postoperative morbidities including nausea, vomiting, febrile morbidity, and ileus was higher in the gelatin sponge group than in the control group. Of the patients with no passage of gas in the first 24 hours, only those with hypoactive bowel sounds or no bowel sounds and with an air-fluid level on abdominal X-ray were accepted as ileus. This may explain the relatively low rate of postoperative ileus despite the prolonged time to first flatus in the gelatin sponge group.

The passage of first flatus is routinely used as a clinical marker for recovery of bowel motility during the postoperative period. The impairment in the recovery of bowel motility may be due to the local hypersensitivity reaction caused by the application of gelatin sponge. Rare cases of anaphylaxis associated with gelatin sponge have been reported [20,21]. The placement of gelatin sponge can result in local edema, which may decelerate intestinal motility. Another underlying factor may be the dislocation of the gelatin sponge. Dutton et al. reported optic nerve pressure associated with the dislocation of local hemostats [22]. As the gelatin sponge has a limited adherence to the bleeding surface, it can be easily displaced [4]. The displaced gelatin sponge may act as a foreign body and, thus, lead to intestinal irritation.

To the best of our knowledge, the present study is the first to demonstrate that the use of GS is associated with a prolonged time to passage of flatus and, thereby, delayed discharge from hospital. However, the main limitation of this study was the retrospective design.

### Conclusions

The findings of the present study indicate that the mean time to first flatus during the postoperative period and the duration of hospitalization are significantly prolonged by the use of gelatin sponge as a local hemostat in cesarean section patients. The delay in the recovery of bowel motility may be due to the local hypersensitivity reaction caused by gelatin sponge and/or dislocation of this local hemostat. These findings imply that the type, amount, and localization of gelatin sponges should be recorded in surgery notes. Women who experience

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a delay in passing the first flatus after cesarean delivery should be assessed for gelatin sponge utilization. Additionally, women who receive gelatin sponge during cesarean delivery should be monitored up closely for the recovery of postoperative intestinal motility. Further research is warranted to clarify the effects of gelatin sponge use on postoperative morbidity of women who undergo cesarean section.

### **Conflict of interest**

The authors of this manuscript report no conflict of interest.

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