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ORIGINAL ARTICLE

SURGICEL compared with simple gauze packing in grade IV liver injury: an experimental study

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Abstract

A number of hemostatic agents such as porcine collagen, topical thrombin, and SURGICEL (oxidized cellulose) can be used to achieve homeostasis in liver laceration. This study aims to compare stereological findings in using SURGICEL vs. gauze packing in grade 4 liver lacerations in Wistar rats. In this experimental study, 20 male Wistar-albino rats weighing 250–300 g were purchased from Shiraz University of Medical Sciences animal laboratory. At the beginning of the study, a 1-cm length and 0.5-cm depth linear laceration was made on the large lobe of the liver in all rats through laparotomy. At least one or more liver tissue samples were obtained from live rats to compare the efficacy of SURGICEL vs. gauze packing. According to our stereological results, normal liver tissue in the SURGICEL group (0.882 ± 0.146) was significantly lower than the controls (0.994 ± 0.007) (p value $< .016$). Liver fibrosis in the SURGICEL group (0.043 ± 0.025) was significantly more than the control group (0.005 ± 0.007) (p value $< .016$). As known, by increase in the fibrosis tissue, the chance of recurrent bleeding decreases; analysis of the results showed that we had more fibrosis tissue after treatment of liver laceration by SURGICEL instead of gauze and it is a new hope in liver laceration treatment methods.

Keywords SURGICEL · Liver injury · Hemostatic agent · Gauze packing

Introduction

Nowadays, liver bleeding is a major problem for surgeons due to its high vascularization and small artery sizes (Nouri and Sharif 2015). Trauma is a risk factor during liver surgery because liver is the organ most commonly injured in blunt abdominal trauma (Amirbeiky et al. 2014; Malhotra et al. 2002; Motie et al. 2009; Tinkoff et al. 2008). In Iran, trauma is the second leading cause of death among the youth (Afifi 2008). In managing trauma patients, the first step is to create a safe airway, immobilize the cervical column, and obtain suitable circulation and breathing. Next, controlling hemorrhage is another critical step (Matsuda et al. 2006; Testai et al. 2002). Despite progresses in surgical science, hemorrhage control, particularly in liver parenchyma, is still one of the major problems with which the surgeons are faced.

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Quick intervention to stop bleeding can reduce the damage and need for blood transfusion (Inaba et al. 2011). The progress in diagnostic imaging has led to a shift towards non-operative management of blunt liver injuries. Bile leak in patients who have undergone surgery to control bleeding has remained a potential complication (Asensio et al. 2000; Singh et al. 2007; Wahl et al. 2005).

A number of hemostatic agents such as porcine collagen, topical thrombin and SURGICEL (oxidized cellulose) can be used to achieve homeostasis (Spotnitz and Burks 2010). Cellulose is a homopolysaccharide of glucopyranose polymerized through β-glucosidic bonds (Pierce et al. 1984). In 1945, oxidized cellulose was first used and since then it has been widely used in surgical fields, which is available in many different forms (Frantz and Lattes 1945). Oxidized cellulose is a hemostatic gauze, which is well accepted because of its sterility, ease of use, bactericidal properties, and favorable biocompatibility (Lewis et al. 2013).

SURGICEL is the product that is more accessible, cost-benefit, easier to obtain, and has more beneficial effects than previous hemostatic agent. In this research, we aimed to compare stereological findings in using SURGICEL vs. gauze packing in grade 4 liver lacerations in Wistar rats.

Materials and methods

In this experimental study, 20 male Wistar-albino rats weighing 250–300 g were purchased from Shiraz University of Medical Sciences animal laboratory. Their health status screening was performed under standard laboratory conditions—temperature 20–24 °C and 12/12 h light/dark cycle. Each rat was housed in separate cages and fed with pellet and appropriate water at libitum.

To control hypothermia, we used rectal temperature (Tr) and the temperature was maintained at 38.0 °C ± 0.5 °C with a heating lamp and resuscitation with warm isotonic saline.

The study was approved by Shiraz University of Medical Sciences local ethics committee. Then, the rats were randomly divided into two groups, each containing 10 rats. Before laparotomy, the rats were anesthetized with intramuscular injection of ketamine (50 mg/kg; Alfasan International, Woerden, the Netherlands) and xylazine (10 mg/kg; Alfasan International). The anesthesia lasted for about 20 to 30 min. After inducing bleeding, we administrated warm isotonic saline (< 10 ml/kg) for resuscitation.

At the beginning of the study, a linear laceration with 1-cm length and 0.5-cm depth (grade 4) was made on the large lobe of the liver in all rats through laparotomy (Tinkoff et al. 2008). After uncontrolled bleeding for 2 and 10 min, one group underwent gauze packing and the other one was packed with SURGICEL in a standardized manner. After10 min, the packs were removed to evaluate the amount of bleeding. A total of six rats in the gauze group and one rat in SURGICEL group expired within 2 weeks of follow-up. Five rats from the SURGICEL group were selected to be compared with live gauze group rats. At least one or more liver tissue samples were obtained from live rats to compare the efficacy of SURGICEL vs. gauze packing. The tissues were fixed in buffered formaldehyde for 1 week and later studied by stereology method. In the first step, the tissue lams were randomly chosen to be checked under microscope, using point counting method. Then, the randomly selected points in each lam were analyzed via video microscope system Nikon E200 Japan, and a video camera Sony SSc Dc18p. This was done to find normal, granulomatous, fibrosis, and amorphous tissues at equal intervals along X- and Y-axis in different resolutions (× 1000) by using stereology application. The data were collected and then analyzed through SPSS version 21 using Mann-Whitney test; p value less than 0.008 was considered to be significant.

Results

Bleeding

There was no statistically significant difference among intraperitoneal bleeding between the SURGICEL (0.99 ± 0.13 ml) and control groups (0.97 ± 0.14 ml) 2 min after the injury (P = 0.74). Also, there was no statistically significant difference among intra-peritoneal bleeding between the SURGICEL (0.11 ± 0.08 ml) and control groups (0.14 ± 0.06 ml) 10 min (P = 0.35) after the liver injury. However, there was a significant difference between the SURGICEL (0.46 ± 0.14 ml) and control groups (0.76 ± 0.18 ml) in intra-peritoneal bleeding 48 h after the liver injury (p value = 0.0006).

Death

One (10%) subject expired after 14 days in the SURGICEL group; however, six (60%) rats expired in the control group. This association was not statistically significant (p value = 0.14).

Stereological study

Weight and volume of the liver in the SURGICEL and control groups were not statically significant ($p > 0.05$). According to our stereological results, normal liver tissue in the SURGICEL group (0.882 ± 0.146) was significantly lower than the controls (0.994 ± 0.007) (p value < .016). Liver fibrosis in the SURGICEL group (0.043 ± 0.025) was significantly more than the control group (0.005 ± 0.007) (p value < .016). Granulation between the two groups was not significant. Also, the amorphous tissue in the SURGICEL group was not significant in comparison with control group (Table 1) (Fig. 1).

Table 1 Mean and standard deviation for normal liver tissue, fibrosis, granulation tissue, and amorphous tissue in the SURGICEL and control groups

Group		*N*	Mean	STD deviation	*p* value
Vvnormal	G	4	.9947	.00707	.016
	S	5	.8827	.14646	
Vvfibrosis	G	4	.0053	.00707	.016
	S	5	.0436	.02508	
Vvgranulation	G	4	.0000	.0000	.190
	S	5	.0206	.02033	
Vvamorphus	G	4	.0000	.0000	1.000 s
	S	5	.0000	.0000	
Liver weight	G	4	5.7100	.59810	.413
	S	5	4.8700	1.16925	
Liver volume	G	4	5.3800	.50180	.413
	S	5	4.5060	1.10287	

Discussion

Today, one of the main problems in healthcare system is liver bleeding, for the management of which many different methods have been suggested. Each method has its own pros and cons. Topical hemostatic agents are used as supplementary option to control bleeding.

Karakaya et al.'s study showed that Ankaferd BloodStopper (ABS) was as effective as SURGICEL in the success of homeostasis following partial liver removal in a rat model (Karakaya et al. 2009). It was reported that collagen preparations were as effective as gauze in decreasing the bleeding time and blood loss after liver trauma. Perihepatic packing to control hemorrhage has undesirable effects, such as intraabdominal sepsis, even though it has some beneficial effects (Feliciano et al. 1986).

Moreover, the results of Bala et al.'s study (Bala et al. 2012) in 2012 showed that biliary complications and bile leak were frequent in blunt liver injuries, and surgical interventions might lead to sepsis, coagulopathy and respiratory insufficiency (Yuan et al. 2014).

Satar et al. (Satar et al. 2013) showed that ABS can cause more positive histopathological changes in comparison to SURGICEL in rat experimental model.

In Okamus et al.'s study, ABS, as a homeostatic agent, successfully stopped hemorrhage in deep tissue without any pathological changes in the tissue after 2 weeks of follow-up (Okumuş et al. 2013). In our study, the amount of bleeding between the surgical and the gauze groups was statistically significant ($p = 0.001$).

In the research conducted by Feretti and co-workers, SURGICEL had no significant effect on controlling aorta bleeding in rats (Ferretti et al. 2012). In Abe's study, SURGICEL was able to stop bleeding in all patients who had undergone rectum surgery (Abe et al. 2015). Also, it was mentioned in Sharma's research that SURGICEL stopped bleeding in 93% of patients with uterine perforation after laparoscopy surgery (Sharma et al. 2003).

However in some studies, the SURGICEL did not act as sufficiently as it was predicted; for example, in Genyk's study bleeding did not stop after 3 min of treatment by SURGICEL in 50% of patients (Genyk et al. 2016). Also, in Kakaei's study 33% of patients had recurrent bleeding after treatment using SURGICEL (Kakaei et al. 2013). Sirlak showed that the SURGICEL was less effective in controlling bleeding in patients who underwent heart surgery compared with treatment by Colgel (Sirlak et al. 2003). It seems that the differences between the results of these studies come from different methods and their research population.

In our study, the mortality rate was 60% (6/10) in the gauze group and 10% (1/10) in the SURGICEL group; however, it was not statistically significant (p value = 0.14).

To the best of our knowledge, few studies have been conducted on the histopathological effect of SURGICEL in the liver tissue. Several studies in Turkey showed that ABS permanently stopped bleeding without any histopathological changes in the liver tissues. In our study, liver fibrosis in the SURGICEL group (0.043 ± 0.025) was more significant than the control group (0.005 ± 0.007) (p value $< .016$). Fibrosis prevents the bile leakage and morbidity such as sepsis and coagulopathy. SURGICEL significantly reduced bleeding in comparison to the group using gauze packing ($p = 0.0006$).

These data show that SURGICEL in experimental liver trauma can cause favorable histopathological changes and

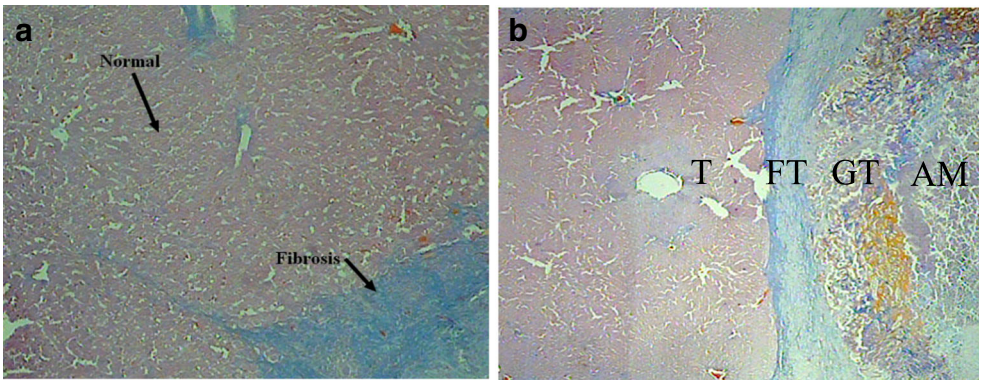

Fig. 1 A) Guaze Group Stereology Study (Heidenhain's AZAN trichrome stain, × 400). B SURGICEL Group Stereology Study (Heidenhain's AZAN trichrome stain, × 400). T, normal tissue; FT, fibroblast tissue; GT, granulation tissue; and AM, amorphous tissue

shorter homeostatic time. However, for confirmation of our results, more investigations are required. Our study had some limitations.

One limitation in our study was the second look after 48 h to remove the gauze from the liver. Although SURGICEL showed its efficacy to control bleeding, the second look while using gauze was inevitable. Hence, finding a proper base for applying SURGICEL on the liver is still a challenging matter. Another limitation was that we did not measure bile leakage during the days following operation, but we assume that due to more fibrosis in the rats packed with SURGICEL group, lesser bile leakage probably occurred in comparison to the gauze packed group.

In conclusion, SURGICEL can be used safely since it might lead to positive pathologic changes and reduced bleeding. Further research in animal and human models is recommended for better evaluation.

Conclusion

As known, by increase in the fibrosis tissue, the chance of recurrent bleeding decreases; analysis of the results showed that we had more fibrosis tissue after treatment of liver laceration by SURGICEL compared with gauze and it is a new hope in liver laceration treatment methods.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval All applicable international, national, and/or institutional guidelines for the care and use of animals were followed. Ethics number: ir.bmsu.rec.1396.418.

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