Background: Controlling parenchymal hemorrhage especially in liver parenchyma, despite the progress in surgical science, is still one of the challenges that surgeons face when trying to save patients’ lives. Researchers in the field are challenging to introduce a more effective method.

Objectives: The current study aimed to determine the haemostatic effect of alum \([\text{KAl(SO}_4\text{)}_2]\) and compare it with that of standard method, suturing technique, in controlling bleeding from liver parenchymal tissue.

Materials and Methods: In this animal model study, 60 male Wistar rats were used. An incision, two centimeters long and half a centimeter deep, was made on each rat’s liver and the hemostasis time was measured once using alum with different concentrations (5%, 10%, 15%, 25%, and 50%) and then the control method, controlling bleeding by suturing, was employed. The liver tissue was examined for pathological changes.

Results: Complete hemostasis occurred in all the groups. There was a statistically significant difference between the two haemostatic times \((P < 0.001)\). The haemostatic times in different concentrations of alum were significantly less than that of the control group \((P < 0.001)\). The pathologic examination showed the highest frequency of low-grade inflammation based on the defined pathological grading.

Conclusions: Alum might be an effective haemostatic agent in controlling liver parenchymal tissue hemorrhage in an animal model.

Keywords: Hemostasis; Alum Compounds; Liver; Rats
lights on from 8:00 a.m. to 8:00 p.m. They had free access to standard rat chow and water ad libitum. Animal handling and all experiments were performed in accordance with the international guidelines for the care and use of laboratory animals (Institute of Laboratory Animal Resources, 1996) and approved by the local research council at Kashan University of Medical Sciences, Kashan, Iran.

3.2. Surgery
Rats were anesthetized by intraperitoneal (IP) injection of a ketamine/xylazine mixture (ketamine 100 mg/kg and xylazine 10 mg/kg). The 10% ketamine and 2% xylazine (Alfasan, the Netherlands) were purchased from pharmacy at Shahid Beheshti Hospital of Kashan. Then the cutaneous and subcutaneous layers in the abdominal zone were opened, and after determining the anatomical position of the liver, the liver lobe was extracted from the abdominal cavity (Figure 1). Next, a two-centimeter long and half-a-centimeter deep cut was made on the liver by a scalpel, the depth was determined by a mark made on the scalpel 0.5 cm from the tip, and the length was measured with a ruler on the liver.

3.3. Alum Administration and Haemostatic Time Measurement
The alum was purchased from Merck (Darmstadt, Germany). Aqueous solution of alum 50%, 25%, 15%, 10% and 5% (w/v) were prepared in distilled water. Half a milliliter volume of solutions were applied to the incision sites by an insulin syringe. In fact, each concentration of alum was used in one of the groups, and the times of hemostasis were measured by chronometer (Figure 2). In the current study, the haemostatic time was considered as the time required for stopping the bleeding with no blood discharge from the incision site. The mean of ten measured times was considered as the haemostatic time for each concentration. Suturing, the standard method, was used in the control group to be compared with the results of the alum concentrations. The time of liver hemostasis was measured using sutures and (all the stitches were made by the same surgeon) on the livers of the ten rats kept and fed similar to the other groups, and the mean of the ten obtained times was compared with the results of different concentrations of alum. After controlling liver hemorrhage, subcutaneous and skin were closed again, and to prevent infection, each rat received 50 mg of kefalin through an intraperitoneal injection ((cefalotin 1 g/Vial), Aspen Pharmacare Australia Pty Ltd, Australia).

3.4. Pathological Study
After one week, the rats were anesthetized by IP injection of a ketamine/xylazine mixture (ketamine 100 mg/kg and xylazine 10 mg/kg) and were placed in a supine position on the operating table. Then an incision was made on the previous site and the rats’ livers were
The pathological effects of alum and suturing technique on the liver tissue were studied through staining with haematoxylin and eosin (H and E) by light microscopy. Acidic property of alum after reaction with blood proteins creates a barrier by coagulated proteins, and prevents the outflow of blood from vessels. On the other hand, it prevents the alum from entering the vessels, and as a result, it does not allow potential systemic complications of alum.

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<th>Table 1. The Hemostasis Time Using Different Concentrations of Alum and Suturing Technique in Liver Parenchyma$\textsuperscript{a}$</th>
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<td><strong>Groups</strong></td>
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<td><strong>Haemostatic times, Sec</strong></td>
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<td>$\textsuperscript{a}$ Data are presented as Mean ± SD.</td>
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<th>Table 2. The Frequency of Liver Pathological Grade After Exposure to Different Concentrations of Alum and Suturing Technique$\textsuperscript{a}$</th>
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<td><strong>Pathological grade</strong></td>
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<td><strong>Grade 1</strong></td>
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<td><strong>Grade 2</strong></td>
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<td>$\textsuperscript{a}$ Data are presented as No. (%).</td>
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Results of the current study showed that, compared with the standard method used in the control group (with a deep suture of the liver parenchyma) alum needs significantly less time to exert its haemostatic effect. Currently, the choice techniques used to minimize bleeding during liver surgery are based on personal preference, physicians’ experience and facilities available in the treatment centers. The standard method is used to control bleeding of the liver lacerations clamps in the vascular area by deep stitches or the pack method (14).

It should be considered that liver bleeding control with sutures could cause more injuries, both parenchymal and ischemic, in the normal liver tissues. On the other hand, the liver parenchymal tissue is not suitable for stitching, and with a low-experienced surgeon, the sutures will exacerbate the rupture of the liver parenchyma. Pack method also has the risk of re-bleeding and abdominal compartment syndrome, which imposes additional surgery to the patient. Intermittent clamping of the portal triad is also associated with more bleeding than continuous clamping (5).
In the current study, after exposing the liver tissues to alum they were sent to the laboratory to evaluate the haemostatic effect of this haemostatic agent. In order to determine the inflammation of the liver, caused by exposure to the alum as a foreign body, a pathological grading was used. This grading was scored from zero to five, according to the severity of the inflammation. Pathological reports showed that the alum, even at very high concentration (50%) did not cause any inflammation greater than grade two, and the immune system reaction against the alum as a foreign body, a pathological grade of 3–4.

Kim and Rethnam stated that a good haemostatic material is the one that stops bleeding in the shortest possible time, one that is easily portable and compatible with life, imposes minimum complications to the patient, does not interfere with tissue healing and has a reasonable price (13). Considering the definition of a haemostatic agent provided by these researchers, the unique mentioned features of alum, such as not requiring normal haemostatic system for function, unlike other haemostatic agents, make this chemical substance an extremely effective topical haemostatic agent to control liver parenchymal tissue bleeding, compared to the other methods.

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References