American Journal of Medicine and Medical Sciences 2025, 15(8): 2505-2509
DOI: 10.5923/j.ajmms.20251508.17

Effectiveness of Hemostatic Agents in Traumatic Liver Injuries

Khamdamov Bakhtiyor Zarifovich*, Ganjiev Farrukh Khairilloevich, Makhmanazarov Orifjon Mirzonazarovich

Bukhara State Medical Institute, Bukhara, Uzbekistan

Abstract The developed and experimentally substantiated model of liver injury enables a comprehensive assessment, including quantitative, behavioral and morphological, which is fundamental when choosing a drug for local hemostasis. At the same time, based on the studies conducted, it was proven that BloodSTOP IX demonstrated the least aggressiveness and the greatest biocompatibility.

Keywords Liver injury, Local hemostasis, Morphology

1. Introduction

Traumatic liver injuries occupy one of the leading places among life-threatening abdominal conditions in emergency surgery, being the main cause of intra-abdominal bleeding. According to modern data, mortality in severe forms of such injuries reaches 20-30%, especially in case of combined trauma, massive blood loss and development of shock [1,3,5].

The evolution of approaches to surgical tactics for liver trauma in recent decades has led to a move away from extensive resections in favor of organ-preserving techniques, including the use of modern local hemostatic agents [2,4,6]. However, despite the variety of available agents, the issue of a reasonable choice of hemostatic drug depending on the morphological substrate of the injury, the nature of the bleeding, and the likelihood of a biliary component remains unresolved [7,9]. Morphological studies in recent years have shown that a number of widely used agents, especially those based on oxidized cellulose, can cause an aggressive tissue reaction with the formation of coagulation necrosis, inflammatory infiltration, biliary extravasation, and subcapsular fibrosis [8,10]. Particularly vulnerable in this context are areas of the liver anatomically associated with the biliary tree, where tissue damage and bile impregnation can significantly complicate the course of the postoperative period [3,11]. On the other hand, a number of agents with pronounced initial adhesion, high flexibility and the ability to spread evenly demonstrate a morphologically soft and physiological type of reparation, accompanied by uniform granulation and the absence of biliary aggression [4,7]. An important criterion for choosing a local hemostatic agent is its operational controllability: ease of placement, degree of adhesion to the wound surface, resistance to respiratory excursions of the liver, as well as the need for additional compression [3,5,8].

The use of agents that do not require fixation allows to reduce the duration of the intervention and minimize repeated blood loss, especially in the conditions of laparoscopic operations and unstable hepatopoietic field [2,9,10].

Despite the existence of studies devoted to the comparison of individual hemostatic agents, the vast majority of them do not take into account the morphological consequences of their use, limiting themselves to clinical and operational parameters. As a result, there is no algorithm that takes into account not only the hemostatic properties of the drug, but also its effect on tissue regeneration, the risk of biliary complications and morphological stability.

Thus, the development of a systematic approach to the comparative assessment of local hemostatic agents based on the combined characteristics of hemostatic efficiency, operational parameters and morphological changes is a relevant and practically significant task. The implementation of such a model will substantiate the choice of the optimal drug for liver injuries, minimize the risks of complications and increase the reproducibility of the surgical result.

Objective of the study. To study the effectiveness of various local hemostatic agents in traumatic liver injuries.

2. Material and Methods

The conducted clinical and experimental study allowed us to objectively evaluate the effectiveness of various local hemostatic agents in traumatic liver injuries, as well as to substantiate the algorithm for their rational choice. The work was based on a comparison of clinical data of 44 patients

* Corresponding author:
xamdamov.baxtiyor@bsmi.uz (Khamdamov Bakhtiyor Zarifovich)
Received: Jun. 12, 2025; Accepted: Jul. 28, 2025; Published: Aug. 4, 2025
Published online at http://journal.sapub.org/ajmms

hospitalized for liver injury and experimental observations on 80 laboratory animals with simulated injuries.

In the clinical part of the study, patients were divided into control (n=23) and main (n=21) groups, comparable by age, gender, type of injury (blunt trauma - 63.6%, incised - 36.4%), nature of bleeding and volume of hemoperitoneum. The frequency of venous and mixed bleeding was 65.9%, which reflects a high hemostatic load. Lesions of the V and IV liver segments prevailed (up to 26.1% of cases), and in 29.5% of cases, bile leakage was detected, requiring the selection of drugs resistant to biliary aggression. The frequency of grade III hemorrhagic shock did not exceed 6.8% in both groups, which made it possible to avoid systemic distortions in the analysis of hemostasis. The experimental model included 10 series on 80 Wistar rats (10-12 weeks old, body weight 260-320 g), with uniform distribution by injury type (blunt or cut trauma) and the drug used: Surgicel® , TachoSil® , Biatravm® and BloodSTOP IX. Observation was carried out on days 3, 7 and 14 with macro- and micromorphological verification. To control natural regeneration without intervention, two additional control series were formed (n=16).

In the experimental part of the study, a reproducible model of liver injury was implemented, covering both clinically significant types of injury - blunt and cut, with subsequent application of local hemostatic agents of various nature. A total of 80 laboratory animals were included in the experiment, evenly distributed over 10 series, which ensured symmetry of observations. The fundamental difference of this model was the comparison of morphological changes in dynamics (3, 7 and 14 days) not only between the drugs, but also with the control series, in which the application of agents was not carried out. This allowed us to objectively assess the effect of each drug on the course of inflammatory and reparative processes, as well as to identify signs of accelerated or delayed regeneration, tissue maceration, bile impregnation, coagulation necrosis and fibrosis.

The results of the morphological analysis served as the basis for constructing a correlation model that compares clinically significant parameters (bleeding duration, hemostasis stability, need for repeated application) with tissue characteristics of the injury zone. The use of a semi-quantitative assessment system made it possible to identify statistically significant relationships between the severity of coagulation necrosis and the protracted nature of hemostasis, between the maturity of granulation tissue and the absence of repeated applications, as well as between the intensity of inflammatory infiltration and the instability of the hemostatic effect. Pearson's correlation coefficients varied from $r = -0.45$ to $r = 0.63$ at a significance level of $p < 0.05$, which confirms the analytical validity of the model. Thus, the data obtained in the experiment provided not only an evidence base for a comparative assessment of local hemostatic agents, but also made it possible to substantiate the morphological criteria for their effectiveness depending on the nature of the injury. These results became the basis for the transition to clinical testing of the proposed algorithm for selecting a drug adapted to the conditions of emergency liver surgery.

Characteristics of the research methods: For the experimental part of the study, outbred white rats of the Wistar line were used, obtained from the certified vivarium of the Bukhara State Medical Institute. All animals were clinically healthy males, aged 10-12 weeks, with a body weight of 260 to 320 g at the beginning of the experiment.

The animals were kept in individual cages on standard bedding, with free access to water and granulated feed, under controlled temperature (22±2℃), humidity (55-65%) and light conditions (12-hour lighting cycle). Before the manipulations, all animals underwent a week-long quarantine period and a visual clinical examination to exclude latent diseases and external defects. The experiments were carried out under conditions of natural light activity in the morning hours, in a specially equipped operating room at the vivarium, in compliance with aseptic requirements. All actions were carried out in accordance with international principles of humane treatment of laboratory animals (Helsinki Declaration, 2011) and were approved by the local bioethics committee of the Bukhara State Medical Institute (protocol No. 18 dated 01/23/2021).

Depending on the type of the simulated injury, all animals were divided into two main experimental groups: with reproduction of blunt liver injury and with the formation of a cut wound of the liver. Each of these groups, in turn, was divided into four subgroups in accordance with the local hemostatic agent used: Surgicel® , TachoSil® , Biatravm® and BloodSTOP IX.

The total number of animals in the experiment was 80 rats: 32 for each injury model using drugs and 8 for 2 control series. All interventions were performed according to a single standard, with identical anesthesia conditions, surgical access and hemostatic protocol, differing only in the type of drug used.

During the experiment, 10 consecutive series were formed, each of which included 8 laboratory animals. The series differed both in the type of reproducible liver injury and in the hemostatic agent used. Series 1 included rats with a model of blunt liver injury, with Surgicel® used in the damaged area.

The 2nd series also represented a blunt trauma model, but with the use of TachoSil® .

The 3rd series corresponded to the same trauma model using the domestic hemostatic agent Biatravm® .

The 4th series completed the blunt trauma block and included the application of BloodSTOP IX.

The 5th series included animals with the reproduction of a linear cut wound of the liver, to which Surgicel® was applied.

The 6th series corresponded to a similar cut wound of the liver, but with the use of TachoSil® .

The 7th series involved the application of Biatravm® to the cut surface.

The 8th series completed the structure of the experiment and included the use of BloodSTOP IX for a cut wound of the liver.

To verify morphological changes caused not only by trauma but also by the action of hemostatic drugs, a separate control group of animals (9th – 10th series) was formed, which did not receive the application of a hemostatic agent after the modeling of liver trauma. These animals were observed for the same periods (3, 7 and 14 days) and underwent the same procedure for collecting material and morphological assessment. This allowed us to establish the background level of inflammatory and reparative activity, as well as to determine the natural dynamics of healing in the absence of drug exposure.

This design provided a symmetrical study model, in which each drug was tested under conditions of both blunt and incised traumatic liver injury, which allowed for not only intragroup but also intergroup comparative analysis of the hemostatic efficacy and morphological consequences of each drug.

Modeling of liver injury was performed under general injection anesthesia. A mixture of xylazine (10 mg/kg) and ketamine (80 mg/kg) was used as an anesthetic, administered intramuscularly into the hind limb. After the onset of the surgical stage of anesthesia, the animal was laid on its back on a sterile surgical field. The hair in the epigastric and right hypochondrium was carefully shaved, the skin was treated with 0.05% chlorhexidine solution in three stages, followed by the imposition of sterile access. A longitudinal skin incision 2.5-3 cm long was made, soft tissues were bluntly and sharply dissected, providing access to the liver, while the surgical field was treated without the use of cauterizing solutions.

In the models of blunt liver injury (series 1–4), a standardized technique was used: a cylindrical weight of 50 g, freely falling from a height of 20 cm through a guide tube, was vertically applied to the exposed surface of segment V or IV of the right liver lobe. This energy (≈0.1 J) provided reproducible parenchymal damage with the formation of a crushed hematoma and diffuse venous or capillary bleeding. In cases where through-and-through destruction of the parenchyma, capsule rupture with profuse bleeding and the inability to stop bleeding within 10 minutes were observed, the animal was excluded from the series as not corresponding to the model in terms of severity. In the models of incised liver wounds (series 5–8), a technique for creating a linear controlled defect was used: a #11 scalpel was used to make a longitudinal incision at a right angle, 5 mm long and 2 mm deep, in the projection of segment V of the liver. The incision line was parallel to the capsule, causing capillary and oozing bleeding without an arterial component. The damage was limited to the subcapsular layer and was not accompanied by the destruction of segmental vessels. Defects with signs of damage to the bile ducts, central veins or a blood loss volume exceeding 0.5 ml also served as grounds for excluding the animal from the experiment due to non-compliance with the model criteria.

After the modeling and application of the hemostatic drug, the animals were observed for three periods: on the 3rd, 7th and 14th days after the operation. Each period included an equal number of animals from all series, which ensured the symmetry of the sample and the possibility of comparing the early, intermediate and late phases of morphological reparation. On the day of material collection, the animals were withdrawn from the experiment by an overdose of anesthesia with subsequent verification of a lethal outcome. The liver was collected within the damage zone together with the adjacent tissues and edges of the drug application.

The evaluation of the results included both macroscopic and microscopic examination. The following were recorded macroscopically: wound shape and consistency, tissue color, presence of bile leakage, degree of adhesion of the hemostatic material, signs of rejection or maceration. The volume of residual bleeding and the presence of adhesions were also recorded. The samples were photographed before and after opening the capsule. Microscopic examination was performed on serial paraffin sections stained with hematoxylin and eosin. The following parameters were studied: presence and extent of coagulation necrosis; severity of inflammatory infiltration; bile impregnation or biliary granulomas; presence of granulation tissue and its maturity; capsular reaction and perisinusoidal fibrosis; signs of completed regeneration.

Additionally, the adhesion of the drug, the need for repeated application, the stability of hemostasis and the presence of residual blood loss (by the volume of impregnation of the surgical field in the first 3 minutes after application) were assessed. All observations were documented and compared with clinical and functional parameters, including the duration of bleeding recorded by a stopwatch from the moment of injury to stable cessation of visual bleeding. Thus, within the framework of the experimental study, a standardized model of liver injury was implemented, including two types of injury in the form of a blunt and incised wound with the ability to reproduce clinically significant bleeding scenarios. Uniform distribution of animals across series, compliance with uniform conditions of injury and the use of hemostatic drugs ensured high reproducibility of the results obtained. The formed model served as a reliable basis for the subsequent analysis of morphological changes, clinical and experimental comparisons and the formation of an algorithm for choosing the optimal local hemostatic agent.

3. Results and Discussion

In the conditions of blunt liver injury modeling, it was found that BloodSTOP IX ensured the achievement of final hemostasis in the shortest possible time, which was less than one minute. The obtained values significantly differed from similar indicators when using traditional drugs. The level of blood loss in the series using BloodSTOP IX remained the lowest among all groups, and there was no need for repeated application, which allowed us to classify this drug as resistant to technical instability of the surgical field.

Analysis of behavioral characteristics in blunt trauma showed differences in the degree of adhesion of the preparations, the need for fixation, and the duration of the delay in action. Preparations based on oxidized cellulose required mandatory compression and demonstrated average

or unstable adhesion upon contact with a wet surface. Biatravm® was fixed without external support, but in some cases was accompanied by local tissue changes in the contact zone. BloodSTOP IX combined immediate fixation, uniform distribution, and minimal displacement under mechanical action. In a model of an incised wound of the liver against the background of a linear and anatomically smooth defect, differences were found in the stability of the application and the density of the adhesion of the materials. Surgicel® and TachoSil® demonstrated a tendency to curl and peel off the edges during the first minutes after application. When using them, there was a need for additional compression, which reduced the reproducibility of the effect. Biatravm® retained its shape, but required uniform application. BloodSTOP IX provided stable adhesion without additional intervention, demonstrating stability even during respiratory excursions of the organ.

Differences in the delay of action were revealed against the background of drug application in conditions of capillary and mixed bleeding. Surgicel® and TachoSil® were activated within 1.5-2 minutes, which required prolonged contact with the tissue. Biatravm® showed an effect within one minute. BloodSTOP IX achieved a visual hemostasis effect within 20-30 seconds, which allowed for the shortest possible time to stabilize bleeding and proceed to the next stage of the intervention. In the macroscopic analysis of the application zone on the 3rd day, differences in the density of adhesion, tissue color, the presence of maceration and edema were observed. When using Surgicel® and TachoSil® , areas with local detachment of the edges and areas of cloudy infiltrate were recorded. In the series with Biatravm® , signs of initial retraction of the capsule were noted. BloodSTOP IX maintained visual integrity of adhesion, with minimal signs of marginal hyperemia and without maceration.

Microscopically, on the 3rd day, the stage of acute inflammatory response was recorded. In the areas of application of traditional agents, massive edema, coagulation necrosis, biliary extravasation and destruction of the bile duct epithelium were observed. In Biatravm® preparations, signs of activation of the connective tissue component and bile stasis were determined. When using BloodSTOP IX, the damage zone retained a beam-sinusoidal structure, infiltration was moderate, without signs of bile impregnation and pronounced necrosis.

On day 7, in the series with Surgicel® and TachoSil® , gray-yellow deposits on the liver capsule with signs of adhesions were visually determined. Biatravm® showed the formation of local retractions and a dense subcapsular zone. The use of BloodSTOP IX was accompanied by the preservation of a smooth surface without signs of adhesions, with minimal changes in the color and structure of the wound field.

Histologically, on day 7, in the series with traditional agents, the fibroblastic reaction continued to dominate, characterized by collagen deposition, formation of strands and local disruption of the beam structure. Biatravm® provoked thickening of granulation tissue and perisinusoidal fibrosis. Against the background of BloodSTOP IX, loose organization of granulation tissue, moderate lymphomacrophage infiltration and full capillary vascularization were preserved.

On day 14, the stage of final regeneration was established. Surgicel® and TachoSil® formed areas of coarse fibrosis, zones of capsular thickening, retractions and, in some cases, calcifications. Biatravm® caused a pronounced subcapsular scar, accompanied by surface deformation. BloodSTOP IX ensured the formation of a thin connective tissue layer with preservation of the architectonics and normal vascularization.

No signs of biliary irritation, biliary hyperplasia or macrophage infiltration were detected on day 14 with BloodSTOP IX. The absence of material residues, minimal capsular reaction and preservation of the hepatocyte shape indicated completed morphogenesis with no signs of late aggression.

Comparative morphological analysis revealed patterns: Surgicel® and TachoSil® were associated with limited inflammatory reactions and fibrosis. Biatravm® demonstrated a tendency towards accelerated scarring, accompanied by disruption of the beam structure. BloodSTOP IX ensured mild morphogenesis, with gradual formation of mature but physiological granulation tissue.

Formation of granulation tissue with BloodSTOP IX occurred according to the type of replacement restoration, in which the microcirculatory framework was preserved, no massive necrosis or infiltrative destruction was observed. This created favorable conditions for subsequent tissue remodeling and reduced the likelihood of adhesions.

Intermodel analysis (blunt trauma and incised wound) showed that at all observation periods BloodSTOP IX demonstrated comparable morphological parameters, which allowed us to evaluate its versatility in conditions of injuries with different biomechanics. At the same time, in conditions of blunt trauma, the effectiveness was maintained against the background of venous impregnation, and in case of an incised wound of the liver in the presence of capillary and biliary components. Four groups of features were selected as critical evaluation parameters: the severity of the inflammatory response, the dynamics of granulation tissue, the degree of fibrosis and the presence of a bile component. According to all these criteria, BloodSTOP IX demonstrated the least aggressiveness and the greatest biocompatibility. This allowed us to use its morphological profile as a reference point for the subsequent clinical stage.

Thus, the conducted studies confirmed that a comprehensive assessment, including quantitative, behavioral and morphological, is fundamental when choosing a drug for local hemostasis. The obtained experimental results provided a sufficient evidence base for the transition to clinical and analytical synthesis. The developed and experimentally substantiated model of liver injury allows for a comprehensive assessment, including quantitative, behavioral and morphological, which is fundamental when choosing a drug for local hemostasis. At the same time, based on the conducted studies, it was proven that BloodSTOP IX demonstrated the least aggressiveness and the greatest biocompatibility, thereby

leading to a decrease in the average duration of the hospital stage of complex treatment of liver injuries.

4. Conclusions

1. When modeling blunt liver trauma, it was found that BloodSTOP IX provides the shortest hemostasis time, minimal blood loss, and no need for repeated application, surpassing traditional agents (Surgicel® , TachoSil® , Biatravm®) in these parameters. The data obtained confirm its high hemostatic activity and technical stability under conditions of diffuse venous bleeding.
2. In the model of a cut liver wound, BloodSTOP IX demonstrated the highest degree of initial adhesion, minimal delay in action, and resistance to displacement without the need for compression. This made it possible to achieve rapid hemostasis even on a smooth and poorly structured surface, which makes this drug preferable for linear capillary injuries.
3. Morphological assessment of the application area showed that BloodSTOP IX at all observation periods (3, 7 and 14 days) causes a moderate inflammatory reaction, not accompanied by coagulation necrosis, biliary infiltration or pronounced fibrosis. The drug ensured restoration of the beam-sinusoidal structure and preserved tissue architecture, which indicates its high biocompatibility compared to other agents.

REFERENCES

[1] Bashegurova E.V., Gayfieva L.N., Styazhkina S.N. Problems of treating abdominal trauma in road traffic accidents. // Modern Science. - 2022. - No. 5-2. - P. 30-33.

[2] Vorontsov A.K., Olshevsky A.A., Korsakov A.V. et al. Development of a prognostic model of liver damage // Actual problems of medicine. - 2024. - Vol. 47. - No. 3. - P. 418-434.

[3] Gushcha T.S., Kapustina A.N. Comparative analysis of hemostasis methods in liver injuries // Collection of conf. - Grodno, 2021. - P. 491-492.

[4] Chubaryan K.A., Groshilin V.S., Lukash Yu.V. Possibilities of Improving the Outcomes of Surgical Treatment of Patients with Severe Liver Injuries. // Polytrauma. - 2024. - No. 3. - P. 19-27.

[5] Shapkin Yu.G., Malakhov S.V., Panov E.V. et al. Tamponade in Surgical Treatment of Severe Liver Injuries // Polytrauma. - 2020. - No. 1. - P. 18-22.

[6] Brigode W, Adra A, Capron G, Basu A, Messer T, Starr F, Bokhari F. The American Association for the Surgery of Trauma (AAST) Liver Injury Grade Does Not Equally Predict Interventions in Blunt and Penetrating Trauma. World J Surg. 2022 Sep; 46(9): 2123-2131. doi: 10.1007/s00268-022-06595-w.

[7] Cadili A, Gates J. The Role of Angioembolization in Hepatic Trauma. Am Surg. 2021 Nov; 87(11): 1793-1801. doi: 10.1177/0003134820973729.

[8] Petrowsky H., Raeder S., Zuercher L. et al. Operative management of complex liver trauma: current status and a critical review // Frontiers in Surgery. – 2022. – Vol. 9. – Article 824410.

[9] Svarich VG, Svarich VA. Gemostaz pri tsentral'nom razryve pecheni u rebenka [Hemostasis for central rupture of liver in a child]. Khirurgiia (Moscow). 2023; (2): 115-119. Russian. doi: 10.17116/hirurgia2023021115.

[10] Thomas MN, Whaba R, Datta RR, Bunck AC, Stippel DL, Bruns CJ. Management und Versorgung von Leberverletzungen nach stumpfem Bauchtrauma [Management and treatment of liver injuries after blunt abdominal trauma]. Chirurgie (Heidelb). 2023 Aug; 94(8): 669-674. German. doi:10.1007/s00104-023-01858-1.

[11] Zhang C., Fu D., Wang F. et al. A randomized controlled trial to compare the efficacy of regenerated and non-regenerated oxidized cellulose gauze for the secondary treatment of local bleeding in patients undergoing hepatic resection. Annals of Surgical Treatment and Research. – 2021. – Vol. 100, No. 4. – P. 202–208.