THE EXPERIMENTAL EVALUATION OF THE EFFECTIVENESS OF HAEMOSTATIC DRUGS FOR ENDOSCOPIC HAEMOSTASIS OF GASTROINTESTINAL BLEEDING

ABSTRACT

BACKGROUND

This article highlights the problems of bleeding from the upper gastrointestinal tract, which appear with a frequency of 100 - 120 cases per 100,000 population. Overall mortality is 10-14%, postoperative - from 12 to 35% and has no tendency to decrease. The article discusses the results of haemostatic effectiveness of drugs used for the injection method of endoscopic haemostasis, which were conducted on laboratory rats, based on the Clinical Experimental Laboratory (CEL) and the B. Atchabarov’s Institute at S.D. Asfendiyarov KazNMU.

METHODS

In the experiment were used methods such as simulation of bleeding from the gastric mucosa; a comparative analysis of the haemostasis effectiveness of 3 drugs (aminocaproic acid, Dicynonum, Tramin) used for local administration in the endoscopic haemostasis. Laboratory blood tests to study the effect of these drugs on thrombogenic and fibrinogenic activity of blood. The study was conducted on 37 white laboratory rats and were conducted two series of experiments in each series animals were divided into 3 groups, depending on the used type of haemostatic medication.

RESULTS

Comparative analysis of haemostatic effect in the experiment demonstrated high effectiveness of Tramin as by time of haemostasis, 3-4 minutes, as well as by quality of formed thrombus. Laboratory studies demonstrated that the introduction of Tramin saves platelet levels within the normal range as well as reduces bleeding time in 1.3 times compared to aminocaproic acid and 1.4 compared to Dicynonum.

CONCLUSION

The obtained results allow to recommend the Tramin for injection endoscopic haemostasis of gastrointestinal bleeding.

KEYWORDS

Gastrointestinal Hemorrhage, Tranexamic Acid, Endoscopic Hemostasis

INTRODUCTION

One of the current problems of modern clinical medicine is bleeding from the upper gastrointestinal tract, which appear with a frequency of 100 - 120 cases per 100,000 population [1, 2]. Overall mortality is 10-14%, postoperative - from 12 to 35% and has a tendency to decrease [3].

Introduction into clinical practice of the widely-channel endoscopes and modern video information systems opened a new stage in the diagnosis and treatment of acute gastrointestinal bleeding. New technologies in endoscopic surgery, provide primarily, a good review, allow productively reveal a source of bleeding and conduct adequate primary haemostasis [3, 4].

The most widely used methods of injection endoscopic haemostasis in which to submucosal space next to the source of bleeding in defect of the gastric mucosa or duodenal ulcer by means of an injector, conducted through the channel of an endoscope, are introduced various haemostatic solutions; Hydrogen peroxide [5], Epinephrine [6], Aethoxysklerol [7].

The disadvantages of these methods include the duration of haemostasis, the necessity to introduce a large number of haemostatic solutions, necrosis development at the injection site of an organ’s paries, with the formation of an acute erosions and ulcers. In this regard, increases risk of occurrence of serious complications of bleedings and perforation, frequently occurring even with conventional therapeutic doses of [8 -11, 18, 20].

The imperfection of the known methods of endoscopic haemostasis, due to technical limitations of separate ones dictate the necessity to improve the known methods of haemostasis, the search for new effective
ways and means, differentiation of indications for their use.

The work represents experimental studies on 37 laboratory rats, performed on the basis of clinical experimental laboratory (CEL) and scientific clinical diagnostic laboratory (SCDL) of B. Atchabarov’s Institute at S.D. Asfendiyarov KazNMU.

**The main objective of the research** – to undertake a comparative evaluation of haemostatic effectiveness of drugs used for the injection method of endoscopic haemostasis.

To solve the above object, the authors set three tasks:

1) Simulation of bleeding from the gastric mucosa,

2) Conduct a comparative analysis of the haemostasis effectiveness of 3 drugs (aminocaproic acid, Dicynonum, Tramin) used for local administration in the endoscopic haemostasis and

3) Laboratory blood tests to study the effect of these drugs on thrombogenic and fibrinogenic activity of blood;

Of listed drugs, scientific and practical interest represents Tramin (the drug of tranexamic acid) is a synthetic derivative of the amino acid lysine. The effect of the drug is associated with its ability to reversibly block the lysine-binding sites in molecule of plasminogen, thereby preventing interaction of plasmin, plasminogen with lysine sites in the fibrin polymer [12-14, 17, 19].

In practical healthcare Tramin is widely known as an effective haemostatic drug and is assigned to the intravenous and intramuscular injections [10, 13, 14]. For endoscopic injection haemostasis, the drug is not previously used. In this connection, the given work is foreground and claims to the invention [14-17].

**METHODS**

**Tasks:**

1) Simulation of bleeding from the gastric mucosa on animals;

2) Undertake a comparative analysis of haemostatic effects of the drugs (aminocaproic acid, Dicynonum, Tramin) after their local administration around the source of bleeding (gastric mucosa);

3) Conduct laboratory studies of blood - to study the influence of drugs (aminocaproic acid, Dicynonum, Tramin) on thrombogenic and fibrinogenic activity;

Experimental studies were carried out on laboratory rats, based on the Clinical Experimental Laboratory (CEL) and the B. Atchabarov’s Institute at S.D. Asfendiyarov KazNMU.

While conducting experiments we followed to the “Guidelines for Ethical Conduct in the Care and Use of Non-human Animals in Research” (or also called “Animal testing regulations”) [9, 15]. The operations were performed under ether mask anaesthesia with premedication of Calypsol, entered intrapleural, at the rate of 10 mg / kg. Laparotomy access along the median line. The experiments were performed in the operating of CEL compliance with the rules of aseptic and antiseptics.

 Conducted 2 series of experiments, in each series animals were divided into 3 groups, depending on the used type of haemostatic medication (Table. 1).

**RESULTS**

In the first series of experiments, included 18 animals in which were simulated a bleeding from gastric mucosa: Upper midline laparotomy (Fig.1). In the wound was outputted and autopsied a stomach. After the evacuation of the gastric contents, were producing scarification of the mucous membrane, thereby causing bleeding (Fig.2). Haemostatic drug was administered to the animal after the beginning of bleeding, and was estimated duration, the massiveness and time of haemostasis of bleeding.

In applying of aminocaproic acid average duration of bleeding was 5-6 min.

When using Dicynonum the average duration of bleeding was 7-9 minutes, the average length of bleeding in using Tramin 3-4 minutes.

Thus, according to the results of study the highest haemostatic efficiency demonstrated Tramin as by time of haemostasis, 3-4 minutes, as well as by quality of formed thrombus (formed, tightly fixed) (Fig. 3)
Table 1. The distribution of animals per group

<table>
<thead>
<tr>
<th>Groups</th>
<th>Haemostatic preparations</th>
<th>Series I</th>
<th>Series II</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Aminocaproic acid</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>II</td>
<td>Dicynonum</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>III</td>
<td>Tramin</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Total:</td>
<td></td>
<td>18</td>
<td>9</td>
</tr>
</tbody>
</table>
In a second series of experiments, in animals were performed laboratory tests of blood with the purpose of comparative analysis on blood parameters, including haemoglobin, erythrocytes, platelets, coagulation time by Sukharev.

For intravenous administration of the drug and the subsequent blood sampling, all animals was performed venesection with the catheterisation of femoral vein (Fig. 4).

For blood sampling was used Vacutainers that collect blood in a predetermined amount and to ensure its tightness (Fig. 5). The fence was conducted every 5, 10, 15 min.

Laboratory studies were carried out in the scientific clinical diagnostic laboratory of B. Atchabaroy’s Institute at S.D. Asfendiyarov KazNMU. To determine the blood test was used hematologic analyser sysmexxs -1000i, which gives the results of the analysis of blood samples by 24 parameters, including haemostatic parameters.

**DISCUSSION AND CONCLUSION**

The results of the conducted laboratory researches lead to the following conclusions; (Fig. 6).

1) Application of compared haemostatic preparations are not adversely affect the basic indicators of the blood (Erythrocytes, haemoglobin, Haematocrit etc.).

2) Intravenous injection of Tramin saves platelet levels within the normal range.

3) Coagulation time and bleeding are reduced in 1.3 times when administered Tramin compared to aminocaproic acid and 1.4 compared to Dicynonum.

**Conclusions:**

1) The comparative analysis of the haemostatic effect
in the experiment has shown high efficiency Tramin as by time of haemostasis, 3-4 minutes, as well as by quality of formed thrombus;

2) Laboratory studies demonstrated that the introduction of Tramin saves platelet levels within the normal range as well as reduces bleeding time in 1.3 times compared to aminocaproic acid and 1.4 compared to Dicynonum.

3) The obtained results allow to recommend the Tramin for injection endoscopic haemostasis of gastrointestinal bleeding.

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