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MUSHENKO V.Ye., KOZLOVA T.V., VOSKRESENSKAYA N.M.
SI "The V.T. Zaitsev Institute of General and Emergency Surgery under NAMS of Ukraine", city of Kharkov

EVALUATION OF GECOTON EFFICACY IN PATIENTS WITH INTRAOPERATIVE BLOOD LOSS

Abstract. *Correction of intraoperative blood loss remains up till now to be one of the pressing challenges due to its concomitant coagulative and metabolic disorders, largely complicating the outcomes of surgical interventions in the abdominal cavity organs. Correction of intraoperative blood loss is performed with the aid of different infusion solutions, ambiguously impacting on both the hemodynamic parameters and the blood coagulative potential, and also on metabolic shifts in consequence of hypoperfusion. The paper reviews the results of studies dedicated to the use of a new infusion drug, combining the properties of hydroxyethyl starches with molecular weight of 130 κD, with the properties of hyperosmolar crystalloid solutions.*
Key words: *intraoperative blood loss, colloids, crystalloids, hemodynamics, lactate.*

Introduction

Replacement of the blood loss still remains to be an immediate problem, despite a great many of infusion solutions available to anesthesiologist – from crystalloid to different-class colloid ones. As a result of numerous investigations into the use of various variants of infusion therapy [1–6, 8] most of investigators came to a conclusion as to the necessity of using colloids to correct hypovolemia because of the blood loss, while the ratio colloids/crystals fluctuates from 1 : 1 to 1 : 3. Discussing the issue of the efficacy and safety of using hydroxyethyl starches (HES) of different classes ended by the adoption of agreement [7] on the safety of HES with molecular weight below 200 kD. Reduction of HES molecular weight to 130 kD makes it possible to increase a dose of colloid to 15–20ml/kg/day. Since in the majority of situations, even a daily admissible dose of colloid solutions is not enough to correct intraoperative blood loss, crystalloid solutions, hypertonic ones inclusive, are used. The use of hypertonic crystalloid solutions per se is nowadays considered not the most effective because of a number of negative factors, accompanying their use: fast (within half an hour) redistribution along the water sectors, diuresis stimulation, water-electrolyte disbalance. There exist combinations of colloid and crystalloid solutions allowing for the increase of the circulating blood volume (CBV), to be maintained increased for several hours. HyperHAES [12] may be taken as an example. However, the colloid base of this solution is HES with high molecular weight (200 kD), which was not today included in the schemes, recommended for using in critical states due to considerable negative effects [9–11]. Further searches for plasma-substitutive drugs resulted in the development of Gecoton solution.

Gecoton is a multicomponent, balanced in its electrolytic composition solution, whose colloid component is presented by 5% HES solution with molecular weight of 130 kD and molecular replacement degree 0.4; hyperosmolarity of the solutions is ensured on account of lactate and sodium chloride and 5% xylitol. Concentration of Na^+ in the solution is 270.7 mmol/l.

An objective of our research was: to study the efficacy of pharmaceutical product Gecoton, used to stabilize hemodynamics in the intraoperative blood loss; to investigate into the dynamics of lactate concentration in intraoperative blood loss in patients, having hypervolemia.

Materials and methods

The study was carried out on the base of Anesthesiology Depatrtment at SI "The V.T Zaitsev Institute of General and Emergency Surgery under the National Academy of Medical Sciences of Ukraine". The study included 16 patients. Criteria of inclusion were:

1. Presumed intraoperative blood loss at least 400ml.
2. Absence of concomitant cardiac pathology.

3. Absence of prouounced baseline disorders of caugulation system.

Before surgery, all patients were given the all-round clinical and biochemical examination. Patients' age was 48 ± 5 years.

All surgical interventions were made to patients on a regular basis. When admitting to the operating room all patients were provided with a permanent intravenous route via peripheral venous catheter; catherization of the central veins was performed after patients' introduction to generall anesthesia. To study hydroynamics, the central vein was catheterzed with a three-lumen catheter Certofix Trio 7 Fr, and the catherer was installed into peripheral artery. Anasthesa was made with sevoflurane. Monitoring of the blood gases (O_2, CO_2, oxygen consumption) was brought abot with the aid of a multigas sensor of anasthetic machine Felix Visio (France). Invasive monitoring of arterial pressure (AP), central venous pressure (CVP) pulseoxymetry and heart rate (HR) was effectuated by means of cardiomonitor Mediana (Korea). Laboratory control during surgical intervention took place at the beginning of operation, at the beginning of its basic, after its basic step was over and after surgical hemostasis, as well as at the end of operation. Hemodynamic indicators were registered at the very same steps. Cardiac output was determined by calculation, based on mesuring oxygen content in the arterial and mixed venous blood, and oxygen consumption level at the moment of the blood sampling for investigation. The blood lactate was measured to evaluate the degree of volemia and the impact of Gecoton administered therewith, on the level of lactate in dynamics.

Within the aforementioned operative steps, hemoglobin and hematocrit were determined under the standard procedure; elctrolytes – on analyzer (AEC-01 by KwertyMed, Ukraine); blood acid-base condition – on apparatus Easy Blood Gas Medica (USA); blood lactate level – under the rapid test procedure, on apparatus Lactate Scout+ by EKF Diagnostica (Germany); condition of the blood cougulation factors – on coagulometer K-3002 OPTIC (Poland).

Infusion therapy was performed throughout the whole operation, with crystalloid solutions, calculated as 4–6 ml/kg/h. In the development of intraoperative hemorrhage, Gecoton was infused in a dose of 400 ml during 15–20 min, if the blood loss was up to 1000 ml, and 800ml within half an hour, if the blood loss exceeded 1000 ml.

Results and discussion

The character of surgical intervention and the volume of intraoperative blood loss in patients under study are presented in Table 1.

Dynamics of hemodynamic indicators (average data) during surgery in the group of patients under study is presented in Fig. 1.

Taking into account the category of surgical interventions and the blood loss volume, we regard the data obtained in the manner like this. Moderate reduction of AAP, CVP and rise of HR by the beginning of the basic step of operation was conditioned by technical peculiarities of performing surgical interventions, where the volumetric overload is undesirable, and the method of controllable hemodilution to prevent the development of hypovolemia in the expected intraoperative blood loss, is not used. Further reduction of AAP, CVP and rise of HR were conditioned by the blood loss. On the basis of the data on correcting hypovolemia due to intraoperative blood loss with the aid of Gecoton, a conclusion may be made that the study drug appears to be perfectly effective to correct hemodynamic disorders. Among positive moments it is possible to note a slight elevation of CVP, perhaps, due to rapid sodium redistribution along the water sectors. Higher AAP indicators at the end of operation as compared to its beginning are because of sevoflurane (sevorane) vasoplegic effects. The last measurement of hemodynamic indicators was made after discontinuation of sevorane delivery into the respiratory circuit of APV apparatus.

Table 1. Character of surgical intervention and volume of intraoperative blood loss

Character and volume of surgical intervention	Number of patients	Blood loss volume, ml	Surgery duration, h
Hemihepatectomy	5	620,0 ± 75,0	5,2 ± 0,5
Pancreatoduodenal resection	1	720,0	6,5
Resection of 2–3 liver segments	3	450,0 ± 50,0	4,5 ± 0,3
Removal of retroperitoneal space tumor	2	1300,0 и 1100,0	4,5 ± 0,5
Choledochous duct resection	2	450,0 и 750,0	6,5 ± 0,5
Gastric resection	1	550,0	3,5
Rectum + liver segment resection	1	850,0 мл	3,5
Resection of transverse column hepatic angle + 2 liver segments	1	1150,0	4,5

Of interest is the study of lactate level in Gecoton infusion. When studying infusion media of different electrolytic composition and with addition of different anionic residues to create a buffer of the reserve alkalinity [13], it is noted that metabolism of these anionic residues (residues of the acetic, citric, lactic citric and apple acids are used in the infusion media composition) requires supplying the necessary amount of oxygen to the cells. The largest amount of oxygen is particularly required for the lactate metabolism. Just for this reason, the use of the Ringer solution lactate in patients with blood loss and hypotension, who are mentally alert and spontaneously breathing, is not regarded a starting therapy of the blood loss. We studied Gecoton use to correct hypotension as a result of the intraoperative blood loss, when patients are under the effect of neuromuscular relaxants and do not require additional amount of oxygen to oxidize abundant lactate. Furthermore, all patients were provided with oxygen supply (controlled with multi-gas sensor), that exceeded its bodily consumption by minimum 1.5–2 times. Lactate metabolism in these situations depended solely on the activity of hepatic tissue. With regard for the category of patients, the use of lactate-containing solution must be knowingly safe. We investigated into the changes of lactate level in the blood serum in dynamics at the same steps of surgery, where hemodynamic indicators were noted. The results of measurements obtained are presented below (Fig. 2).

While commenting on the mentioned schedule, it should be noted that the increase in lactate level in the blood serum since the beginning of the basic step of operation depends upon a number of factors, conditioned by not only the infusion of lactate-containing solutions.

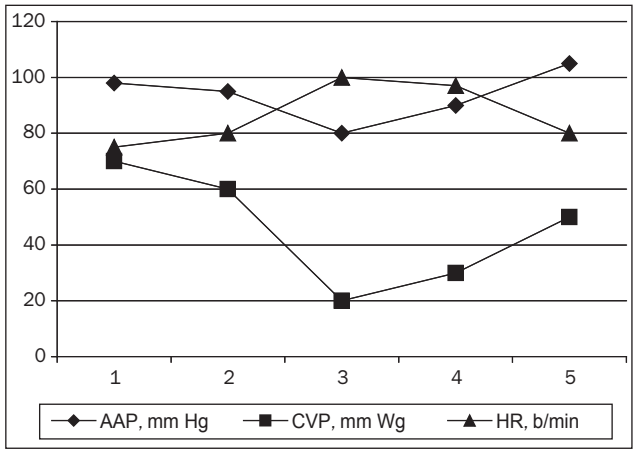

Figure 1. Change of hemodynamic indicators during surgery: here and in Fig. 2:
1 – beginning of operation; 2 – beginning of the basic step of operation; 3 – blood loss and beginning of Gecoton infusion; 4 – end of the basic step of operation; 5 – end of operation
Notes: AAP – average arterial pressure (mm Hg); CVP – central venous pressure (mm Wg); HR – heart rate (b/min)

Before all, it is the intraoperative hypothermia, which cannot be always avoided, the specificities of surgical interventions on the hepatoduodenal area (the study presents average figures of lactate level measurements) and the blood loss. Gecoton infusion made it possible to reduce hypovolemia manifestations and, consequently, to improve the blood flow, this being reflected in the decreased lactate concentration in the blood serum by the end of surgical intervention. Postoperative studies did not take place in view of normalization of the blood pH indicators; none of the study patients revealed any hemodynamic disorders in the postoperative period.

Also, of interest is the study of the dynamics of coagulogram indicators. Out of 16 patients, whose hypovolemia due to intraoperative blood loss was corrected by Gecoton infusion, only 3 did not undergo surgical intervention on the liver. These patients did not reveal changes in the coagulgram indicators, both during surgical intervention and in the early postoperative period. In the rest 13 patients, the decrease in prothrombin level (minimal decrease was seen at the level of 66.6% in patients who underwent hemihepatectomy) was conditioned both by the blood loss and partial hepatic tissue resection.

However, after Gecoton infusion in the control study of coagulogram indicators at the end of surgical intervention, this group of study patients did not reveal any further disorders in the system of coagulation. Dynamics of coagulogram indicators in the study patients (average data) is presented in Table 2.

When analyzing the data presented in Table 2, it may be noted, that despite a considerable blood loss, the decrease in the level of fibrinogen and prothrombin was not way beyond the limits, where the deficit of coagulation factors may be regarded as consumption coagulation, i.e. fibrinogen level reduction was in conformity with its absolute loss. Gecoton use to correct the blood loss also did not lead to the development of consumption coagulation, this confirming the fact that there is no Gecoton negative

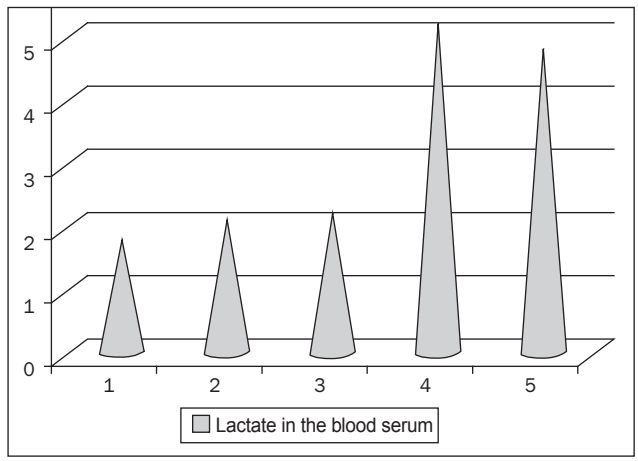

Figure 2. Lactate concentration dynamics in intraoperative blood loss

Table 2. Coagulogram indicators in intraoperative blood loss and its Gecoton-assisted correction

Indicator, study step	Beginning of operation	Beginning of basic step	Blood loss, Gecoton infusion	End of basic step	End of operation
Coagulation time, min	12,3 ± 1,2	13,2 ± 1,8	16,2 ± 2,1	19,4 ± 2,1	17,1 ± 1,5
Prothrombin, %	88,6 ± 2,4	89,3 ± 2,7	73,6 ± 1,8	71,3 ± 1,5	77,3 ± 3,1
Fibrinogen, g/L	4,8 ± 0,3	4,4 ± 0,2	2,7 ± 0,8	2,2 ± 0,7	3,1 ± 0,6

effect on coagulative system. The decrease in prothrombin level by the end of operation was due to the specificities of surgeries, in which this study was carried out. The fact that this category of patients revealed no negative impact of Gecoton infusion on the system of coagulation in the intraoperative blood loss, made for the purpose of its correction, confirms Gecoton safety even for patients with decreased synthetic hepatic function.

Conclusions

The use of Gecoton in order to correct intraoperative blood loss in patients with surgeries on the abdominal cavity organs made it possible to stabilize hemodynamic indicators with no negative effect on the system of hemostasis. Gecoton dose of 400-800 ml, administered intraoperatively, was safe to patient, did not lead to excessive lactate level in the blood serum and did not cause the lesser circulation overload.

On the basis of the study carried out, a conclusion may be made of a sufficiently high efficacy of drug Gecoton in treating intraoperative blood loss and of its safety when used in a dose of up to 800 ml during surgery. With regard for the data obtained, Gecoton may be recommended for correction of intraoperative blood loss in operations on the abdominal cavity organs.

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Мушенко В.Є., Козлова Т.В., Воскресенська Н.М.
ДУ «Інститут загальної та невідкладної хірургії ім. В.Т. Зайцева НАМН України», м. Харків

ОЦІНКА ЕФЕКТИВНОСТІ ЗАСТОСУВАННЯ ГЕКОТОНУ В ПАЦІЄНТІВ З ІНТРАОПЕРАЦІЙНОЮ КРОВОВТРАТОЮ

Резюме. Корекція інтраопераційної крововтрати до сьогодні залишається однією з актуальних проблем у зв'язку з розладами коагуляційного та метаболічного стану, що супроводжують крововтрату. Ці розлади значно погіршують результати оперативних втручань на органах черевної порожнини. Корекція інтраопераційної крововтрати виконується за допомогою різноманітних інфузійних середовищ, що неоднозначно впливають як на показники гемодинаміки, так і на коагуляційний стан крові та метаболічні розлади внаслідок гіпоперфузії. У даній статті розглядаються результати досліджень, присвячених проблемі використання нового інфузійного препарату, що поєднує в собі властивості як гідроксіетилкрохмалів із молекулярною масою 130 кД, так і гіперосмолярних кристалоїдних розчинів.

Ключові слова: інтраопераційна крововтрата, колоїди, кристалоїди, гемодинаміка, лактат.

Mushenko V.Ye., Kozlova T.V., Voskresenskaia N.M.
State Institution «Institute of General and Emergency Surgery named after V.H. Zaitsev of National Academy of Medical Sciences of Ukraine», Kharkiv, Ukraine

EVALUATING THE EFFECTIVENESS OF GECOTON IN PATIENTS WITH INTRAOPERATIVE BLOOD LOSS

Summary. Correction of intraoperative blood loss still remains one of the pressing problems due to concomitant coagulative and metabolic disorders, greatly complicating the outcome of surgical interventions on the abdominal organs. Correction of intraoperative blood loss is carried out using various infusion media ambiguously affecting both the hemodynamic parameters, and the coagulative potential of blood and metabolic changes due to hypoperfusion. This paper considers the results of studies on the problem of using new infusion solution that combines the properties of hydroxyethylstarch with a molecular mass of 130 kDa and properties of hyperosmolar crystalloid solutions.

Key words: intraoperative blood loss, colloids, crystalloids, hemodynamics, lactate.