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**Application of tranexamic acid in operations with cardiopulmonary bypass.**

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The article describes the experience of the use of tranexamic acid during surgery with cardiopulmonary bypass. Proved the efficacy and safety of its use in clinical practice, the effect on the hemostatic system and the need for perioperative blood transfusion.

**Key words:** tranexamic acid, blood loss, cardiopulmonary bypass, blood transfusion.

**Background.** Excessive bleeding and inflammatory response (IR) after cardiopulmonary bypass (CPB) are common complications of cardiac surgery [1]. Although tranexamic acid (TA), a lysine analog competitive inhibitor of plasmin and plasminogen, is effective in reducing bleeding after cardiac surgery, its anti-inflammatory effect in fibrinolysis blockade has been less studied. According to foreign authors, the use of TA to prevent intra- and postoperative bleeding, showed its effectiveness. This is reflected in a reduction of perioperative blood loss and, as a consequence, the frequency of complications and death, as well as a decrease in blood transfusions [1, 2, 3]. TA reversibly blocks lysine binding sites on plasminogen molecule and thereby prevents its conversion into plasmin. As a consequence, fibrin is not destroyed and the strength of a blood clot increases. However, it still remains unknown, and the optimal safe dose, as well as the method of use (before surgery, start during CPB).

**Purpose of the study.** Study the effect of TA on the dynamics of intra- and postoperative blood loss. Evaluate the efficacy and safety of its use.

**Materials and methods.** From July to December 2014 were analyzed 44 case histories of patients who underwent various surgical procedures using CPB. This group consisted of patients with valvular heart disease (mitral and aortic), combined with ischemic heart disease (IHD) and the defeat of the valve apparatus, aneurysm of the ascending thoracic aorta.

Exclusion criteria: left ventricular aneurysm, glomerular filtration rate of 50 mL / min or less, repeated cardiac surgery, acute coronary syndrome, hepatic dysfunction (alanine aminotransferase less than 40 U/l, aspartate aminotransferase less than40 U/l), preoperative coagulopathy, baseline hemoglobin less than 100 g / l.

Was selected 30 case that satisfy these criteria. Patients were divided into 2 groups: Group 1 - patients who intraoperatively and postoperatively used TA; Group 2 - patients which anesthetic management was conducted according to standard procedures.

All operations were performed under combined anesthesia with sevoflurane and propofol (when CPB was connected ). Mechanical ventilation was performed in the mode normoventilyatsii under the control of arterial pCO2. Fentanyl was used for analgesia - 5 mg / kg for induction and 3-5 mg / kg / hr to maintain anesthesia stage. To achieve miorelaxation used rocuronium bromide: 0.6 mg / kg for intubation of the trachea followed by administering a dose of 1 mg / kg after the administration of heparin. The dose was 300 IU heparin / kg. Intraoperative monitoring – invasive arterial blood pressure, CVP, electrocardiography registration with ST-analysis, pulseoximetry. Laboratory control: hemoglobin, hematocrit, erythrocytes, leucocytes, platelets, total protein, glucose, creatinine, urea, electrolyte, acid-base status and the blood gas, blood coagulation with the determination of activated partial thromboplastin time (APTT).

**Results and discussion.** All patients were performed various surgical interventions with CPB. General characteristics of the patients included in the study are presented in Table 1**.**

**Table 1**

**Clinical data of the study groups.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Group 1, n=15,  M±SD | Group 2, n=15,  M±SD | p |
| Age, years | 62±5,7 | 61,8±5,2 | 0,92 |
| Diabetes mellitus | 3(20%) | 3(20%) |  |
| Operation time, min | 311±62 | 278±41 | 0,097 |
| Duration of CPB, min | 188,5±25,5 | 173,6±20 | 0,086 |
| Duration of aortic clamp, min | 124,3±12 | 121,3±14 | 0,53 |
| Glomerular filtration rate, ml/min | 79,3±12,1 | 80,5±10,6 | 0,77 |
| EUROSCORE, % | 2,94±1,05 | 2,50±1,44 | 0,34 |

All the patients of the first group prior to surgery was introduced TA 10 mg / kg intravenously. Subsequently, the TA was administered continuously at a dose of 1 mg / kg / hr for 10-12 hours, but not more than 2 grams / day of total dosage. Volemic support in both groups was carried out using crystalloid (0.9% sodium chloride solution and Ringer's solution). Gelofusin used as a base for filling CPB and intravenously. CPB performed during in moderate hypothermia (29-32 ° C nasopharyngeal temperature) and perfusion rate of 2.2 - 2.4 l / min / m². After the main phase of the operation the patient is warmed to a temperature of 37 ° C and after hemodynamic stabilization unit CPB disconnected. Heparin was neutralized with protamine sulfate (1.5 mg of protamine per 100 units of heparin). After the introduction of protamine sulfate, check the aPTT.

Intraoperative fluid balance did not differ significantly between patients groups 1 and 2 (2578 ± 560 ml and 2663 ± 947 ml, respectively). Intraoperative blood loss was significantly lower in the patients in group 1 (731 ± 69 ml and 853 ± 78ml respectively). Significantly lower amount of exudate appeared during the first 4 hours (151 ± 32 ml and 260 ± 55 ml), 12 hours (210 ± 37 ml and 343 ± 74 ml), 24 hours (270 ± 51 ml and 459 ml ± 112 ) and the total amount of time spent fluid drains (404 ± 74 ± 791 ml and 155 ml). Hematological data of patients is presented in Table 3.

The above data is possible to reduce the need for blood transfusion in patients using TA (442 ± 178 ml and 653 ± 179 ml of packed red blood cells, respectively). In both groups, the abolition as antiplatelet agents and anticoagulants occurs more than 10 days prior to surgery.

Duration of hospital stay after surgery was significantly lower in patients of the first group: 8,6 ± 1,6 days and 10,3 ± 2,1 days.

The data obtained are presented in Table 2.

**Table 2.**

**Clinical study results.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Group 1, n=15,  M±SD | Group 2, n=15,  M±SD | p |
| Intraoperative fluid balance, ml | 2578±560 | 2663±947 | 0,76 |
| Intraoperative blood loss, ml | 731±69 | 853±78 | 0,0001 |
| Amount of exudate for 4 hours after surgery, ml | 151±32 | 260±55 | <0,05 |
| Amount of exudate for 12 hours after surgery, ml | 210±37 | 343±74 | <0,05 |
| Amount of exudate for 24 hours after surgery, ml | 270±51 | 459±112 | <0,05 |
| The total amount of exudates, ml | 404±74 | 791±155 | <0,05 |

**Table 3.**

**Perioperative haemotologic data**

|  |  |  |  |
| --- | --- | --- | --- |
| Показатель | Group 1, n=15,  M±SD | Group 2, n=15,  M±SD | p |
| Hemoglobin, the beginning of the operation, g/l | 120±10 | 123,6±9 | 0,3 |
| Hemoglobin, the end of the operation, g / l | 104±10,8 | 96±10,3 | 0,04 |
| Hemoglobin, 12 hours after surgery, g / l | 114±13,1 | 102,5±9,2 | 0,009 |
| Hemoglobin, 24 hours after surgery, g / l | 110,1±7,8 | 101,9±9,2 | 0,01 |
| Hemoglobin, 48 hours after surgery, g / l | 108,7±7,4 | 99,8±9,4 | 0,007 |
| Platelet count, the beginning of the operation\*10^9/l | 228±24 | 225,6±23.1 | 0,78 |
| Platelet count, the end of the operation\*10^9/l | 165±34,3 | 123,6±26,6 | 0,0009 |
| Platelet count 12 hours after surgery \*10^9/l | 199±40,4 | 145,6±20.8 | 0,0001 |
| Platelet count 24 hours after surgery \*10^9/l | 177±24,4 | 153,7±23 | 0,01 |
| Platelet count 48 hours after surgery \*10^9/l | 176±22,4 | 149±22,2 | 0,02 |
| Blood transfusions, ml | 441±178 | 653,8±178 | 0,002 |
| APTT, the end of the operation, sec | 29,2±3,1 | 29,1±2,7 | 1 |

Hemoglobin levels in patients in group 1 was significantly higher in all stages of research since the end of the main phase of the operation. As can be seen from Table 3, patients in group 1 had greater platelet count as in step closure operation, and in the first 48 hours after surgery. This effect of TA is theoretically possible, since blocking plasmin and plasminogen molecule not degraded fibrin and thus fibrin degradation products do not inhibit platelet function. Therefore, in addition to the use of TA antifibrinolytic action, and we have obtained protection effect platelets.

Hyperfibrinolysis process due to an increased release of tissue plasminogen activator from the vascular endothelium. This process begins by cutting the skin and is aggravated with further surgical procedures. Therefore, the appointment of TA after induction of anesthesia and before surgery to intervention seems to be the most optimal.

The most common complication of the use of TA in postoperative period - generalized seizures. However, according to the foreign authors, the risk of seizures increased using TA in a total dose of more than 100 mg / kg [4, 5]. According to others, when compared to 2 methods of use of tranexamic acid (a "high" dose - bolus injection of 30 mg / kg after induction of anesthesia and the same dose was added to the CPB and a "low" dose - 15 mg / kg after systemic heparinisation and 1 mg /kg/h infusion before the extended end of the operation). The authors found no benefits for patients "high" dose, which was reflected in the absence of a difference in blood loss and transfusion requirements between groups [2].

The maximum daily dose of TA in patients of group 1 was 2 grams, which should not exceed 25 mg / kg.

**Conclusions.**

1. The use of TA effectively and safely during cardiac surgery with CPB.

2. The use of TA in the studied regime has allowed us to reduce both total blood loss and need for transfusion of packed red cells in the perioperative period.

3. TA showed a positive effect on the hemostatic system, but primarily the focus should be on quality surgical hemostasis.

**References.**

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