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# PREVENTION OF VENOUS THROMBOEMBOLIC COMPLICATIONS AFTER TRAUMATOLOGICAL AND NEUROSURGICAL HIGH – TECH OPERATIONS.

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**Abstract:**Venous thromboembolic complications include deep vein thrombosis of the legs, pulmonary embolism, and asymptomatic thromboembolic complications. They are extremely life-threatening after traumatic and neurosurgical operations, including total hip arthroplasty and knee arthroplasty. According to most authors, a sharp increase in venous thromboembolic complications from 4.5% to 40-60% was observed within 35-40 days after these mini-technological operations without prophylaxis. (Phlebology 2015 2-52).

**Relevance of the problem:**
Since 1984, anticoagulant therapy methods have been used for preventive purposes when venous troboembolic complications are observed in traumatological and neurosurgical high-tech operations, as they are extremely dangerous for life. According to worldwide statistics, 2.5 million people undergo endoprosthetic surgery of the large joints of the legs per year. For example: in Germany, in 2018, 548,886 hip and knee joint replacement operations were performed, while in the United States, it is expected that by 2030, about 4 million upper joint replacement operations will be performed. Most developed countries are seeing an increase in the number of endoprosthetic surgeries, which is due to the increase in human life expectancy, the general aging of the population, and the increase in the number of people suffering from obesity. Factors such as reducing the volume of surgical trauma, shortening the duration of the operation, shortening the time of hospitalization of patients, getting patients up early can reduce the risk of developing venous thromboembolic complications, but at the same time, large hematomas can be observed when anticoagulants are used in the operative fields in major traumatological and neurosurgical operations. and superficial and deep periprosthesis leads to the development of infectious processes.

**The main goal of the topic:**
Based on the information on the use of direct-acting oral anticoagulant drugs, the use of modern anticoagulant drugs that do not affect the blood coagulation system in the prevention of venous thromboembolic complications in high-tech traumatological and neurosurgical operations

**Materials and methods:**
In 2018-2021, 66 patients with femoral neck fractures were treated at the Khorezm branch of the Republican Research Centre of emergency medicine. Among them, 38 (57.5%) had femoral neck fractures, 28 (42.4%) had subcapital fractures. The age of patients ranges from 28 to 90 years, with an average of 60 years. Women make up 33 (50%), men make up 33 (50%).
According to contemporary foreign and domestic literature, different durations of thromboprophylaxis are recommended after endoprosthesis of hip and knee joints and spine operations.

**Comparative characteristics of thromboprophylaxis after total hip and knee arthroplasty in Russian and international manuals**

| Manuals, year | Recommended preparations | Duration |
|---|---|---|

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| | | Knee joint | Hip joint |
|---|---|---|---|
| Russian Association of Traumatologists and Orthopedists ,2016 | Low molecular weight heparin, dabigatran, rivaroxaban, unfractionated heparin, acetylsalicylic acid | 5-6 weeks | |
| Russian Association of Cardiologists, Cardiovascular and Phlebologists, 2015 | Low molecular weight heparin, dabigatran, rivaroxaban, apixaban, unfractionated heparin | | |
| American College of Chest Physicians (ACCP) 2012 | Low molecular weight heparin, dabigatran, rivaroxaban, apixaban, unfractionated heparin, anti vitamin K anticoagulants , acetylsalicylic acid - in cases where it is impossible to use other anticoagulants | 10-14 days (with extension up to 35 days) | |
| American Academy Orthopaedic Surgeons ( AAOS) 28 /08-2017 | Without a specific drug recommendation | Individual duration | |
| National Institute for Health and Care Excellence ( NISE ) 2015 | Low molecular weight heparin, dabigatran, rivaroxaban, unfractionated heparin | 10-14 days | 28-35 days |
| The Scottish Intercollegiate GuidelinesNetwork (SIGN ) 2010. | Unfractionated heparin, dabigatran, rivaroxaban, ASA-not used as monotherapy. | Duration is not specified | |

The above periods of using anticoagulants are associated with changes in the coagulation system of the blood, which are preserved for several weeks after traumatic operations, that is, a decrease in the fibrinolytic activity of the blood, a decrease in the amount of natural anticoagulants, that is, AT-3, and activation of coagulation.

Venous thromboembolic complications are observed more in the ambulatory stage after discharge of patients from the hospital due to the shortened hospital stay. Therefore, it is necessary to carry out pharmacological thromboprophylaxis in ambulatory conditions along with anticoagulant drugs and constant elastic compression of leg veins.

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Unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), vitamin K antagonists are among the drugs used in the prevention of venous thromboembolic complications in traumatology. Although they have been used for more than 30 years, they are not without a number of disadvantages, that is, because UFH and LMWH are used parenterally, financial and injection for ambulatory conditions requires a lot of cocktail.

**UFH** has an indirect mechanism of action - heparin molecules combine with its cofactor (antithrombin-3) through the pentasaccharide active center, and antithrombin turns from a slow-acting thrombin inhibitor into several activated fast-acting inhibitors of the coagulation system. UFH - disadvantages: use several times a day, some complications - thrombocytopenia, osteoporosis, bleeding can be observed.

**LMWH** - has a direct anti-XA effect, inhibits a small amount of direct thrombin, due to the long half-life of LMWH - its use is reduced to 1 time per day. It is used parenterally.

**Vitamin K antagonists (warfarin and phenylin)** – anticoagulant effect is aimed at reducing blood clotting factors, which depend on the production of Vitamin K. Used orally, it has a low therapeutic effect and requires constant monitoring of the level of coagulation (INR).

**ASA** is used orally as an antiaggregant, it is convenient for ambulatory patients, it is used cheaper than anticoagulants, in many manuals there are some restrictions on the order and amount of administration. There are objections to the use of ASA in traumatological operations.

**NOAC (new oral anticoagulants) - POAC (primary oral anticoagulants)** - these drugs include dabigatran etexilate, rivaroxaban-xarelto, apixaban, racxabans, which are used to prevent thromboembolic complications after traumatological and neurosurgical operations.

**Dabigatran etexilate** - as a direct inhibitor of thrombin - is considered the first oral anticoagulant with a direct effect registered for the prevention of thrombosis of the deep veins of the legs, thromboembolism of the superficial artery after traumatic operations. By inhibiting free and bound thrombin contained in thrombi, it stops the conversion of fibrinogen to fibrin. The antithrombotic effect develops quickly and is observed within 2-3 hours after taking the drug.

**Rivaraxaban - Xarelto** - this drug is considered to be a direct, highly selective inhibitor of factor Xa, one of the main enzymes of the coagulation cascade, at the main key point of thrombus formation. It has a very rapid onset of action, quickly appears in the tissues of the body when used orally, and has strong pharmacokinetics.

Even though the above-mentioned drugs belong to the same group, they are characterized by a number of pharmacokinetic properties and may affect their clinical effectiveness and safety.

**Pharmacokinetic characteristics of the use of anticoagulants belonging to the POAC group in the period after traumatological and neurosurgical operations.**

| Whole Molecule | Dabigatran | Rivaroxaban | Roxaban |
|---|---|---|---|
| | II-a | Xa | Xa |
| Dosing order, per day | 110 mg on the day of operation, then 220 mg - 1 time | 10 mg - 1 time | 2,5mg – 2 imes |
| 1st dose after surgery | 1-4 hours after hemostasis is observed | 6 -10 hours | 12-24 hours |

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| | | | |
|---|---|---|---|
| Bioavailability | 6 % | 80-100 % | 50 % |
| Relationship with blood plasma proteins | 35 % | 92-95 % | 87 % |
| Half-life | 12-14 hours | 9-13 hours | 8-15 hours |
| Metabolism | It binds with glucuronic acid through the liver and forms 4 active metabolites in the plasma. | Through the liver - oxidative metabolism through the cytochrome system | Through the liver - oxidative metabolism through the cytochrome system |
| Renal excretion | 80 % | 66% (36% unchanged, 30% inactive metabolite) | 25 % |
| Excretion by other means | - | 28% - through the gastrointestinal tract (18% - as an inactive metabolite, 10% unchanged, | 25% - through the gastrointestinal tract |

New special specific tests have been developed to determine the exact level of activity of POAC drugs in the blood.

**Use of coagulogram indicators to evaluate the anticoagulant effect of POAC drugs:**

| Test | Name of the drug | | |
|---|---|---|---|
| | ACA – acetylsalicylic acid | Roxaban | Rivaroxaban – Xarelto |

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| | | | |
|---|---|---|---|
| Pt-Prothrombin time | Not applicable. | Not applicable. | Increased - may indicate a high risk of bleeding. |
| APTt- Activated partial thromboplastin time | An increase of 2 times the upper limit of the norm | Not applicable. | Not applicable. |
| Tt - thrombin time | The norm is a low level of pharmacologically significant hypocoagulation. | Not applicable. | Not applicable.. |
| Diluted thrombin time | ST: > 200 ng/ml or >65 s | Not applicable. | Not applicable.. |
| MNO- International normalized ratio - coagulation level | Not applicable. | Not applicable. | Not applicable. |
| Ecarin clotting time | ST: 2 times the upper limit of normal | It doesn't change. | Not applicable. |
| Anti-Xa activity | Not applicable.. | Not applicable.. | ST- special test |

**Conclusions:**

Today's current thromboprophylaxis methods lead to an extreme reduction in fatal venous thromboembolic complications. Since the appearance of direct-acting oral anticoagulants, these drugs have been widely used in the prevention of venous thromboembolic complications after traumatological and neurosurgical operations, which have been included in their manuals in many countries of the world.

Among the advantages of POAC are oral administration, long-term administration, no need for constant laboratory monitoring, low interaction with food products and other drugs. On the other hand, POAC drugs, i.e., rivaroxaban - xarelto, have some disadvantages when using them: they have interactions with many drugs, and they require correction in patients with kidney failure due to renal

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excretion. Thus, despite the history of pharmacological thromboprophylaxis in traumatology and neurosurgery, there are many unsolved issues that require serious investigations.

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