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MAIN CHARACTERISTICS OF ORAL ANTICOAGULANT THERAPY IN PATIENTS WITH ISCHEMIC HEART DISEASE

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ABSTRACT

Anticoagulants are drugs that prevent blood clots by acting on plasma coagulation factors. Anticoagulants mainly inhibit the appearance of fibrin filaments and contribute to the cessation of the growth of already formed thrombi, counteracting the effect of thrombin on fibrin. They also enhance the effect of endogenous fibrinolytic enzymes on blood clots.

KEYWORDS: *Clinical Significance, Unfractionated (Standard) Heparin, Anticoagulants, Direct Anticoagulant, a Synthetic Drug.*

INTRODUCTION

Anticoagulants are divided into two groups: a) direct anticoagulants - (i.e., interacting directly with blood coagulation factors), effective in vitro and in vivo; b) indirect anticoagulants (vitamin K antagonists) - long-acting, act only in vivo and after a latent period.

Direct-acting anticoagulants include heparin, which can be unfractionated (UFH) and fractionated (low molecular weight) - (LMWH), as well as selective direct-acting thrombin inhibitors. In addition, fondaparinux sodium is a direct anticoagulant, a synthetic drug that has a similar effect to heparin.

Unfractionated (standard) heparin (heparin sodium) is obtained from the lungs of cattle and the intestinal mucosa of pigs. Heparin binds to antithrombin III (ATIII), causes conformational changes in its molecule, and accelerates the complexing of antithrombin III with serine proteases of the coagulation system; as a result, thrombin, the enzymatic activity of activated factors IX-XII, plasmin and kallikrein are blocked.

The highest bioavailability is observed with intravenous administration. After intravenous administration, the action begins immediately, the half-life (T1 / 2) is 1 hour. With subcutaneous administration, bioavailability is low (10-40%), T1 / 2 is 1-2 hours.

Heparin in plasma is mainly in a protein-bound state, is intensively taken up by endothelial cells and cells of the mononuclear-macrophage system, which is the reason for the variable anticoagulant effect of the drug.

Excretion of heparin occurs through the kidneys in the form of metabolites, and only with the introduction of high doses is it possible to excrete unchanged.

Heparin reduces blood viscosity, reduces vascular permeability stimulated by bradykinin, histamine and other endogenous factors, and thus prevents the development of stasis.

Anticoagulants of indirect action (AND) do not affect the blood outside the body, are effective when taken orally, their action is realized through the proteins of the prothrombin complex, they have a common antagonist - vitamin K. The time of appearance is also common.

When characterizing the mechanism of action of oral anticoagulants, it should be noted that, unlike other drugs that inhibit the formation of fibrin (heparin, defibrinators), AND prevent the formation in the hepatocyte of II, VII, IX and X coagulation factors, causing a hypo-coagulable state.

According to the chemical structure, indirect anticoagulants can be divided into 3 subgroups: monocoumarin derivatives (warfarin, acenocoumarol), dicoumarin (ethyl biscumacetate), and indandione (phenindione).

From a clinical point of view, these drugs differ from each other in terms of their ability to be adsorbed in the gastrointestinal tract, the duration of the half-life, and the frequency of side effects caused.

Warfarin is the drug of choice, providing the most stable anticoagulant effect, in addition, warfarin has the best evidence base in terms of efficacy and safety of use. Acenocoumarol is inferior to warfarin in terms of efficacy and safety. Indandione derivatives have anticoagulant activity similar to coumarins, but often cause side effects (toxic effects on the liver and various skin manifestations). Indandione derivatives can be prescribed to patients who have had allergic reactions to coumarin derivatives or who tolerate long-term use of the drug well.

Atrial fibrillation (AF) is one of the most common cardiac arrhythmias: its frequency in the general population is 1-2%, while the frequency of AF increases with age – up to 15% at the age of 80 years [9, 5]. In the coming years, an even greater increase in the number of patients with AF is predicted due to an increase in life expectancy [9, 5]. According to the results of the Framingham study, the risk of developing AF at the age of 40 years and older is about 25% [5]. This study included all participants in the Framingham Heart Study who did not have AF at the time of indexation, aged 40 years or older. The lifetime risk (up to 95 years of age) of developing AF (plus atrial flutter) was calculated, with death without AF taken as a control outcome [5]. A total of 3999 men and 4726 women were followed up between 1968 and 1999. (176166 patient-years), 936 study participants developed AF, and 2621 participants died without AF. At age 40, the lifetime risk of developing AF was 26.0% (95% confidence interval (CI) 24.0-27.0) for men and 23.0% (21.0-24.0) for women [6].

The clinical significance of AF is due to the fact that its presence is associated with an increase in mortality, the incidence of ischemic stroke and other thromboembolic complications, heart failure and hospitalizations, deterioration in the quality of life, a decrease in exercise tolerance, impaired left ventricular function, and the development of cognitive dysfunction [3]. This

problem also has a large social aspect: the presence of AF leads to high healthcare costs [4]. Thus, 5333 patients with AF from 35 European countries took part in the Euro Heart Survey on AF [8], cost studies were conducted in 5 participating countries with the largest number of patients.

The average costs associated with hospitalization for AF per patient per year were €1507, €3225, €1010, €2315, and €2328 in Greece, Italy, Poland, Spain and the Netherlands, respectively. The main cost components (they accounted for more than 70% of the total annual costs in all five countries) were medical care in a hospital setting and interventional interventions [8]. A dedicated systematic review of the literature on AF costs (1990-2009), which included the results of 37 studies, confirmed the high level of costs associated with AF (up to €7241 in Sweden), with the maximum cost also accounted for hospitalizations - they accounted for about 50-70% of all annual costs [10].

New oral anticoagulants are divided into two classes: oral direct thrombin inhibitors (such as dabigatran) and oral direct factor XA inhibitors (such as rivaroxaban, apixaban, etc.). Unlike vitamin K antagonists, which block the formation of several active vitamin K-dependent coagulation factors (factors II, VII, IX, and X), these drugs block the activity of one coagulation step.

Indications for the prophylactic use of anticoagulants in therapeutic patients have not been studied enough. Prophylactic administration of heparin is recommended in patients with ischemic stroke and in the presence of such risk factors as: myocardial infarction, severe heart and respiratory failure, malignant tumors, etc. UFH is prescribed s / c 5000 IU 2-3 times / day within 1-2 weeks or LMWH for the same period.

In the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), the use of anticoagulants is mandatory. Treatment begins with the appointment of UFH according to the scheme: intravenously - a bolus of 80 U/kg, then an infusion of 18 U/kg/h (but not less than 1250 U/h) for 48 hours, with the selection of a dose that maintains an APTT value of 1, 5–2.5 times higher than the normal value of this indicator for the laboratory of this medical institution. If it is not possible to provide continuous infusion therapy with heparin, it is acceptable to use heparin in the form of s / c injections according to the scheme: intravenously - a bolus of 3000-5000 IU, then s / c 250 IU / kg, then 250 IU / kg 2 r / day with dose selection according to the value of APTT. The duration of heparin therapy should be at least 7 days. With DVT and PE (except for the severe form), it is acceptable to use LMWH instead of UFH in the form of s / c injections.

Anticoagulants of indirect action are prescribed simultaneously with heparin 3–4 days before its withdrawal, starting from the minimum therapeutic doses. So, warfarin is prescribed at an initial dose of 2.5-5 mg / day. Heparin is canceled when the level of INR = 2.0–3.0 is reached, which persists for two consecutive days.

The duration of AED therapy after an episode of DVT and PE depends on the persistence of risk factors and causes of thrombosis and should be from 3 months to lifelong use of the drug.

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