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ANTICOAGULANT TREATMENT OF AF: FOCUS ON THE WARFARIN DOSAGE

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Summary

Authors analyzed the results of some studies of AF and warfarin dosing. Than investigation of 75 patient with AF (permanent type) was performed. According to demographic, anthropometric data and related conditions (diabetes mellitus type 2, myocardial infarction, acute cerebrovascular ischemia, pulmonary embolism, alcohol abuse - drinking more than one ounce of ≥3 weekly) predictive model of warfarin dosing was developed: warfarin dose = 0.097 * BMI - 0.03 * AGE + 0.30 *ASS.Status+ 0.02 *WC+ 1, 88. After testing of final model authors concluded what derived formula was representative, to determine the optimal dose of warfarin given to patient based on demographic characteristics. Considering all of the abovementioned, this model can be recommended for use determining the treatment strategy in patients with AF.

Keywords: anticoagulant treatment, warfarin, atrial fibrillation.

Framingham study is one of the largest sources of understanding the development, prevalence and risk factors of many cardial pathologies. In this analysis the authors evaluated

the incidence, prevalence and risk factors of such pathology as atrial fibrillation (AF) in the period from 1958 to 2007.

The data of 50-year follow-up was analyzed (202417 person-years). That includes 9511 patients which at startpoint of follow-up had no AF. During the period of observation 1544 cases of AF were recorded. In the period from 1958 to 1967 years the AF incidence was 20.4 / 1000 person-years amoung men and 13.7 / 1000 person-years amoung women. In the last decade of analysis (1998-2007 years) prevalence of AF increased 4 times and reached 96.2 / 1000 person-years amoung men and 49.4 / 1000 person-years amoung women.

Also significantly changed the distribution of some risk factors for AF. The authors pointed out the reduce of smoking and alcohol abuse, while the prevalence of obesity and diabetes have increased. At the same time the quality of arterial hypertension treatment had improved, accompanied with decreasing amount of cases with left ventricular hypertrophy or heart failure. The survival rate of patients with diagnosed AF became higher.

It should be noted that the increase of AF prevalence could certainly be the result of better detection of arrhythmia and more frequent use of ECG monitoring. However, counting on significant increase of obesity and diabetes - two important risk factors for AF - likely prevalence of arrhythmias had really increased through these years. High level of AF incidence and prevalence is essential both for individual patients as well as for society. The AF presence among cordial pathologies has significantly affect morbidity and mortality and increases the risk of stroke and heart failure.

Currently guidelines for the use of anticoagulants written by many cardial organizations differ one from another. Thus, according to the recommendations of the European Society of Cardiology (ESC), Asia Pacific Heart Rhythm Society and NICE in case of 1 point for male patient, and female patient - 2 points on a scale CHA2DS2-VASc (it is known, that female gender is a risk factor) anticoagulants therapy is indicated. On the other hand, the recommendations of American College of Cardiology (ACC) / American Heart Association (AHA) / Heart Rhythm Society (HRS) state that patients with one additional risk factor may not need administration of antithrombotic therapy, or oral aspirin or the type of anticoagulant can be used.

Results of a small one-year study showed that in patients who suffer from obesity, the risk of massive bleeding requiring hospitalization compared with patients without obesity was on 84% higher. Moreover, the risk of massive bleeding gradually increases depending on the degree of obesity.

These data indicates that the rate of body mass index (BMI) can be a predictor of bleeding risk in patients under warfarin. According to the researchers, further research should answer questions about the mechanism of increased risk due to obesity and whether this increased risk observed in the application of new oral anticoagulants.

Thus the main our task was to determine the effect of different body mass index on dosage of warfarin in order of rapid achievement of target international normalized ratio (INR) and the maximal reduction of possible complications of anticoagulant therapy. To derive the most significant prognostic factors of influence we analyzed data from 75 patients with different BMI which had permanent form of AF and the native were under warfarin therapy at the time of inclusion. For all patients saturating dose of vitamin K antagonist (5 mg)- warfarin was selected. For the purity of research design and to facilitate dose adjustment for all patients the same manufacturer warfarin dosage of 2.5 mg / tab was recommended. Patients underwent dosage adjustment based on indicators of blood coagulation on 1,3,5,7,14,21 and 30 days of investigation. Further examination of the patients were conducted once a month. Optional additional controls were also conducted outside the schedule of INR control.

We analyzed all available data on the impact of demographic, anthropometric data and related conditions using the method of multiple regression. We have established the most predictive indicators that had a decisive influence on 5th day of treatment of indirect anticoagulant such as warfarin. These indicators revealed gender, height, BMI, waist circumference (WC) and the associated status (diabetes mellitus type 2, myocardial infarction, acute cerebrovascular ischemia, pulmonary embolism, alcohol abuse - drinking more than one ounce of ≥3 weekly). Within these parameters we developed a predictive model that reflects the need to achievement a target INR levels

warfarin dose = 0.23 * SEX - 0.04 * AGE - 0.05 * WEIGHT+0.04 * Height + 0.25 * BMI+ 0,015 * WC + 0.28* ASS.Status -28.55

However, after the removal from the formula less informative indicators we got the final model for predicting of warfarin dose, which is the following –

warfarin dose = 0.097 * BMI - 0.03 * AGE + 0.30 *ASS.Status+ 0.02 *WC+ 1, 88.

This formula was tested due to prescribing of warfarin to 30 patients with AF who were treated at Railway hospital №2 st.Kyiv. In 13 patients AF was combined with concomitant obesity, 9 patients were overweight, the rest had normal BMI. The 18 patients had from 1 to 3 abovelisted associated conditions that were taken into account in the derivation formula. The examination of the patients was conducted within 30 days of the drug

administration with the definition of INR – daily one week, after stabilization of INR rate within the therapeutic window – once a week. INR was inside therapeutic window for all of these patients, only 3 patients mentioned INR 2.0-3.0 go beyond that required small warfarin doses correction. No case of hemorrhagic complications was recorded.

So the derived formula is representative, to determine the optimal dose of warfarin given to patient based on demographic characteristics. Considering all of the abovementioned, this model can be recommended for use determining the treatment strategy in patients with AF.