THE ROLE OF CLINICAL PHARMACIST IN REDUCTION OF RISK DEVELOPING OF CARDIOVASCULAR TOXICITY OF SELECTIVE AND NON-SELECTIVE NSAIDs

Serdyuk I. S., Yevtushko A. S.
Scientific supervisor: Davishnia N. V.
National University of Pharmacy, Kharkiv, Ukraine
inna.knopka96@yandex.ua

Introduction. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most common prescribed medications purchased over the counter for treatment of acute and chronic pain and inflammation associated with a list of medical conditions. Like any drugs, the benefits of NSAIDs should be considered in tandem with the potential adverse effects: dyspepsia, gastric or duodenal ulceration, sodium retention and subsequent arterial hypertension, as well as increased incidence of cardiovascular (CV) adverse events. Unfortunately, all NSAIDs, as selective (COX-2) and non-selectivity (COX-1 and COX-2) have been associated with an increased risk of adverse CV events.

Aim. To conduct a systematic analysis of sources of modern scientific literature about the manifestations of cardiotoxicity of NSAIDs and develop an algorithm of actions for clinical pharmacist to minimize the possibility of CV side effects.

Materials and methods. For realization of research were used methods of systematic analysis of 20 scientific literature sources (articles) about the manifestations of cardiotoxicity of NSAIDs. All articles were published from 2007 to 2017. The criteria for inclusion in the analysis was the availability of data about clinical trials, observation studies, systematic reviews or CV side effects of NSAIDs. The data should be containing information about serious coronary heart diseases (myocardial infarction, any stroke, CV death, composite CV outcomes), as their baseline risk of CV events is increased. For further study, rofecoxib, ibuprofen, naproxen, diclofenac were selected, because they had similar risk assessment criteria. In this group, rofecoxib was classified as a selective COX-2 NSAID, all other drugs were non-selective NSAIDs. An algorithm of actions for clinical pharmacist was based on such sources: EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update and The American College of Cardiology/American Heart Association recommendations.

Results and discussion. According to the results of the analysis, selective and non-selective NSAIDs have a risk of developing of CV outcomes. The connection between the risk of developing of myocardial infarction was significantly described in 55 % of analyzed data for rofecoxib, in 40 % for diclofenac, in 35 % for ibuprofen.

The development of stroke in patients who used NSAIDs was significantly noted in 50 % of analyzed data for rofecoxib, in 40 % for diclofenac, in 25 % for ibuprofen.

A provocation of CV death was significantly marked in 40 % of analyzed data for rofecoxib, in 30 % for diclofenac, in 25 % for ibuprofen. The cardiovascular toxicity of naproxen has not been proven. In different 7 studies negative impact of the CV development was not been found. The most commonly prescribed doses of naproxen were 500-1000 mg/d or greater, and there was no evidence of increased CV risk at these higher doses. The reviews suggested that 5 key variables affect the extent of CV risk associated with NSAIDs: 1) COX-2 selectivity, 2) dose responsivity, 3) plasma half-life, 4) blood pressure and 5) interaction with acetylsalicylic acid (ASA). Available data on platelet effects suggest no reduction in cardioprotection when ASA is used concomitantly with naproxen, diclofenac or celecoxib; however, ibuprofen may interfere with ASA. Based on the obtained data and international recommendations, the algorithm of actions for clinical pharmacist should include such basic principles: 1) It is not recommended the appointment of prescription and non-prescription NSAIDs refineries to patients who have preliminarily CV outcomes. If severe pain syndrome exists, acetaminophen will be the drug of choice for them. 2) If it is necessary to use NSAIDs, they should be administered at the lowest effective doses. 3) To recommend prescribing 500-1000 mg/d doses of naproxen, there was no evidence of increased CV risk for them. 4) Strictly, to consider plasma half-life when NSAIDs are co-administered with other drugs. 5) To inform the doctor about the neediness for constant blood pressure monitoring. 6) To avoid any potential negation of ASA antiplatelet effects, it should be administered a minimum of 30 minutes prior to or 8 hours after ibuprofen or others NSAIDs. 7) According to international guidelines there is additional evidence showing a reduction of CV risk in patients treated with disease-modifying antirheumatic drugs: methotrexate or TNF inhibitors. 8) Total cholesterol and high-density lipoprotein cholesterol should be measured in CV risk assessment. 9) When elaborate the lifestyle recommendations to emphasize the benefits of a healthy diet, regular exercise and smoking cessation. 10) To inform the patients about negative consequences of the disturbance of antihypertensives and statins admission regimens, that will increase the patient's compliance to the therapy.

Conclusions. To summarize briefly, conducted systematic analysis showed that such NSAIDs, as rofecoxib, diclofenac and ibuprofen had significantly increase of cardiotoxicity. It was proved in 55 % to 25 % of data of scientific literature sources. In regular practical activities, as an algorithm of actions, a clinical pharmacist should use the statements of international recommendations and guidelines, which will lead the minimization of side effects and will increase the safety of NSAIDs using.