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NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND RENAL DISEASES

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Abstract

Non-steroidal anti-inflammatory drugs (NSAIDs) have always been used to treat pain, even though studies exist reporting and verifying undesirable effects especially nephrotoxicity and alimentary tract toxicity. The mechanism of action of NSAIDs is based on nonselective inhibition of isoenzymes of cyclooxygenases: Cyclooxygenase-1 (COX-1), Cyclooxygenase-2 (COX-2), and Cyclooxygenase-3 (COX-3). The most common side effects of NSAIDs affect the alimentary tract, renal system, liver, and respiratory system (in the form of various allergies), etc. The purpose of this scientific research paper is: to document and report the side effects of NSAIDs upon the kidneys. Materials and methods: In a cohort study, 60 patients with an average age of 58 years old (± 5.00 years) have been examined. Of the examined patients, 35 patients were females and 25 were males. The average duration of the pathophysiological state was 48 years (± 2.00 years). The study also included the control group of patients [healthy individuals (voluntary blood donors)] compromising 60 individuals, of which 30 were females and 30 were males. The average age of the control group patients was 58 years old (± 5.00 years). During the duration of the study, all of the patients were treated with NSAIDs (with short breaks) and Methotrexate (MTH) with dose of 7.5 – 10 mg (for 10 weeks). During the laboratory examination which were utilized and performed to discover nephrotoxicity, we tested for concentration of erythrocytes (Rbc), haemoglobin (Hb), haematocrit (Htc), urea, creatinine, GFR (by Cockcroft-Gault formula), albuminuria, C-reactive protein (CRP), rheumatic factor (RhF), and urinary enzymes (cystatin-C, βNAG (N-acetyl-B-D-glycosaminidase), AAP (Alanine aminopeptidase), γ-GT). For examination of concentration of all tested biomarkers, the colorimetric analysis method was applied on a Cobas Integra 400® plus device.Results: All of the patients treated with NSAIDs, regardless of the type of drug, showed an increase of all of the examined biomarkers, with a *significant difference* of $p<0.0005 – 0.0001$, in comparison to the control group, consisting of healthy individuals. Statistical processing: We applied the standard deviation measure(X±DS), arithmetic mean value, and the Mann-Whitney U test in order to analyse and process the obtained values and parameters. Conclusion: From this scientific work we may conclude that our results are in accordance and compliance with the already published results on the undesirable and noxious effects of the NSAIDs upon the kidneys. Thus, we suggest NSAIDs utilization, application, and administration be extremely rational, especially for patients suffering from diabetic nephropathy, and other renal pathologies.

Keywords: NSAID, pain, renal diseases

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are medicaments with analgesic, anti-inflammatory and antipyretic effects. The term non-steroid is used to distinguish steroid medication. The mechanism of action of non-steroidal anti-inflammatory drugs is based on non-selective inhibition of cyclooxygenase enzymes that inhibit isozymes: Cyclooxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2) and Cyclooxygenase-3 (COX-3) side effects, allergic reaction to the drug, headache, dizziness, increased blood pressure cardiovascular side effects (detected in recent years), diarrhea, diarrhea, therefore, when using the NSAID, it is necessary to first take a patient history of the above mentioned diseases. Non-steroidal anti-inflammatory antirheumatics are the most commonly used in: rheumatic diseases and pains of

a rational aetiology. Non-steroidal antirheumatics have been used since 1500, NSAIDs have the following effects: - an anti-inflammatory effect-an antiretatic effect - antipyretic effect (reduces / normalizes high body temperature. Each treatment with NSAIDs is aimed at reducing the duration of pain as well as keeping the symptoms of the disease. NSAIDs are the most used antiretomers, despite the discovery of CoX-2 inhibitory orophs their nephrotoxicity remains a topic of investigation and scientific research (Perezella *et al.,* 2001). The negative effects of non-steroidal antiretomers are favored by the reduced synthesis of prostaglandins of arachidonic acid with the non-specific blockade of the enzyme of cyclooxygen, which leads to vasoconstriction and reversibly slight damage to the kidney leading to acute necrosis of tubules with acute renal failure. Nonsteroidal antirheumatics are a common cause of interstitial nephritis with nephrotic syndrome. Non-steroid anti-inflammatory drugs due to hypoperfusion of the kidneys that may cause acute renal failure, but in addition to the above, they can lead to hypoperinemias with hypoaldosteronism by decreasing the tubular flux which is also cause of hyperkalemia with congestive heart failure and nephrotic syndrome (Ejaz *et al.*, 2004, Clive *et al.,* 1984). NSAIDs continue to be nephrotoxic medications manifesting renal tubular necrosis, tubulointresticio pyelonephtitis, papillary renal neoplasia, acute renal failure (ARF) and chronic glomerulonephritis, hypertension, hyperrenineia (Parezella *et al.,* 2001).The impact of NSAIDs on the appearance of chronic renal insufficiency remains still questionable (Gault *et al.*, 1998).

Purpose of care

The goal and task of the effort is to pass through the activity of certain enzymes, analyzed in urine and blood, to determine the negative effects and harmful effects of non-steroidal anti-inflammatory drugs on their kidneys, ie their nephrotoscopy, in patients without kidney damage and forced by rheumatic, polyarthritis or rheumatoid arthritis to use non-steroidal antirheumatics in therapy.

MATERIALS AND METHODS

In a cohort study, 60 patients with an average age of 58 years old (± 5.00 years) have been examined. Of the examined patients, 35 patients were females and 25 were males. The average duration of the pathophysiological state was 48 years (± 2.00 years). The study also included the control group of patients [healthy individuals (voluntary blood donors)] compromising 60 individuals, of which 30 were females and 30 were males. The average age of the control group patients was 58 years old (± 5.00 years). During the duration of the study, all of the patients were treated with NSAIDs (with short breaks) and Methotrexate (MTH) with dose of 7.5 – 10 mg (for 10 weeks). During the laboratory examination which were utilized and performed to discover nephrotoxicity, we tested for concentration of erythrocytes (Rbc), haemoglobin (Hb), haematocrit (Htc), urea, creatinine, GFR (by Cockcroft-Gault formula), albuminuria, C-reactive protein (CRP), rheumatic factor (RhF), and urinary enzymes (cystatin-C, βNAG (N-acetyl-B-D-glycosaminidase), AAP (Alanine aminopeptidase), γ-GT). For examination of concentration of all tested biomarkers, the colorimetric analysis method was applied on a Cobas Integra 400® plus device.

RESULTS

All of the patients treated with NSAIDs, regardless of the type of drug, showed an increase of all of the examined biomarkers, with a *significant difference* of $p<0.0005$- 0.0001, in comparison to the control group, consisting of healthy individuals.

Statistical processing: We applied the standard deviation measure(X±DS), arithmetic mean value, and the Mann-Whitney U test in order to analyse and process the obtained values and parameters. Conclusion: From this scientific work we may conclude that our results are in accordance and compliance with the already published results on the undesirable and noxious effects of the NSAIDs upon the kidneys. Thus, we suggest NSAIDs utilization, application, and administration be extremely rational, especially for patients suffering from diabetic nephropathy, and other renal pathologies.

DISCUSSION

Non-steroidal anti-inflammatory rheumatics (NSAIDs) bundle into the second group after nephrotoxicity following aminoglycosides as the cause of acute renal failure (ARF).) NSAIDS are known drugs that can provoke ARF, interstitial nephritis accompanying haematuria and proteinuria. last year, a large number of studios that the use of non-reactive antirheumatics in the treatment of rheumatic diseases shows a certain toxic effect on the kidney's function due to possible accumulation in them. Even though we have a wide range of NSAIDs drugs available for renal safety is necessary and is still a number of studies and studies. It has been shown that prostaglandins protect the renal blood flow and glomerular filtration rate (GFR), especially in those places that are impoverished with fluid. The locally synthesized prostaglandin PGE12 (Prostacyclin), PGE2, and PGD 2 leads to vascular dilatation, reduces vascular resistance, and contributes to strengthening renal perfusion by redistribution of blood flow from the renal cortex to the nephrons and the juxta medullary region. PGE2, and to a lesser extent PGF 2, causes diuresis and sodium bromide through the inhibited sodium and chloride transport in the ascending portion of the Henley loop. PGE 1 tends to antagonize the action of antidiuretic hormone (vasopressin). Lastly, prostacyclin together with PGE2 serves for the normal maintenance of the glomerular filtration rate. In the last years, quite a number of experimental studies and examinations for the nephrotoxicity of NSAIDs have been made to follow the toxic effect of non-steroidal anti-tumors on the function of kidney. The results obtained and the examination of these examinations are used as a basis and for the monitoring of the effects and effects of non-steroidal anti-inflammatory drugs on the kidneys or other organs. . The recommended dose of non-steroidal anti-inflammatory drugs is often not adapted to the condition of the patient, which can lead to urinary effects associated with a decrease in renal function as a result of the accumulation of the drug in the kidneys and their corresponding harm . The toxic effect of NSAIDs is most commonly encountered in the long-term therapy of NSAIDs. The past trials indicate that there is no indication of a delayed indication of the nephrotoxicity occurring during the therapy itself and the dosage of NSAIDs. A large number of studies have shown that the incidence of acute renal failure due to the use of NSAIDs is about 15.5% of cases (Grifin *et al.,* 2000). All NSAIDs are nephrotoxic independently in which group they belong. ADAMS et al. (Adams *et al.,* 1986) in their study have proven that NSAIDs with prolonged half-life of disintegration are with greater nephrotoxicity due to the constant inhibition of prostaglandins which is manifested by a sustained and progressive decrease in renal blood flow while short-hemisphere NSAIDs with a lower nephrotoxicity due to rapid elimination, Wheleton (Klienknecht *et al.*, 1986), a cohort, has found that long-acting drugs such as Ibuprofen can also contribute to renal impairment for several days. A large number of nephrolozes have the lifespan of NSAIDs taken early NSAIDs resulting in four types of damage to the debilitating impairment: 1. acute ischemic renal failure, 2. acute interstitial nephritis, 3. analgesic-related nephropathy, 4. unusual side pain syndrome, and cancellation of renal impairment. Renal function using ibuprofen.NSAIDs also affects the concentrations of sodium, potassium, and water homeostasis. There have been published studies confirming that increased blood pressure may be caused by the interaction of NSAIDs with antihypertensive

drugs and cause deterioration in renal function. The most common form of renal dysfunction more rapidly with nephrotoxicity than NSAIDs is acute renal failure caused by the haemodynamic effect. Diseases, illnesses or drugs that cause a decrease in current or effective circulation cause a homeostatic increase in the production of catecholamines such as norepinefrin and the activation of the renal angiotensin system. Within the renal blood supply and secretion of catecholamines, vasoconstriction is regulated inversely by the compensatory release of prostaglandin to provide adequate renal permeability (Warren *et al.*, 2000 – Koseki *et al.,* 2001). In this state, the action of NSAIDs results in a reduced blood flow to the kidney and a glomerular filtration rate, which is usually observed after giving initial doses to NSAIDs. However, if renal function damage is not detected in the early phase of therapy, the prolonged renal ischemia that can cause acute tubular necrosis and permanent damage to the kidneys (Segasothy *et al.*, 1995, Brater *et al.,* 2001). The National Kidney Foundation (NKF) recommends shampoos and NSAIDs (pherucoid aspirins and acetaminophenes) to patients with chronic cerebral palsy. Abusive laws and the NSAID can lead to analgesic nephropathy, a condition that is often irreversible after cessation of therapy. NSAIDs disadvantage ally interact with some commonly prescribed medicines, including diuretics, ACE inhibitors, blocker receptors ter angiotensin, leading to effectiveness reduction, along with increased risk of kidney damage.

CONCLUSION

From this scientific work we can conclude that our results are consistent with the already published results of the adverse and harmful effects of NSAID on the kidneys. Thus, we suggest using, administering and administering NSAIDs to be extremely rational, especially for patients suffering from diabetic nephropathy and other renal pathologies. Patients with renal impairment, essential arterial hypertension and asthma status should have particular and long-lasting care the use of non-anti-inflammatory drugs should always take into account the nature of the medication and its elimination.

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