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Case Report

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Iatrogenic Drug and Kidney Graft: About A Case

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Summary

The Kidney is vulnerable organ to the drug toxicity, due to the interstitial accumulation of toxic agents, expose the kidney to higher concentrations. The nephrotoxicity develops by a variable degree renal failure, it may be evolved quickly and spontaneously towards the terminal stage and unfortunately lately discovered. Following the studies of indesirable effects of an unwanted circumstance at the EHUO's pharmacovigilance service; we could show the involvement of many nephrotoxic substances as Nonsteroidal anti-inflammatory drugs, during the aggravation of the chronic end stage of the renal failure. As a conclusion, and to reduce the incidence of the renal complications, it is essential to prevent the occurrence of the iatrogenic-based nephrotoxic effects, because that can be a real primary prevention, which is why the recommendations while using this drugs must be respected.

Keywords: Indesirable effects; Nephrotoxicity; Prevention; Recommendation

Introduction

The chronic end stage of the renal failure is a major problem to the public health conditions. In Algeria, we consider that it can affect plus than 13000 persons, a prevalence of about 374 pmh [1].

One of the major problems of the chronic end stage of the renal failure diagnosis is that it can remain asymptomatic for a very long time, until a nearby DFG of 15 ml/min/1,73 m² of the body surface. It is often diagnosed in a very late stage in the disease evaluation [2]. The point of this work is to show the involvement of the Nonsteroidal anti-inflammatory drugs through the studies of indesirable effects of an unwanted circumstance at the EHU-Oran's pharmacovigilance service during the aggravation of the chronic end stage of the renal failure.

Patients and Methods

We report that a patient: B.W, 29 years old; hospitalized in the nephrology service, after a chronic interstitial nephritis was suspected.

The patient was suffering a severe and frequent ophthalmic pain since a young age and a chronic anemia, she was administrated since she was aged 17 (12 years ago), a Nonsteroidal anti-inflammatory in self-medication which is the Nopain® DS [Naproxen Sodium 550 mg] and that high dosage up to four tablets daily. And for anemia she took Folic Acid at 10 mg/ day.

And to save weight, the patient has been using a product called Ginseng purchased from an herbalist. In 2013, she was admitted at the Mostaganem hospital for an altered state of consciousness after taking 4 tablets Ginseng®, a renal failure diagnostic was made following a serum creatinine greater than 40 mg/ml which corresponds to a renal clearance in MDRD of 14.10 ml/ mn and 14.27 en CKD-EPI.

In September 2015, the patient started hemodialysis, with a diuretic prescription label, the Furosan®[1/4 Furosémide 500 mg]. After few months, the patient developed an infection on fistula, treated by Claforan® [Cefotaxim], but the deterioration in renal function confirmed by ultrasound atrophied kidney led to a chronic renal failure in a terminal stage of where the use of kidney transplantation scheduled for 8 March 2016 in the EHU-Oran, The Kidney Graft Unity

Results

The intrinsic accountability score for Nopain® and Furosan® was: I3, according to the French method. Similarly, the known effect is describer for the AINS leading to an extrinsic accountability to B2. According to the method Naranjo and al. (Anglo-Saxon method), the score was +7 for both drugs which means that each of them is probably responsible for the effect.

It should be noted that the associations Naproxene® and Furosémide® are considered because it can cause a renal failure in patients at risk by reducing glomerular filtration. And that it may progress to chronic renal failure in patients at risk

Discussion

Chronic interstitial nephritis represents about 10% of chronic kidney disease; they are the cause of the end stage renal failure in 5-10% of patients treated with iterative dialysis. They may be of urological origin (chronic pyelonephritis) or non-urological (drug, toxic) (Table 1).

Infectious causes	Infectious stones Chronic urinary infection associated with an anatomical abnormality of the urinary tract Renal tuberculosis
Urological causes	Nephropathy of vesico-ureteral reflux, Chronic obstacle stones, adenoma or cancer of the prostate, bladder tumor (or the pelvis), retroperitoneal fibrosis;
Metabolic causes	nephrocalcinosis: distal renal tubular acidosis, primary hyperparathyroidism, hypercalciuria, primary hyperoxaluria ... Chronic hypokalemia;
Toxic causes	Medications: Lithium, cyclosporin A, nephropathy analgesic, Chronic lead poisoning and cadmium Chinese herbs nephropathy (aristolochic acid) Balkan endemic nephropathy (mycotoxin);
Dysimmune causes	sarcoïdose, Sjögren
Hematologic causes	tubulopathy myeloma, sickle cell anemia;
Hereditary causes	Autosomal dominant polycystic kidney disease, autosomal recessive polycystic kidney disease, nephronophthisis, cystic disease of the spinal cord.

Table 1: Etiologies of chronic interstitial nephritis.

Naproxen is a nonsteroidal anti-inflammatory drug derived from arylpropylique acid [3], its effectiveness as its main side effects are related to its main mechanism of action which is inhibition of cyclooxygenase enzymes responsible for the synthesis of prostaglandins that contribute to the regulation of intrarenal hemodynamics, in order to maintain the glomerular perfusion. The nephropathies due to AINS are frequently secondary to acute kidney injury generally immuno-allergic origin and occur irrespective of the dose, they are rarely accompanied by systemic symptoms and that just persists the time of treatment [4].

The responsibility of AINS in the occurrence of the NIC is more or less clear, heir administration on a chronic basis over the years is responsible for serious chronic interstitial renal parenchymal willingly complicated urinary tract infections, papillary necrosis and very long-term tumor of urinary tract, it is true unknown abuse and triggered by painful menstruation and/or frequent headaches that reminds our case. It affects almost exclusively women [6,7].

After analyzing the statement, we can conclude that kidney disease can still be caused and / or aggravated by the taking of the food supplement (Ginseng Tablets based) because this type of Chinese herbs containing likely to aristolochic acid, known by its potential toxicity to the kidneys.

Recommendations for the proper use of non-steroidal anti-inflammatory [according to ANSM]: [9]

The "French Agency for the Safety of Health Products" (FASM) issued in July 2013, a reminder of the rules of proper use of nonsteroidal Anti-Inflammatory Drugs (AINS), and the choice of an AINS is based on the consideration of individual risk factors as well as the safety profile of each AINS schedule (Table 2).

Risk factors related to drug	Intrinsic nephrotoxicity Combination with other nephrotoxic drugs Dose and rate of administration unsuitable, prolonged duration of treatment;
Risk factors related to the patient	Age, Pre-existing renal insufficiency, Comorbidities (diabetes, heart failure, multiple myeloma) Fluid and electrolyte disorder ... etc.

Table 2: Risk factors for nephrotoxicity [8].

Before prescribing, consider the risk of gastrointestinal, cardiovascular risk and renal risk because AINS increase the risk of fluid retention, may favor a small increase in arterial thrombotic risk in case of prolonged use, are capable of inducing acute renal failure.

When prescribing, observe the indications and systematically inform the patient of the risks associated with AINS use and precautions to be followed in case of self-medication. Should be prescribed and used AINS at the lowest effective dose for the shortest duration possible and respect the against-indications.

When the monitoring of treatment, it is essential to monitor gastrointestinal adverse reactions: according to ANSM, the occur-

rence of epigastric pain or other gastrointestinal symptoms require discontinuation of treatment, monitor cardiovascular adverse effects: The ANSM specifies that any symptoms worsening or onset of cardiovascular disease AINS requires firstly stopping treatment, the other a reassessment of the adequacy of the indication in the pathology concerned; To be attentive to possible skin manifestations: any AINS treatment should be discontinued at the onset of skin rash, mucosal lesions or any other manifestation of hypersensitivity.

These reactions usually occur during the first month of treatment; To be attentive to any infectious event: The ANSM draws the attention of health professionals on the fact that AINS are able to obscure the first signs of infection and thus worsen the prognosis of some of them: as dental infections, chicken pox, pneumonia and ORL infections.

Conclusion

Potentially nephrotoxic drugs are either prescribed or available self-service in pharmacies such as AINS.

These can aggravate IRC through glomerular hemodynamic changes: If effective hypovolemia, extracellular dehydration, diuretic use, the DFG is maintained through vasodilatation related, mechanism that was stopped by AINS. In these circumstances, an increase in kidney failure may occur. Meanwhile, the pharmaceutical industry strives to develop less toxic therapies that reference products (appearance of AINS anti-COX-1) [5].

Do not overlook the herbal drugs that are active drugs that can also produce side effects and even exhibit some toxicity.

Similarly, individual risk factors of each patient must be identified before introduction of a nephrotoxic treatment and preventive measures put in place to prevent that risk. So the existence of a renal failure must encourage great caution when using drugs. It is always advisable to avoid polytherapy. Indeed, acute renal toxicity can have serious consequences in the short term and long term. A renal failure indeed increases the risk of developing chronic kidney disease or end stage renal disease and mortality, the risk increasing with the severity of the renal failure.

Finally, it is essential to perform a monitoring of renal function, by estimating the glomerular filtration rate, preferably with the MDRD formula, before, during and after treatment. The various settings of renal function (abnormal urinary sediment, proteinuria) will also be monitored. Dose adjustment of treatment in renal function is of course imperative. Prevention measures type of hydration should be implemented.

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