Ketoprofen-Induced Irreversible Renal Failure

P.A.	Patricio A.	Pazmiño
P.B.	Patricio B.	Pazmiño

Nephrology, Internal Medicine and Hypertension Center, Department of Medicine, Texas Tech University Health Science Center School of Medicine, El Paso, Tex., USA

P. Pazmiño, PhD, MD, NIH Center, Suite 101, 1701 N. Mesa & Schuster, El Paso, TX 79902 (USA)

Dear Sir,

Ketoprofen (Orudis®, Wyeth) is a new nonsteroidal anti-inflammatory agent with analgesic properties which was recently released for clinical use in the USA. We report here a case of irreversible renal failure after treatment for 10 days with ketoprofen. Clinicians should be aware of this potential nephrotoxicity and use caution in its administration, especially in patients with preexistent renal disease, hypertension or compromised intravascular volume status.

Case Report

An 84-year-old white male was admitted to the hospital for evaluation of nausea, vomiting, azotemia, and hyperkalemia. There was no history of hematuria, rash, fever, or urinary complaints.

As an outpatient, he was on treatment for 3 years with Dyazide® (hydrochlorothiazide 25 mg, triamterene 50 mg) p.o. b.i.d., multi-vitamins (1 p.o. q.d.), and dipyridamole (75 mg p.o. b.i.d.). Ten days prior to admission, he was given ketoprofen (75 mg p.o. t.i.d.), because of arthritic complaints, and a week later the dose was decreased to 75 mg/day for 3 additional days. Because of flu-like symptoms, Symmetrel® (amantadine 100 mg p.o. b.i.d.) was added and laboratory tests were obtained by the referring physician that eventually prompted hospitalization.

On admission all medications were discontinued. The blood pressure was 136/80 mm Hg, the temperature was 36°C, the pulse was 86/min, and the respiratory rate was 18/min. The remainder of the physical exam was noncontributory except for mild prostatic hypertrophy and dryness of the mucosae. The urinalysis showed a pH of 5, a specific gravity of 1.014, 8-9 WBCs/high-power field and no casts or bacteria. A Hanzel stain of the urine sediment showed 5% eosinophils. The hematocrit was 32.8%, WBC count was 14,800/mm³ with 47% segmented neutrophils, 8% bands, 23% lymphocytes, 7% monocytes, 9% eosinophils, and 6% metamyelocytes. The potassium was 6.3 mEq/l (6.3 mmol/l), chloride 112 mEq/l (112 mmol/l), CO₂ 9.7 mEq/l (9.7 mmol/l), glucose 94 mg/dl (5.05 mmol/l), BUN 111 mg/dl (39.63 mmol/l), and creatinine 12.4 mg/dl (1096 µmol/l). Three months earlier, on a previous admission due to pneumonia,

the BUN was 31 mg/dl (11.06 mmol/l), creatinine was 1.7 mg/dl (150.28 µmol/l).

An ultrasound of the kidney did not reveal hydronephrosis. A 24-hour urine collection showed a creatinine clearance of 3 ml/min/1.73 m² and 897 mg of protein. The following tests were normal or negative: urine toxicology and heavy-metal screen, urine culture, electrocardiogram, chest X-ray, hepatitis profile, CPK, LDH, immunoglobulin E, and SGOT. A repeat creatinine

clearance, 10 days after admission was 2 ml/min/1.73 m² and the protein excretion was 336 mg/24 h.

The patient was a Jehovah witness and declined to have a kidney biopsy. Treatment was given for hyperkalemia and dehydration, but there was no significant improvement of the renal insufficiency and eventually chronic hemodialysis was required. After 3 weeks in dialysis the patient developed a pericarditis and expired.

Acute renal failure secondary to prostaglandin inhibitors is becoming a common occurrence in clinical nephrology [1–4]. Ketoprofen has been in clinical use for a relatively short time and to our knowledge, this is the first reported case of acute renal failure since ketoprofen was introduced into the American market. A recent review of the literature includes 1 case of acute interstitial nephritis and one of papillary necrosis attributable to ketoprofen [5]. Moreover, there are reports in European literature of reversible and irreversible renal failure associated with ketoprofen [6, 7]. Sixteen months after our original report to the manufacturer, further inquiry revealed 6 additional cases of acute renal failure reported to them so far.

The lesion causing renal insufficiency could not be determined in this case because of the patient's refusal to have a percutaneous kidney biopsy due to his religious beliefs and the possible need of blood transfusion. The presence of eosinophils in the peripheral blood and in the urine sediment, provides indirect support for our interpretation that the renal failure and proteinuria may have been secondary to an acute interstitial nephritis, possibly associated with glomerular lesion [8]. Further studies,

Ketoprofen-Induced Irreversible Renal Failure

71

Abraham, P.A.; Keane, W.F.: Glomerular and interstitial disease induced by non-steroidal anti-inflammatory drugs. *Am. J. Nephrol.* 4:1–6(1984).

Pazmiño, P.: Suprofen-induced acute renal failure. *Tex. Med.* 55:32–33(1987).

Carmichael, J.; Shankel, S.W.: Effects on non-steroidal anti-inflammatory drugs on prostaglandins and renal function. *Am. J. Med.* 75:992–1000(1985).

Ducet, F.; Pointel, P.; Martin, D.; Villermet, B.: Reversible acute renal failure induced by ketoprofen. *Néphrologie* 3: 105–106(1982).

Windeck, R.; Bock, K.D.; Jakubowski, H.D.: Irreversible failure of a transplanted kidney. Was this induced by ketoprofen? *Dt. med. Wschr.* 705:720–721 (1983).

Garella, S.; Matarese, R. A.: Renal effects of prostaglandins and clinical adverse effects of non-steroidal anti-inflammatory agents. *Medicine* 65:165–181 (1984).

Zipser, R.D.; Henrich, W.L.: Implications of non-steroidal anti-inflammatory drug therapy. *Am. J. Med.* 80:O suppl. 1 A, pp. 78–84 (1986).

including kidney biopsies are required in future cases to clarify the etiopathogenesis of the renal insufficiency associated with ketoprofen.

Since ketoprofen is a widely advertised new addition to the nonsteroidal anti-inflammatory drugs, suggested guidelines to minimize the nephrotoxic effects of these drugs should be followed [8, 9] and urinalysis should be done [4]. Thus, the possibility of inducing renal failure in the patients at risk should be considered when ketoprofen is prescribed. 7

Acknowledgement

The author gratefully acknowledges the referral of this patient by Dr. Eliseo Hervas.

References

Schrier, R.W.; Henrich, W.L.: Non-steroidal anti-inflammatory drug. Caution still indicated. *J. Am. med. Ass.* 251:1301–1302 (1984).