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Case Report

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ACUTE RENAL FAILURE AFTER USING DEXKETOPROFEN: 3 CASE REPORTS

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ABSTRACT

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used all over the world. Acute renal failure (ARF) is a known complication of NSAIDs. Especially in cases of hypovolemia NSAIDs inhibit the enzyme cyclo-oxygenase that regulate the synthesis of prostaglandins from arachidonic acid and it may result vasoconstriction and reversible renal failure. Dexketoprofen is enantiomer of ketoprofen and is a nonspecific NSAID in aryl-proprionic acid group. In this article we present 3 patients with acute renal failure and with history of the use of dexketoprofen.

KEYWORDS: Non-Steroidal Anti-Inflammatory Drug, Dexketoprofen, Acute Renal Failure.

INTRODUCTION

Although the incidence of nephrotoxicity with the use of NSAIDs is low, but commonly prescription and the widespread use of NSAIDs increases the risk of nephrotoxicity,[1] The severity and frequency of renal side effects increase in the cases of diabetes, heart failure, old age, and patients with renal failure and dehydration.[2] Acute renal failure secondary to the use of NSAIDs can occur as a result of various mechanisms. Functional hemodynamic deterioration of renal functions and reversible kidney failure is the most common form . Renal pathologies such as acute interstitial nephritis, acute tubular necrosis, papillary necrosis, renal vasculitis, nephrotic syndrome, hypertension due to salt and water retention, edema and hyperkalemia may also be seen due to NSAIDs.[3]

Nonsteroidal anti-inflammatory drug dexketoprofen is S (-) enantiomeric form of ketoprofen and both are arylpropionic acid derivatives.[4] Except rhabdomyolysis and acute renal case due to deksetoprofen, there are no renal toxicity cases related to this molecule.[5] In this article we present 3 patients with acute renal failure and with history of the use of dexketoprofen.

MATERIAL AND METHODS

Case 1: 35-year-old female patient with rectal carcinoma tumor resection and ileostomy used dexketoprofen in the postoperative period twice a day intravenous for 1 week and oral for 10 days. Preoperative and postoperative serum creatinine levels were normal, but rised after 15 days after discharge. During the acceptance of the patient's to the clinic with complaints of nausea and vomiting, blood pressure was 110/70 mmHg, pulse rate: 76/min and there was no signs of dehydration. The patient's laboratory tests were hemoglobin 11.2 g/dL, white blood cell count: 9030/ mm^3, platelet count: 427000/ mm^3, aspartate aminotransferase (AST): 17 IU/L, alanine aminotransferase (ALT): 10 IU/L, lactic dehydrogenase (LDH): 215 U/L, creatinine phosphokinase (CPK): 20 U/L, urea 88 mg/ dl, creatinine 5.5 mg/dl, Na: 141 mmol/L, K:5.2 mmol/L, respectively. Urinalysis was normal. Abdominal ultrasonography revealed grade 1 hydronephrosis in the right kidney collecting system. Intravenous fluid therapy was started, fluid intake and urine output were monitored on a daily basis. During follow-up, the amount of urine did not decrease. Daily urine output of patient was 2500-3000 cc. Her urea, creatinine and electrolytes were daily followed- up. Despite the continuation of hydronephrosis in the same manner, with the appropriate fluid therapy on 7th day her biochemical parameters decreased as blood creatinine 3.9 mg/ dL, urea 42 mg/ dl, respectively and on 14th day, blood creatinine was 1.5 mg/ dl and urea was 24 mg/ dl. Without urological catheterization, two months later, renal ultrasound was normal and creatinine was 0.8 mg/ dl.

Table 1. Labaratory findings of patient 1 on consecutive days.

Urea (mg/dl)	Creatinine (mg/dl)	Sodium (mmol/L)	Potassium (mmol/L)
88	5.5	132	5.2
74	5.8	141	5.0
53	4.3		5.5
24	1.5		4.5
42	0.81	138	4.4
42	0.54	141	4.4

Case 2: 56 year old male patient was under medication of metoprolol 25 mg tablet/ day and losartan potassium-hydrochlorothiazide 100/25 mg tablet/ day due to ischemic heart disease and hypertension and he started to use ciprofloxacin tablet 500 mg twice a day and ornidazol three times a day because of diarrhea for about 1 week. The patient had used 16 tablets of dexketoprofen twice a day for 2 weeks because of osteoarthritis. The patient complained loss of appetite and weakness for 10 days. He had no history of kidney disease and serum creatinine tests were detected normal 1 month ago and at the time of his admission his laboratory parameters were; urea: 133 mg/ dL, creatinine: 6.82 mg/ dl, Na: 135 mmol/ L, K: 4.9 mmol/ L, ALT: 19 U/ L, AST 18 U/ L, gamma-glutamyltransferase: 48 U/ L, alkaline phosphatase: 64 U/ L, creatinine phosphokinase: 73, respectively. In physical examination, arterial tension was 110/ 70 mmHg, and renal ultrasonography revealed bilateral grade 1 increase in parenchymal echo. After the initiation of intravenous hydration progressive decline in serum urea and creatinine levels were observed. One week after administration of hydration serum creatinine was 2.1 mg/ dl. Three months later creatinine level was 0.73 mg / dl.

Table 2: Labaratory findings of patient 2 on consecutive days.

Urea (mg/dl)	**Creatinine** (mg/dl)	**Sodium** (mmol/L)	**Potassium** (mmol/L)
133	6.82	135	4.9
172	3.2	140	4.2
150	2.1	132	3.9
43	0.73	142	4.0

Case 3: A 50-year-old male patient with the history of chemotherapy for resected gastric carcinoma was on remission for 4 years and he used dexketoprofen tablet twice a day for 10 days because of chest pain. He complained with anorexia, vomiting and his labaratory investigation was; urea: 93 mg/ dl, creatinine 4.2 mg/ dl, Na: 130 mmol/ L, K: 3.4 mmol/ L, ALT: 19 U/ L, AST 16 U/ L, gamma-glutamyltransferase: 21 U/ L, alkaline phosphatase: 70 U/ L, creatinine phosphokinase: 56 U/ L respectively. No any other reason that can cause creatinine elevation except dexketoprofen use was determined. Creatinine levels approached to normal limits with supportive fluid therapy.

DISCUSSION

NSAIDs are widely used because of their analgesic, antiinflammatory, antipyretic influences. Despite the low risk profile of nephrotoxicity, due to widespread use many people are at risk for renal side effects of NSAIDs.[1-3] In subjects with normal renal functions, prostaglandins have relatively limited role to maintain sufficient renal hemodynamic functions. Especially in cases of lack of fluid, prostaglandins asist in maintaining the renal blood flow and glomerular filtration rate.[6] Use of NSAIDs can cause renal functional damages such as inhibition of renal prostaglandin production, fluid and electrolyte disorders, acute renal failure, nephrotic syndrome, interstitial nephritis and renal papillary necrosis.[3]

Dexketoprofen is water-soluble salt and dextro enanthiomer of ketoprofen and is widely used for analgesia. Orally administered dexketoprofen is well tolerated and highly effective agent to control acute and chronic pain.[4,7] Dexketoprofen at the same time as all the other NSAIDs inhibits renal tissue vasodilator prostaglandin secretion. Dexketoprofen, as well as side effects on gastrointestinal and central nervous systems, has also side effects on kidneys such as acute kidney injury. Dexketoprofen can also cause acute renal failure due to rhabdomyolysis.[5] In the literature, except for the case of rhabdomyolysis-induced acute renal injury we could not find case reports of acute renal injury related to the use of dexketoprofen.

In this article we present 3 cases with previously normal renal function and ARF after the use of dexketoprofen. None of these 3 patients had a known history of renal disease. During the admission patient were not oliguric and during follow-up no of three patients developed oliguria. Urologic intervention was not executed to the patient with history of anterior resection because of rectal carcinoma and right hydronephrosis on USG, because in control sonography hydronephrosis was decreased. Unilateral hydronephrosis, recently operation history and simultaneously long-term use of NSAIDs were the factors that predispose to the development of ARF. Studies have shown that increased prostaglandin production is associated with hydronephrosis. Therefore in these cases the use of NSAIDs by inhibiting the production of prostaglandins can lead to impairment of kidney function.[2] Also high doses of NSAIDs are more risky than medium and low dose for the development of ARF on a daily basis.[8] Especially in the first case, the use of postoperative dexketoprofen for a long time in repeated doses is considered to increase hemodynamic ARF. Sodium deficiency states such as gastrointestinal losses and diuretic therapy, hypovolemia, congestive heart failure, nephrotic syndrome, urinary tract obstruction, advanced age, chronic renal failure are predisposing conditions for acute renal failure due to NSAIDs.[1] Concurrent use of NSAIDs with diuretics, beta-blockers and angiotensin-converting enzyme inhibitors (ACEI) may adversely affect blood pressure control by interfering the positive effects of renal prostaglandins. Also simultaneously use of NSAIDs with ACE inhibitors, angiotensin receptor blockers, diuretics increases the risk of acute renal failure.[6] In physical examination of the three patients there was no signs of dehydration. However in second case, use of diuretics and the history of diarrhea was thought to contribute to ARF. With hydration and supportive therapy renal functions returned to normal in long-term follow-up. During hydration, especially in patients with oliguria or anuria carefull follow-up is necessary in terms of

volume overload. In cases of acute renal failure due to NSAIDs, quick diagnosis and discontinuation of the responsible agent in 72-96 h may reverse the status to normal. However, unless early recognition is provided, condition may progress rapidly and patients may need dialysis.[1] Deterioration of renal function is associated with NSAID exposure time and dose of the drug. In patients with asymptomatic renal insufficiency half of therapeutic doses of NSAIDs may induce ARF.[9] Parenteral administration of NSAIDs cause high peak blood levels and cause acute renal side effects via the increased inhibition of prostglandins.[2] In the elderly population it is known that ARF associated with the use of NSAIDs increases hospitalization and these drugs affect glomerular and microvascular autoregulation mechanisms of the kidney due to the high sensitivity of elderly kidney to nephrotoxic damage. In addition changes in volume of distribution may cause an increase in blood levels of NSAIDs. Elderly patients have decreased total body fluid.[2] Elimination of dexketoprofen is decreased in the elderly and in patients with mild and moderate renal impairment.[10] In patients with impaired renal function and in elderly population dose regulation for dexketoprofen is recommended because of decreased renal functions.[11] Especially in patients with a history of systemic disease, avoidance of recurrent, long-term and high doses dexketoprofen administration for postoperative pain control would be a sensible approach.

CONCLUSION

As result, if possible, it should be avoided to use dexketoprofen in cases that can cause renal hypoperfusion such as renal disease history, old age, post-operative process, dehydration, heart failure and cirrhosis. In high risk patients the lowest effective dose with caution and using the drug for possible short time period could be recommended and patients should be monitored during dexketoprofen treatment for renal functions. During postoperative period in patients at risk for acute renal failure, physicians should pay attention to hydration and NSAIDs should not be prescribed if possible.

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