Case Report

Diclofenac induced acute renal failure in a decompensated elderly patient

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ABSTRACT

Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly prescribed drugs in post-operative period worldwide. Their nephrotoxic effects are documented and accounts for around 15.5% of all cases of drug induced renal failure. Acute renal failure following NSAIDs usage are reported in volume depleted patients which is further precipitated by co-morbid conditions like hypertension and various drug interactions that increase plasma level of NSAIDs and worsens the condition. This highlights the importance of hydration in post-operative period as well as assessment of co-morbid conditions before administration of NSAIDs to prevent acute renal failure.

Key words: Drug interaction, hypertension, volume depleted

INTRODUCTION

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are one of the most commonly prescribed drugs and their nephrotoxic effects are well known.[1] Diclofenac is widely used as analgesic and anti-inflammatory drug. Reports of renal dysfunction have been documented mostly in volume decompensated patients and are favored by various drug interactions. Renal dysfunctions are more prominent in geriatric population with falling renal functions.[2] We would like to report a case of diclofenac induced acute renal failure which was favored by the presence of co-morbid conditions namely, hypertension, falling renal function due to aging and drug interaction in a already volume decompensated patient.

Access this article online	
Quick Response Code:	Website: www.jpharmacol.com
	DOI: 10.4103/0976-500X.110916

CASE REPORT

A 69 year old male patient was a known case of hypertension and receiving tablet atenolol 25 mg once a day since 3 years. He was diagnosed with spindle cell carcinoma on left thigh and was operated for it. Before surgery, he was given tablet furesemide 40 mg once a day and his anti-hypertensive drug was continued. On discharge after surgery, he was asked to continue his antihypertensive therapy with tablet atenolol 25 mg once a day and was also prescribed tablet ranitidine 150 mg twice a day, a combination of diclofenac 50 mg with serratiopeptidase 10 mg thrice a day and another combination of ampicillin 250 mg and cloxacillin 250 mg thrice a day for a total duration of 7 days.

After 7 days, he visited outpatient department with complaints of swelling over legs and decreased frequency of micturition. On examination, the patient was alert and his pulse and blood pressure were within normal limits. He had no pallor, icterus, lymphadenopathy or clubbing but he had pedal edema. His respiratory, cardiovascular and central nervous systems were within normal limits.

On investigation, it was found that his plasma creatinine and urea were raised to 9.4 mg/dl and 99 mg/dl respectively. Among

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the electrolytes, plasma potassium and sodium were 4.9 mEq/L and 133 mEq/L, respectively. These values of these tests when done 4 days prior to surgery were creatinine 1 mg/dl, urea of 17 mg/dl, potassium 4.6 mEq/L and sodium 141 mEq/L. Urine proteins were within normal range with total protein 6.8 g/dl (normal 6.0-8.3 g/dl) urine albumin 3.47 g/dl (normal 3.2-5.0 g/dl) and urine globulin 3.34 g/dl (normal 3.2-5.0 g/dl). Urinary sodium was decreased 14.1 mEq/L (normal 25-50 mEq/L) and so the osmality to 34.2 mEq/L (normal values 100-260 mEq/L).

Following the deranged report, his diclofenac was stopped and his investigations were repeated the following day, on day 5, day 10 and after 1 month. His plasma creatinine and urea levels didn't show significant change on the following day but on day 5 the values started to drop towards normality with plasma creatinine 3.2 mg/dl, potassium 3.6 mEq/L and sodium 137 mEq/L. His pedal edema was also subsiding showing clinical improvement.

On subsequent visit, on day 10, his creatinine level further came down to 1.5 mg/dl, urea to 21 mg/dl, potassium 3.2 mEq/L and sodium 140 mEq/L. After one month, all the values returned within the normal range with creatinine 1.5 mg/dl and urea 16 mg/dl.

DISCUSSION

Non-steroidal anti-inflammatory drugs alter renal functions through their effects on renal prostaglandins leading to reversible renal ischemia.[3,4] Although NSAIDs related hypertension, salt and water retention, edema and hyperkalemia are highly infrequent but they remain a concern in patient who are at risk and can develop acute renal failure.[5]

Prostaglandins do not play a physiologic role in maintaining renal blood flow in normal subjects; but it plays a role in maintaining glomerular filtration rate (GFR). In intravascular depleted states, renal plasma flow is maintained by a balanced between the vasoconstrictor influence of the renin–angiotensin system and the vasodilatory effects of prostaglandins.[4] In fluid depleted states, prostacyclin (PGI_2) mostly affects renal homeostatic mechanisms. PGE_2 and PGD_2 cause dilatation of the renal vascular bed along with the lowering of renal vascular resistance. Thus, it enhances renal perfusion with redistribution of blood flow from the renal cortex to nephrons in the juxta-medullary region.[3] So, Prostaglandins become critical in maintaining GFR in volume depleted states. Hence, when the production of prostaglandins is blocked due to NSAIDs, it may lead to hyperkalemia, peripheral edema, increased blood pressure, weight gain and acute renal failure.[6]

In this case, the patient had no pre-existing renal disease but he was a known case of hypertension and received diuretic therapy prior to diclofenac admistration. Age-related decline in renal blood flow in hypertensive person and volume depletion due to diuretics are further worsened by NSAIDs.[2] This was clinically evident in our case as this patient belonged to the geriatric population so he was more susceptible to nephrotoxic drugs with his ageing kidneys. On presentation, his blood pressure was within normal range but he had marked pedal edema and decreased frequency of micturition. There was sudden rise of plasma creatinine, urea and potassium. He also had low urine output, low sodium excretion and low urinary osmolality which signifies kidney's decreased ability to concentrate urine.

In the above setting, course with NSAIDs therapy i.e., tablet diclofenac 50 mg three times a day (150 mg/day) was sufficient to precipitate acute renal failure as this dose appears to impair the renal blood flow and glomerular filtration rate.[7] Diclofenac has antagonizing effect on atenolol which decreased its antihypertensive effect which further precipitates ARF.[8] This interaction may have had occurred in this case. Thus, the hemodynamically mediated acute renal failure caused by NSAIDs was further exacerbated with interaction with anti-hypertensive drug. According to Naranjo adverse drug reaction probability scale, diclofenac is the probable cause of this hemodynamically mediated acute renal failure.

Hemodynamically-medicated acute renal failure due to NSAIDs in volume depleted patients is reversible and is mostly related to the dose and duration of exposure.[9] In our case, patient's plasma creatinine and urea started to decline after 7 days of drug discontinuation and his pedal edema subsided subsequently with improvement in urine output. Within one month, on subsequent visit to outpatient department his investigation came within the normal range.

In the above condition, either the NSAIDs (nonselective and coxibs) should have been given in lower doses as much as possible without re-titrating the anti-hypertensive drug dosage or "renal-sparing" NSAIDs (like nabumetone) could have been preferred. Adequate hydration of the patient should be maintained prior to initiation of NSAIDs therapy along with restriction of the dietary salt.[10]

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How to cite this article: Dhanvijay P, Misra AK, Varma SK. Diclofenac induced acute renal failure in a decompensated elderly patient. J Pharmacol Pharmacother 2013;4:155-7.
Source of Support: Nil, **Conflict of Interest:** None declared.