World Inventia Publishers

Journal of Pharma Research

http://www.jprinfo.com/

Vol. 7, Issue 10, 2018 ISSN: 2319-5622 USA CODEN: JPROK3

Case Report

NSAID INDUCED NEPHROPATHY IN A PATIENT WITH DIABETES – A CASE REPORT

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Received on: 04-10-2018; Revised and Accepted on: 30-10-2018

ABSTRACT

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are one of the most commonly prescribed drugs and their nephrotoxic effects are well known. We describe a case of a 60-years female patient with diabetic who presented with increasing fatigue and decreased physical endurance attributable to deterioration in renal function. The renal biopsy revealed drug-induced nephropathy and chronology of the events suggested the aetiology to be a recent intake of paracetamol 325 mg + aceclofenac100 mg in a combination for body pains since 3 months. We did not come across a case of NSIAD - induced nephropathy on extensive electronic search of literature. This is probably the first case report of nephropathy associated with the use of paracetamol and aceclofenac, potent non-steroidal anti-inflammatory drugs.

KEYWORDS: *NSAIDS, Nephropathy, Paracetamol, Aceclofenac.*

INTRODUCTION

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are one of the most commonly prescribed drugs and their nephrotoxic effects are well known. Diclofenac is widely used as analgesic and anti-inflammatory drug and Paracetamol is used as antipyretic along with analgesic activity [1]. 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 NSAID induced nephrotoxicity which was favoured by the presence of co-morbid conditions namely, diabetes, falling renal function due to aging and drug interaction in a already volume decompensated patient.

CASE REPORT

The index case was a 60-year female patient who had diabetes since 7 years. She was on medication in the combination of metformin 500mg + glipizide 5 mg twice daily for last 1 year and her diabetes control was satisfactory.

She visited outpatient department with complaints of swelling over legs and decreased frequency of micturition. On examination, the patient was alert and her pulse and blood pressure were within normal limits. She had no pallor, icterus, lymphadenopathy or clubbing but she had pedal edema. Her respiratory, cardiovascular and central nervous systems were within normal limits. So, she admitted in IP general medicine department.

On investigation, it was found that her plasma creatinine and urea were raised to 9.4mg/dl and 99mg/dl respectively. Among the electrolytes, plasma potassium and sodium were 4.9mEq/L and 133mEq/L, respectively. Other investigations were creatinine 1mg/dl, urea of 17mg/dl, potassium 4.6mEq/L and sodium 141mEq/L. Urine proteins were within normal range with total protein 6.8g/dl (normal 6.0-8.3g/dl) urine albumin 3.47g/dl (normal 3.2-5.0g/dl) and urine globulin 3.34g/dl (normal 3.2-5.0g/dl). Urinary sodium was decreased 14.1mEq/L (normal 25-50 mEq/L) and so the osmolality to 34.2mEq/L (normal values 100-260mEq/L).

Following the deranged report, NSAID was stopped and her investigations were repeated the following day, on day 5, day 10. Her 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 3.6mEq/L and sodium 137mEq/L. Her pedal edema was also subsiding showing clinical improvement.

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

DISCUSSION

Non-steroidal anti-inflammatory drugs alter renal functions through their effects on renal prostaglandins leading to reversible renal ischemia [3]. 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 nephrotoxicity.

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) [4]. 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 [5]. 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 [6]. 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, nephrotoxicity and acute renal failure [7].

In this case, the patient had no pre-existing renal disease. This was clinically evident in our case as this patient belonged to the geriatric population so she was more susceptible to nephrotoxic drugs with his ageing

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DOI: https://doi.org/10.5281/zenodo.1476392

kidneys [6]. On presentation, her blood pressure was within normal range but she had marked pedal edema and decreased frequency of micturition. There was sudden rise of plasma creatinine, urea and potassium. She also had low urine output, low sodium excretion and low urinary osmolality which signifies kidney's decreased ability to concentrate urine [5].

In the above setting, course with NSAIDs therapy i.e., tablet paracetamol 325 mg + aceclofenac 100 mg two times a day was sufficient to precipitate nephrotoxicity as this dose appears to impair the renal blood flow and glomerular filtration rate. According to Naranjo adverse drug reaction probability scale, diclofenac is the probable cause of this hemodynamically mediated nephrotoxicity [8].

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. In our case, patient's plasma creatinine and urea started to decline after 7 days of drug discontinuation and her pedal edema subsided subsequently with improvement in urine output [9]. Within one month, on subsequent visit to outpatient department her 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. Adequate hydration of the patient should be maintained prior to initiation of NSAIDs therapy along with restriction of the dietary salt.

The most important issues in nephrotoxicity patient management is withdrawal of the offending medication, substituting it with safer alternatives and correction of electrolyte abnormalities. Decision to use steroids should be guided by the clinical course following withdrawal of offending medications. Small studies have demonstrated rapid diuresis, clinical improvement and return of normal renal function within 72 h after starting steroid treatment, although some indicate lack of efficacy, especially in cases of NSAID induced Nephrotoxicity. Recently a large multicentric retrospective study was carried out to determine the influence of steroids in patients of biopsy-proven drug-induced nephrotoxicity. Delayed steroid treatment has less pronounced therapeutic benefit[7]. The dose of prednisone is 1 mg/kg/day orally for 2–3 weeks, followed by a gradually tapering dose over 3–4 weeks. Overall prognosis of drug-induced ATIN is favourable and at least partial recovery of kidney function is normally observed.

CONCLUSION

In conclusion, now a days these adverse drug reactions are increasingly being reporting day by day, here we reported a case of NSAIDS induced nephropathy, which is common global problem causing significant morbidity and mortality. To prevent such type of ADR's clinicians should seek to minimise NSAID exposure in people particularly susceptible to AKI due to age, CKD or because of the co-prescription of other nephrotoxic drugs.

ACKNOWLEDGMENTS

The authors thank Mr. M. Venkata Subbaiah, Dr. P. Venkata Ramana and Dr. S. Kareemulla from Rami Reddy Memorial college of Pharmacy for their support in manuscript preparation.

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How to cite this article:

Deepti. M, et al. NSAID INDUCED NEPHROPATHY IN A PATIENT WITH DIABETES – A CASE REPORT. J Pharm Res 2018;7(10):236-237. **DOI: https://doi.org/10.5281/zenodo.1476392**

Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nil