

NSAID INDUCED NEPHROPATHYShilpa Anand Hakki¹¹Associate Professor, Department of General Medicine, SDMMCS & H, Sattur, Dharwad.**ABSTRACT****BACKGROUND**

The aim of the study was to study the prevalence of NSAID Induced Nephropathy in patients coming to CHC, Haliyal.

MATERIALS AND METHODS

More than 15000 rural population patients were studied prospectively during December 2015 to March 2017 who were on NSAIDS for a period of more than 2 years.

Inclusion Criteria - Patients on NSAID treatment for more than 2 years were included in the study. Patients with underlying comorbidities like HTN, DM and Nephrolithiasis were also included in the study.

Settings - This was a prospective study undertaken in a Community Health Centre; where patients from peripheral villages came for treatment and were addicted to NSAIDS due to easy availability and OTC (over the counter) prescription. Majority of the patients were laborers; dependant on analgesics to get rid of Generalized Body Ache (GBA) due to extensive labour.

RESULTS

The combined data showed the percentage of patients NSAID induced nephropathy was 2.68%.

CONCLUSION

Judicious use of drugs especially NSAIDS is required to prevent its untoward side effects particularly on kidneys.

KEYWORDS

1) NSAIDs: (Non-Steroidal Anti-Inflammatory Drugs) 2) OTC: Over the Counter; 3) ESRD: End Stage Renal Disease. 4) GBA: Generalized Body Ache; 5) COX: Cyclooxygenase; 6) PG: Prostaglandin; 7) CRF: Chronic Renal Failure; 8) DM: Diabetes Mellitus; 9) HTN: Hypertension.

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BACKGROUND

Nonsteroidal anti-inflammatory drugs (NSAIDs) are very commonly prescribed Analgesics, widely used in the treatment of pain. Easy availability of these drugs over the counter and ignorance about the consequences lead to NSAID induced complications. Complications may be in form of gastritis or nephritis ending up even in chronic renal failure (CRF) and end stage renal disease (ESRD).¹

NSAIDS exert anti-inflammatory, analgesic and anti-pyretic effects through the suppression of prostaglandin (PG) synthesis. Mechanism of action is by inhibiting the enzyme cyclooxygenase (COX). Two isoforms of this enzyme COX-1 and COX-2 are known to exist. The gastrointestinal tract and the kidneys are very vulnerable systems affected by NSAIDs. Nonselective NSAIDs inhibit both COX-1 and COX-2. COX-2 is regulated in response to intravascular volume. Renal hemodynamic and glomerular filtration rate

(GFR) is mainly affected and controlled by COX-1 while COX-2 functions primarily affect salt and water excretion.¹

These enzymes therefore on blockage can have different effects on renal function.

Therefore the chronic users of NSAIDS have an increased risk of developing specific kidney injuries, namely renal papillary necrosis and chronic interstitial. Nephritis Analgesic nephropathy is a disease resulting from the frequent use of combinations of analgesic medications over many years, leading to significant impairment of renal function. In many studies it was noted that a large number of cases of renal failure in patients abusing analgesic mixtures containing more than one analgesic led to nephrotoxicity from the use of analgesics.² Same was with our study. Patients in our study were on more than 2 analgesics over a period of more than 2 yrs. Also, if patients had underlying comorbidities like HTN, DM, Nephrolithiasis or CKD the risk of NSAID induced Renal damage is more.³

Aims and Objectives

Our aim was to study NSAID induced gastritis and Nephropathy.

Out of these two studies NSAID induced Nephropathy is highlighted here.

Main objective was to see incidence of renal damage by NSAIDS in chronic drug abusers and addicts. Also, our aim was also to take measures to prevent NSAID induced

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complications by taking preventive measures and by proper counseling.

MATERIALS AND METHODS

In this prospective study from December 2015 to March 2017, total 15023 patients were examined. Out of them 1830 patients were included and studied in detail. Inclusion criteria was NSAID abuse for more than 2 yrs. Detailed clinical history and complete physical examination was done. Study was taken in rural area at a Community Health Centre, where labour was the main source of earning and people were more dependants on analgesics and already addicted to NSAIDS due to easy availability of drugs and over the counter prescription. Our study involved patients taking drugs for more than 2 years.² Surprisingly patients taking NSAIDS from Decade were also found!

Inclusion Criteria

Patients on NSAID treatment for more than 2 years were included in the study. Patients were on following NSAIDS- paracetamol, diclofenac sodium and Ibuprofen. Patients with NSAID abuse with underlying comorbidities like DM, HTN and Nephrolithiasis were also involved in the study. Serum Blood Urea, Creatinine and urine Albumin tests were done. As study was conducted in CHC with no facility for kidney biopsy, none of patients underwent kidney biopsy. Later NSAID induced nephropathy patients were referred to higher centre for further needful.

RESULTS

Out of 15023 patients 1830 patients (12.18%) were on NSAIDS for Generalized Body Ache. (GBA). Out of those 1830 patients, 49 patients (2.68%) had NSAID induced nephropathy.⁴ Out of 15023 patients 6712 were male patients while 8311 were female patients.

Out of 49 patients with deranged renal functions, 17 patients has underlying co morbidities in the form of DM, (8 patients), HTN (6 patients), Nephrolithiasis (3 patients).

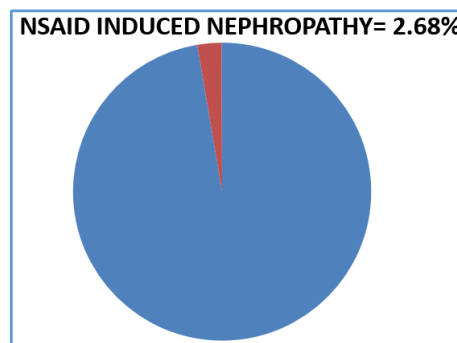
Diclofenac was the most commonly implicated NSAID used by almost all selected patients (99%). Nearly 65.70% patients were on combination analgesics of diclofenac and Ibuprofen. While 2.2% patients were on three analgesics.

Sl. No.	Month/year	Pts on Analgesics	Drug Induced Nephropathy
1.	DEC 2015	21	1
2.	JAN 2016	152	7
3.	FEB 2016	112	2
4.	MAR 2016	180	9
5.	APRIL 2016	109	3
6.	MAY 2016	94	5
7.	JUNE 2016	81	2
8.	JULY 2016	170	1
9.	AUGUST 2016	1021	1
10.	SEPT 2016	1274	1
11.	OCT 2016	551	2
12.	NOV 2016	1107	3
13.	DEC 2016	1120	1
14.	JAN 2017	1050	4
15.	FEB 2017	910	6
16.	MAR 2017	700	1

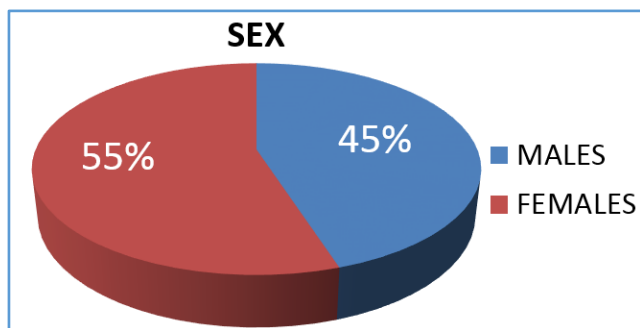
Table 1

Total Duration of Study	Total Patients	Patients on Analgesics	Patients with Nephropathy	Percentage of Analgesic Nephropathy
Dec 2015 to March 2017	15023	1830	49	2.68%

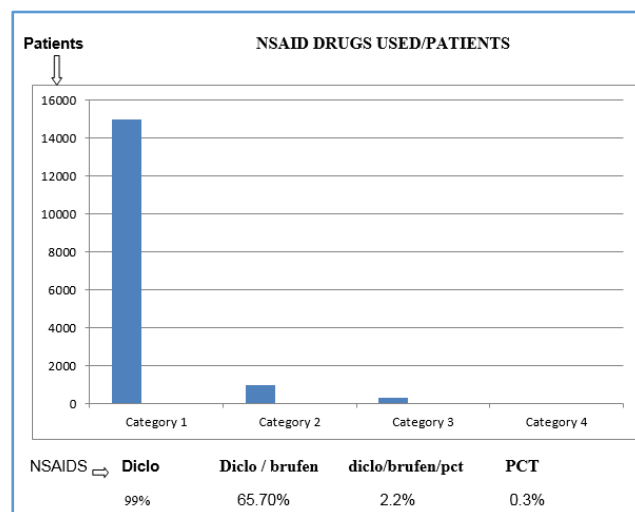
Table 2



Graph 2



Graph 1



Graph 3

Total Patients with deranged KFT	Pts with BUN/CREAT = 20/1.5 TO 30/5.0	Pts with BUN/CREAT = 30/5.0 TO 60/ 6.0	Pts with BUN/CREAT= >60/7.0	Patients with comorbidities DM/HTN/NEPHROLITHIASIS
49	13	13	23	8 DM 17 → 6 HTN 3 NEPHROLITHIASIS

Table 3. Data of Patients on NSAIDS with Deranged Renal Function Tests

DISCUSSION

NSAIDs can cause two different forms of acute kidney injury.⁵

1. Haemodynamically Mediated Kidney Injury

Prostaglandins have a vasodilatory effect on renal vasculature. Prostaglandin mediated vasodilatation is probably of little importance in euvolemic patients with normal kidney function tests, but these prostaglandins (PGI2/PGE2) attenuate the vasoconstricting effect of Renin angiotensin system and sympathetic nervous system in following underlying conditions and comorbidities

A. Decreased Intravascular Volume

- a. Sepsis
- b. Haemorrhage
- c. Diuretic therapy.

B. Diseases

- a. CCF
- b. Cirrhosis
- c. Nephrotic Syndrome

C. Comorbidities

- a. DM
- b. HTN
- c. Nephrolithiasis.⁶

Lack of these vasodilatory prostaglandins due to cox inhibition by NSAIDS may put stressed kidneys at risk for azotaemia and renal insufficiency.

ARF is rare after NSAID overdose but NSAID overdose may place a stressed renal system at risk for failure. This was evident in our study also. Patients with underlying co morbidities were vulnerable group for renal insufficiency.

2. Immune Mediated Kidney Injury

Incidence of Acute interstitial nephritis may be up to 5 to 10%⁷ of patients hospitalized for acute renal failure.⁴ Presentation may be varied, Classic findings of fever, rash, and arthralgias may be absent in up to two thirds of patients. Patients with underlying co morbidities with drug abuse may present with complications which were otherwise normal before drug abuse. Renal biopsy though remains the gold standard for diagnosis. But it may not be required in mild cases and when clinical improvement is rapid after removal of an offending agent or medication. In our study none of patients underwent renal biopsy. There was no follow up of patients who were referred to higher center. Acute kidney injury represents a continuum of renal injury ranging from

clinically asymptomatic changes in renal function to renal failure.⁸

CONCLUSION

The incidence of chronic renal failure continues to increase. NSAIDs remain one of the causes. Analgesic nephropathy can occur in two forms, one in chronic users with renal dysfunction characterized by a dense interstitial fibrosis and the insidious development of renal failure. The second form of analgesic nephropathy is typically an acute renal failure associated with the use of nonsteroidal anti-inflammatory drugs, in patients who are at-risk population of patients who are more vulnerable to developing it, due to underlying co morbidities.⁹ That means, patients with chronic use may end up in renal failure and ESRD or if with acute presentation with acute renal failure, underlying co morbidity may be the triggering factor.

Apart from many other drugs, NSAIDs remain one of the risk factors for Acute Interstitial Nephritis.¹⁰ In cases where it is secondary to NSAID induced, prevention remains an important strategy for the control of this disease. The widespread use of analgesics remains one of potential risk factors for chronic renal disease and risk increases further in patients with underlying co morbidities. Physicians need to be cautious when treating with NSAIDs. Awareness of the dangers of using NSAIDs could reduce the episodes of nephrotoxicity. Before prescribing NSAIDS baseline renal function tests is mandatory in pts with underlying comorbidities³ and in patients with age >45 yrs.¹¹

Preventive Measures

Drug-induced nephrotoxicity tends to occur more frequently in patients with underlying comorbidities.³ Therefore preventive measures are important. It requires screening of patients for underlying risk factors and education /counseling wherever needed. Prevention strategies should target the prescribing and monitoring of potential nephrotoxins in at-risk patients.⁷

General Preventive Measures Include-

1. Using equally effective but non-nephrotoxic drugs whenever possible.
2. Assessing baseline renal function before initiating analgesic therapy.¹²
3. Adjusting the dose of medications for renal function.
4. Avoiding nephrotoxic drug combinations.
5. Renal function should be monitored in at risk patients.¹²
6. If acute kidney injury occurs, the NSAID should be stopped.
7. NSAIDs should be avoided in patients who develop or have a history of interstitial nephritis.

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