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Analgesic Nephropathy: Clinical Profile and Radiological correlation

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ABSTRACT

Introduction: In the recent years , there has been an increase in the incidence and prevalence of End-Stage Kidney Disease throughout the world. Identification of these modifiable risk in the early period can help in prevention of many cases to land into End Stage Disease. Non steroidal anti-inflammatory drugs (NSAIDS) and many other over the counter analgesics are the most commonly used drugs, particularly by the elderly patients who are at high risk of analgesic nephropathy.

Material and Methods:

This prospective study was conducted at Department of Nephrology, Mahatma Gandhi Hospital between January 2017 and January 2019. All patients with a strong history of analgesic use (defined as intake of analgesics for more than 5 years) were evaluated; all patients who had features of analgesic nephropathy on radiological assessment were included in the study.

Results:

Among the patients evaluated for analgesic nephropathy, 16 patients had evidence radiological changes evident on Non Contrast CT for analgesic nephropathy. Mean age of patients in our study was 56.2 years. Females outnumbered males in terms of gender. 56.2% (09) patients had history of hypertension , 43.7 % (07) were diabetic (mean duration 10.2 years) , history of arthritis was present in 68.7 % (11) patients . Mean creatinine was 5.4 mg/dl . 43.7 % patients had proteinuria with 24 hours urinary protein excretion more than 1 gm/day. All patients underwent a Non Contrast Helical CT for the diagnosis of analgesic nephropathy. Following points were taken into consideration:

SICK (Small intended calcified kidney) was observed in 56.2 % cases, irregular counter was observed in 43.7 % cases and focal calcification was observed in 43.7 % cases.

All patients who had evidence of SICK on Non contrast CT (Table 01) had history of analgesic use for an average of more than 5.5 years. All these patients had history of intake more than one analgesic use for more than 5.4 years (mean) . Out of the 56 % cases, 4 had history of Diclofenac use for more than 6.7 years.

Conclusion:

There has been a pressing need for studies and multicenter trials to evaluate the true incidence of analgesic nephropathy more so because if diagnosed early patients can be prevented to progress to advanced renal failure..

Keywords: NIL.

INTRODUCTION

Analgesic nephropathy is a preventable disease which results from the irrational and frequent consumption of combinations of analgesic medications, when taken over many years. This chronic drug use can lead to significant impairment of renal function. In the past decades, there have been observations of a large number of cases presenting with renal failure in patients having history of analgesic mixtures mainly containing phenacetin , leading to the recognition of nephrotoxicity . This drug, phenacetin was subsequently blamed for this disease. Even the use of classic analgesics like acetaminophen (paracetamol) and even salicylates which are commonly used for minor pain , whereas

NSAIDs which are considered as the first-line drugs for the treatment of various arthritis and musculoskeletal disorder However, at many occasions , the role of a single analgesic as an only reason of analgesic nephropathy was challenged, and many studies have attempted to evaluate the extent of involvement of other drugs including paracetamol , non steroidal anti-inflammatory drugs (NSAIDs) and aspirin.

This study was conducted to evaluate the demography of patients, history of drug use, radiological assessment of patients with analgesic nephropathy.

Material and Methods:

This prospective study was conducted at Department of Nephrology, Mahatma Gandhi Hospital between January 2017 and January 2019. All patients with a strong history of analgesic use were evaluated (defined as intake of analgesics for more than 5 years), all patients who had features of analgesic nephropathy on radiological assessment were included in the study.

A detailed history of co morbidities, drug history, biochemical parameters and correlation with CT findings was done. Non– contrast enhanced CT scans were performed using a standardized protocol.

Three parameters were used to identify patients who might have "analgesic-induced" kidney disease: Size, indentations, and calcification. (Figure 02).

Results:

Among the patients evaluated for analgesic nephropathy, 16 patients had evidence radiological changes evident on Non Contrast CT for contrast nephropathy.

Demography and History:

Mean age of patients was 56.2 years. Females outnumbered males in terms of gender , 10 women had evidence of analgesic nephropathy as compared to males.

Co morbidities: 56.2% (09) patients had history of hypertension , 43.7 % (07) were diabetic (mean duration 10.2 years) , history of arthritis was present in 68.7 % (11) patients .

Drug History: History of receiving Methotrexate was present in 5 cases (31 %), Paracetamol was taken by 13 out of 16 cases. Diclofenac use was present in 68.7 % (11) , Mefenamic acid was used by 09 – 56.2 % cases , almost 43.7 % patients had history of alternative medications (homeopathic or ayurvedic medications)

The average quantity of Paracetamol drug used was 200 tablets per month, followed by diclofenac 180 tablets per month. All patients on methotrexate were receiving 7.5 mg per week (mean duration 5.4 years) . Mefenamic acid use was seen in 160 capsules per day. 87.5 % patients had history of ingestion of mixture of analgesic drugs- defined as two or more drugs.

Laboratory Profile:

At the time of presentation, Mean hemoglobin was 8.5 mg/dl, Mean creatinine was 5.4 mg/dl . 43.7 % patients had proteinuria with 24 hours urinary protein excretion less than 1 gm/day.

Radiological findings:

All patients underwent a Non Contrast Helical CT for the diagnosis of analgesic nephropathy.

Following points were taken into consideration:

SICK (Small intended calcified kidney) was observed in 56.2 % cases, irregular counter was observed in 43.7 % cases and focal calcification was observed in 43.7 % cases.

Correlation of findings with demographic profile and drug history:

All patients who had evidence of SICK on Non contrast CT (Table 01) had history of analgesic use for an average of more than 5.5 years. All these patients had history of intake more than one analgesic use for more than 5.4 years (mean). Out of the 56 % cases, 4 had history of Diclofenac use for more than 6.7 years and a mean consumption of more than 150 tablets of diclofenac per month. These patients also had increased creatinine levels with mean creatinine of 4.5 mg /dl.

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Table 01: Criteria for SICK – Small Intended Contracted Kidney

Criteria
- small: bilaterally decreased kidney size[b] by at least one of three methods
  - ellipse volume: men <93.2 cm^3; women <73.9 cm^3
  - voxel volume: men <102 cm^3; women <77.5 cm^3
  - parenchymal thickness: men <1.44 cm; women <1.27 cm
- indented: at least three indentations on each kidney, with at least one major indentation (≥5 mm deep) on one side
- calcified: papillary calcifications in each kidney involving at least four papillae or at least 2 mm in size

Classification
- grade 1: both kidneys are small and indented
- grade 2: both kidneys are small and calcified
- grade 3: both kidneys meet all three criteria

Figure 1: CT classification of findings of Analgesic- nephropathy

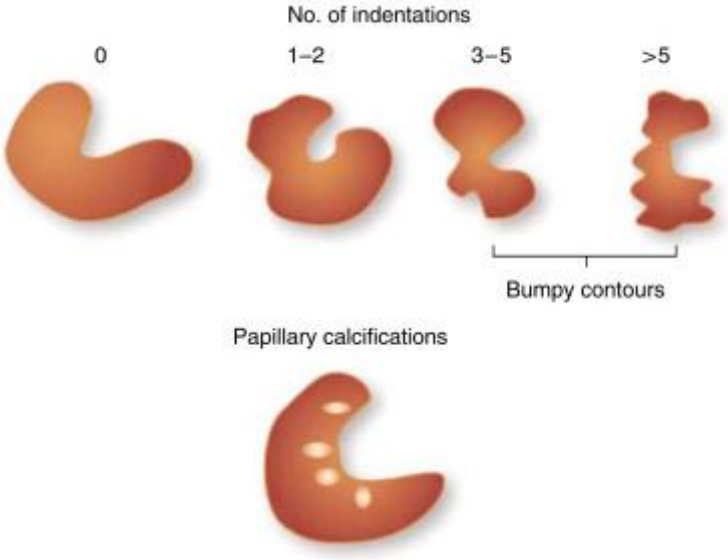

Figure 2: Non contrast CT scan of KUB region showing small indented, calcific kidneys (SICK Stage III), a characteristic finding that is associated with analgesic nephropathy.

Discussion:

Our results demonstrate that there is a strong association between heavy analgesic ingestion and findings of analgesic nephropathy in the form of SICK on Non Contrast CT. Many of the previous follow-up and case-control studies have also shown a significant association between heavy analgesic use and kidney disease . However, the diagnostic reliability of Non contrast CT was increased after the work of Elseviers, DeBroe, and colleagues with the introduction of the criteria of Small Intended Contracted Kidney. Their studies also suggested that the a Non contrast CT scan has high sensitivity and specificity for certain changes which can point towards Analgesic Nephropathy including a reduction in kidney volume, parenchymal scarring, and papillary calcification.

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We found that majority of the patients were more than 45 years of age with mean age of presentation 56.2 years and the number of females were more than males. This was similar to findings by Segasothy M, Kong Be et al [1] , who found similar results with mean age of presentation being 53 years and females outnumbering the number of male patients .

In our group of patients, 56 % had history of hypertension, 43 % had history of diabetes and 68% had history of joint pains in the form of arthritis. These findings co related well with the study by Segasothy M et al who found that patients suffering from Rheumatoid arthritis and PIVD who had history of chronic analgesia were at a higher risk of developing analgesic nephropathy.

Majority of the patients in our group (87.5% had history of ingestion of two or more analgesics . These group of patients had evidence of more renal failure and demonstration of changes of analgesic nephropathy on Non contrast CT . Perneger et al investigated 716 patients with renal failure, and concluded that increased paracetamol use was associated with an enhanced risk of renal failure in a dose-dependent manner. Approximately 9% of renal failure cases were attributable to increased paracetamol use. However, this study failed to adjust for the potential for patients using paracetamol to be concurrently using either phenacetin or NSAIDs when assessing association with renal failure.

Another study by Henrich, W.L et al , found that CT scan was helpful in early detection of features of analgesic-induced nephropathy and correlated with the degree of renal impairment and history of analgesic abuse .

Conclusion

There has been a pressing need for studies and multicenter trials to evaluate the true incidence of analgesic nephropathy more so because if diagnosed early patients can be prevented to progress to advanced renal failure.

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