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ORIGINAL ARTICLE

Utilization Of Nephrotoxic Drugs In Post-Operative Patients Of Urolithiasis

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ABSTRACT

Background of Study: Renal (or kidney) stones have been around for centuries. Egyptian mummies have been found to contain stones. Around the 5th century B.C., physicians at a medical school in Asia Minor described renal colic or pain in detail. Much information has been gathered about the condition in recent years, but more is to be learned about the cause and treatment. Urolithiasis is quite common in developing countries, especially in Nepal. This problem is particularly important in the Nepalese context, perhaps because of the climate, terrain, the living condition of the people and economic aspects. A large number of drugs are also responsible for causing urolithiasis or kidney damage.

Aim of Study: To screen the cases of urolithiasis which were operated in the past two years, and to find and establish whether nephrotoxic drugs were used in the treatment.

Materials and Methods: This is a retrospective study of hospital records of over two years, from January 2001- December 2002. 193 cases were operated for urolithiasis, which were the targeted cases of this retrospective study, and a prescription audit was done on the post operative prescriptions and follow up treatment given by surgeons at Nepal Medical College Teaching Hospital (NMCTH), a major teaching hospital of Katmandu valley, with a view to observe whether nephrotoxic drugs were prescribed for urolithiasis, and a suggestion for avoiding their use so that the reoccurrence of disease is prevented.

Results: A majority of subjects (57.51%) had urolithiasis from the productive age group. Four cases of renal damage were observed among the urolithiasis subjects.

31.08% (60 out of 193) of the urolithiasis subjects were prescribed nephrotoxic drugs. Diclofenac sodium was given in 18.13% of the total subjects, including three subjects of renal damage even being given a potent nephrotoxic drug.

Conclusion: Nephrotoxic drugs have to be avoided in pre-operative, post-operative, and follow up prescriptions in urolithiasis patients.

Key Words: Nepal, Nephrotoxic drugs, renal damage, Urolithiasis

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Introduction

Urolithiasis refers to accretion of hard, solid, non-metallic minerals in the urinary tract. About 1 million people suffer from Urolithiasis each year, and 12% of the people living in the United States will have at least one stone in their

lifetime [1]. Of those who develop stone, 50% will have a recurrence of forming another stone within the next six years. Urolithiasis is quite common in developing and under developed countries, where the recurrence of endemic bladder stone is quite common due to the dietary proteins being mainly derived from plant sources. The problem of stone is more predominant in the productive age groups, as reported earlier [2]. In Nepal, the problem is quite common due to climate, terrain, living

conditions of the people, and economic aspects. Endocrinal and metabolic disorders, racial factors, and variation in dietary habits predisposes to urolithiasis. [3][12]. Besides the above factors, drugs are also responsible for urolithiasis, especially struvite stones [13]-[15] and kidney damage [16]. The present retrospective study was done on the post operative prescriptions and follow up treatment being given by the surgeons in NMCTH, a major teaching hospital of Kathmandu valley, with a view to observe whether nephrotoxic drugs were prescribed in the post-operative and follow-up period after removal of stone, and a suggestion to avoid their use, as it might further aggravate the problem.

Materials and Methods

This is a retrospective study of hospital records of over two years from January 2001 to December 2002 of the cases of urolithiasis that were operated in NMCTH. The total number of subjects who underwent surgical removal of calculi was 193. The criteria of selection of the subjects were based on:

Exclusion Criteria

- (a) Prospective cases
- (b) Cases of other diseases.

Inclusion Criteria

- (a) Hospitals records of the last two years
- (b) Post-operative urolithiasis patients and their follow up treatment.

The case sheets of the subjects were retrieved from the Department of Medical Records, and the post-operative prescriptions and follow up treatment given by the surgeons were audited. An informed consent was taken from the subjects who participated in the study, and was pre-approved by the institutional ethical committee board of Kathmandu University, Nepal.

The absolute data was collected and entered in Microsoft Excel for Windows 98.

Results

The total subjects were 116 males and 77 females. The age varied from 3 years to a

maximum of 74 years, with a mean \pm SD of 40.17 ± 18.69 years. Of the total study group subjects a majority of subjects ie.57.51% (111 out of 193) who had urolithiasis were from the productive age group from 21-40 years [Table/Fig 1]. There were 60 patients in whom nephrotoxic drugs were used, comprising of 46 males and 14 females, as shown in [Table/Fig 1].

[Table/Fig 1] Characteristics of the study group

Age Group	Males (n=116) (Mean \pm SD)	Number of urolithiasis cases where nephrotoxic drugs was used (n=46)*	Females (n=77) (Mean \pm SD)	Number of urolithiasis cases where nephrotoxic drugs was used (n=14)*
1-10 (n=1)	3 (n=1)	-	-	-
11-20 (n=12)	15.57 \pm 2.14 (n=9)	3	16.87 \pm 2.38 (n=3)	-
21-30 (n=69)	26.87 \pm 2.57 (n=42)	16	26.84 \pm 2.87 (n=27)	5
31-40 (n=42)	35.68 \pm 1.89 (n=27)	10	32.58 \pm 4.57 (n=15)	3
41-50 (n=11)	45.87 \pm 2.35 (n=4)	4	45.68 \pm 4.63 (n=7)	2
51-60 (n=23)	54.67 \pm 2.38 (n=10)	5	54.18 \pm 2.58 (n=13)	1
61-70 (n=18)	62.47 \pm 1.58 (n=11)	5	64.12 \pm 1.35 (n=7)	2
71-80 (n=17)	54.67 \pm 2.38 (n=12)	3	54.18 \pm 2.58 (n=5)	1

Values in the parenthesis indicates the total number of subjects diagnosed of urolithiasis in the different age groups

* indicates the total number of cases where nephrotoxic drugs were used of the total cases

The distribution of types of stones is shown in [Table/Fig 2].

[Table/Fig 2.] Distribution of types of stone cases

Types of Urinary Stone	Males (n=116)	Females (n=77)
Left renal	9	13
Right renal	28	19
Urinary bladder	21	17
Vesico ureter junction	8	5
Left ureteric	15	7
Right ureteric	27	8
Urethral	8	8

There were four cases of renal damage as indicated by the serum urea and creatinine concentration of the subjects shown in [Table/Fig 3].

[Table/Fig 3] Biochemical parameters of the study group

	Male (n=116)	Female (n=77)
Urea and Creatinine concentration above normal	1	3
Urea and Creatinine concentration within normal	115	74

The pattern of nephrotoxic drugs beings used in urolithiasis patients is shown in Table 4. Diclofenac sodium, though it is a potent nephrotoxic drug, was used in 58.33% (35 out of 60) cases of renal stone compared to other nephrotoxic drugs which were used, as shown in [Table/Fig 4].

[Table/Fig 4] Distribution pattern of nephrotoxic drugs used in urolithiasis patients

Nephrotoxic drugs used	Males (n=46)	Females (n=14)
Gentamycin	3	-
Diclofenac sodium	32	3
Trimethoprim	4	-
nimesulide	1	-
ampicillin and cloxacillin	3	-
Norflaxacin	1	-
metformin	2	4
glibenclamide	-	4
Amphicillin	-	3

There were five patients in whom two nephrotoxic drugs, namely Megapan and Diclofenac sodium were prescribed while the remaining cases with a single nephrotoxic drug [Table/Fig 5].

[Table/Fig 5]. Analysis of nephrotoxic drugs used

Number of Nephrotoxic drugs used	Males (n=46)	Females(n=14)
One nephrotoxic drug used	42	13
Two nephrotoxic drug used	4	1

The postoperative medications used in urolithiasis patients are shown in [Table/Fig 6].

[Table/Fig 6] Post-Operative medications in urolithiasis patients

Post-Operative Medications	Males (n=116)100%	Females (n=77)100%
Ciprofloxacin	(n=27)23.77 %	(n= 10)12.98 %
Ranitidine	(n=7)6.03 %	(n=4)5.19 %
Gentamycin*	(n=3)2.58 %	-
Vitamin B complex	(n=11)9.48 %	(n=8)10.38 %
Ketorolac trometamine	(n=20)17.24 %	(n=8)10.38 %
Diclofenac sodium*	(n=32)27.58%	(n=3)3.89 %
Iron preparation	-	(n=8)10.38 %
Floaxalate	(n=1)0.86 %	-
antidiabetic	-	(n=4)5.19 %
Trimethoprim*	(n=4)3.44 %	-
antidiabetic	-	(n=4)5.19 %
Nimesulide *	(n=1)0.86 %	-
Amphicillin and Cloxacillin *	(n=3)2.58 %	-
metoclopramide	(n=1)0.86 %	-
Norflaxacin*	(n=1)0.86 %	-
Ibuprofen and Paracetamol	-	(n=4)5.19 %
Vitamin B complex with zinc	(n=1)0.86 %	-
Paracetamol	(n=1)0.86 %	-
Metformin *	(n=2)1.72 %	(n=4)5.19 %
Glibenclamide*	-	(n=4)5.19 %
Ciproflaxacin	(n=1)0.86 %	-
Omeprazole	-	(n=4)5.19 %
Etophylline +Theophylline	-	(n=4)5.19 %
Amphicillin*	-	(n=3)3.89 %
Hyoscine butylbromide	(n=1)0.86 %	(n=4)5.19 %

* potent nephrotoxic drugs

Discussion

A majority of the urolithiasis subjects were from the productive age group, and the findings of the present study correlate with those previously reported by Ansari et al (2003) [2]. It revealed that incidence of stone disease is predominant in the productive age group. In the current study, it was observed that most of the cases of urolithiasis were confined to damage of the right kidney. The findings were similar to the cross-sectional study conducted in Tabriz, Iran, where Ahmadi et al (2007) [17] reported the prevalence of right sided renal stone in the patients. In the present study, only four of our patients had urea

and creatinine levels above the normal reference range. An earlier study conducted in the United States reported serum creatinine to be higher in blacks than in white individuals and people of other races or ethnicities. The differences have been assumed to be largely related to race-related differences in body composition, especially muscle mass. Black patients were roughly four-fold more likely to have a serum creatinine concentration >10 mg/dl, and were six-fold more likely to have a serum creatinine concentration >15 mg/dl. Higher serum creatinine concentrations were associated with a lower relative risk for death (0.93; 95% confidence interval 0.88 to 0.98 per mg/dl); the association was slightly more pronounced among non black patients. In the present study, there were four cases of renal damage, as they were due to long standing calculi that might have caused altered renal functions, and in these cases in particular, nephrotoxic drugs had to be avoided. A study conducted by Hemal et al (1989) [18] cautions the use of diclofenac sodium in Urolithiasis, but the present study revealed that 18.13% of the subjects with urolithiasis were prescribed diclofenac sodium. Another study conducted by Mohkam et al (2008) [19] in the paediatric age group, also reported the toxicity associated with the use of ceftriaxone in paediatric age groups. A recent study conducted by Pannu et al (2008) [20] reported the damage of kidney in up to 25 % of all cases of severe acute renal failure in critically ill patients, due to the nephrotoxic drug used for treatment. Another study by Guo et al (2002) [21] highlighted the toxicity caused by nephrotoxic drugs, and suggested on, the prevention of such toxicity by recognizing and treating the cases of nephrotoxicity due to drugs. From the present study, it is recommended that nephrotoxic drugs should be avoided in cases of urolithiasis, either preoperatively or post-operatively, or in follow up prescriptions. The third generation Cephalosporins (cefotaxime, ceftizoxime, ceftriaxone, ceftazidime, cefoperazone), Quinolones and Fluoroquinolones (norflaxacin, ciprofloxacin, ofloxacin, pefloxacin, lomefloxacin, sparfloxacin) are relatively safe drugs that can be used in urolithiasis due to their specific susceptibility to gram negative bacteria and resistant strains of

pseudomonas and hospital borne resistant strains, to which these subjects may have been exposed to, and therefore these antibiotics should be prescribed. As far as antipyretic drugs are concerned, aspirin may be the safest and efficacious drug that could be used.

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