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Monitoring of Serum Creatinine in Post Surgical Patient Prescribed with Gentamicin

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Research Article

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Abstract

Background: Gentamicin (GM) is the mainstay of antimicrobial treatment of infections caused by gram negative bacilli, including intra abdominal and urinary tract infections and diverse hospital acquired infections. Although various side effects have been reported, including ototoxicity and neuromuscular junction blockade, the major drawback of GM usage is nephrotoxicity. The reported rates of GM nephrotoxicity vary widely from as low as 1.2% up to as high as 55%, although most studies report rates of between 8% and 26%. So the monitoring of SCr, during GM therapy is essential.
Objective: The study aimed to determine the elevation of Serum Creatinine (SCr) from its base line value and to determine the relationship between rise in SCr value with factors such as age and gender in patients during GM therapy .
Methodology: A non-interventional prospective study was conducted in Dhulikhel Hospital, Kathmandu University Teaching Hospital, Dhulikhel, Kavre, Nepal. Outcome of interest was the rise in SCr value from its baseline value in post surgical patient prescribed with GM. The obtained data were entered in Statistical Package for Social Sciences (SPSS 10) and were analyzed.
Result: A total number of 30 patients were enrolled in the study. Rise in SCr value from baseline was not significant on 3rd day of GM therapy (P = 0. 257). However there was significant rise in SCr value from baseline after completion of the therapy (P = 0.005). Among 30 patients there were 21(70%) male and 9(30%) female, however gender difference showed no role in rise in SCr value (p=0.576). Significant difference in rise in SCr value was found with advanced age.
Conclusion: A significant rise in SCr value was observed after completion of GM therapy as compared with baseline SCr value.

Key words: Gentamicin, Serum creatinine, Nepal

INTRODUCTION

Gentamicin (GM) is an aminoglycoside antibiotic, used to treat many types of bacterial infections, particularly those caused by gram-negative bacteria [1]. It is highly effective against gram negative bacilli with a concentration dependent antibacterial action and post-antibiotic effect (ability to suppress bacterial growth for a period of time after the drug level has fallen below the minimal inhibitory concentration (MIC) of the bacteria) [2].

Aminoglycosides, like GM have been widely used in clinical situations because of its efficacy and low cost. However, aminoglycosides present a serious drug induced nephrotoxicity which is linked to their accumulation in renal cortex and their capacity to bind the phospholipids and to induce intracellular lesions. Evidence suggests that aminoglycoside-induced nephrotoxicity occurs after a few days of therapy. Patients treated with aminoglycosides for 4 consecutive days preceding nephrectomy showed that GM had significant tissue accumulation, lysosomal overloading, and loss of lysosomal phospholipase A1 [3]. Clinical nephrotoxicity is defined as a rise in serum creatinine (SCr) to 50% above its baseline value during GM therapy or within 96 h of its discontinuation thus SCr value was used in different studies to access the kidney function after GM administration [4]. Several risk factors for development of complication have been identified including diabetes mellitus, duration of treatment, dehydration and advanced age [5].

As the serum concentration of GM goes up, so does the concentration of GM in the GFR. Because GM is toxic to the kidneys, an increased GM concentration means that even more of the kidney cells are damaged, less glomular filtrate is formed, and the serum concentration of GM goes up even further. Therefore, monitoring kidney function by monitoring

SCr is considered very important not only before initiating GM therapy, but periodically after the therapy has begun. As the serum concentration of GM goes up, there is increasing risk of damage to the vestibular system. Thus, uncorrected or unnoticed kidney failure in a person receiving GM is often quickly followed by ototoxicity [6]. So this study was carried out to serve as a reference to find out whether the therapeutic dose of GM administered to post operative patient cause nephrotoxiciy or not, based on the change in SCr value.

MATERIAL & METHODS

A non-interventional prospective study was conducted in Dhulikhel Hospital, Kathmandu University Teaching Hospital, Dhulikhel, Kavre, Nepal. Total numbers of patients included in the study were 30. Consent was taken from Department of pharmacy, Kathmandu University for conducting the study. Similarly informed verbal consent was taken from patient before enrolling them in the study. GM are commonly used in the hospital as an empiric therapy and in infections caused by Gramnegative bacilli. So post operative ward was selected for study as use of GM was high in particular ward as compared to other wards. Patients were selected according to the inclusion criteria which were patients receiving GM in surgery ward, patients receiving GM for more than three days and patients of either gender. And those patients receiving one day GM course for prophylaxis, patient with baseline SCr value higher than normal at the time of screening, patient with pre existing renal disease were excluded from the study. The tools used was a set of prepared questionnaire for each patients on GM. Patient demographic information, drug information and other required information were received by direct patient interview as well as from patient medication cardex and patient medical file. Patients demographic data including age, gender, baseline SCr value, SCr value on 3rd day and after completion of GM therapy were noted. The obtained data were entered in Statistical Package for Social Sciences (SPSS 10) software. The different test such as pair sample t- test, wilcoxon rank test and correlation were applied as appropriate to analyze the data. P value less than 0.05 was considered statistically significant.

RESULTS

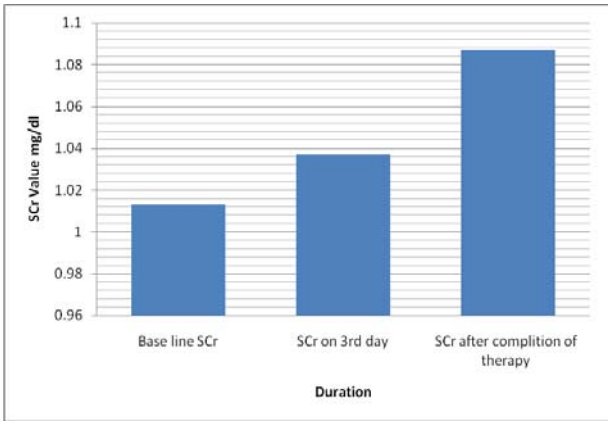
The total numbers of patients enrolled in the study were 30. In the study 21(70%) patients were male and 9 (30%) were female. Rise in mean SCr value was not significant from mean baseline SCr value to mean SCr value on 3rd day of GM therapy (p= 0.257) [Table/Fig 1]. However there was significant rise in mean SCr from baseline to after completion of therapy (p= 0.005) [Table/Fig 2]. The mean baseline SCr value was 1.013 mg/dl, mean SCr value on 3rd day of therapy was 1.037 mg/dl and mean SCr value after completion of therapy was 1.087 mg/dl [Table/Fig 3]. Gender shows no difference in rise in SCr value (p= 0.576) [Table/Fig 4]. However age shows positive correlation with rise in SCr value [Table/Fig 5].

Table/Fig 1: Paired samples statistics between baseline SCr and SCr on 3rd day of therapy

Pairs (n=30)	Mean	Std.deviation	Std.error mean	p-value
Base line SCr value	1.013	0.125	2.286	0.257
SCr on 3rd day of GM therapy	1.037	0.127	2.323	

Table/Fig 2: Paired samples statistics between baseline SCr and after completion of therapy

Pairs (n=30)	Mean	Std.deviation	Std.error mean	p-value
Base line SCr value	1.013	0.125	2.286	0.005*
SCr after completion of therapy	1.087	0.127	2.826	



Table/ Fig 3: Mean SCr value at different time intervals

Table /Fig 4 Wilcoxon rank test (SCr and gender)

Gender	N	Mean Rank	Sum of Ranks	P-value
Male	21	16.070	337.500	0.576
Female	9	14.170	127.500	
Total	30			

Table/Fig 5 Correlation between age and peak SCr

		Age	Peak SCr
Age	Pearson Correlation	1	0.277
	N	30	30
SCr value	Pearson Correlation	0.277	1
	N	30	30

DISCUSSION

GM induced nephrotoxicity is considered to occur after several days of therapy and not immediately, particularly seven days after therapy. The above result shows insignificant rise in SCr value which is further supported by the study conducted by Sweileh WM which found the significant elevation in SCr value from baseline only on the fourth day of treatment with GM on continuous SCr value monitoring [3]. However rise in SCr value was significant after completion of therapy. This result was supported by the study conducted by Bello SO and Chika A. in 2009 which found out that in albino rats given a daily doses of GM 80 mg IM, a significant ($p<0.05$) and progressive rise in SCr levels was observed. The values obtained were 1.33±0.22, 3.38±0.22, and 4.78±0.46 mmol/l at days 0, 5 and 10 respectively [7]. The onset of renal failure caused by aminoglycosides is usually slower and the daily rise of SCr tends to be lower than acute renal failure due to other causes. SCr and BUN characteristically increase 7 to 10 days after initiation of aminoglycoside therapy. In more than half of the cases with nephrotoxicity, the decline in renal function occurs only after the therapy has been completed [8]. Similarly few studies have found that the rate of nephrotoxicity increased by 2% after 6 days and 3.3% after 11 days [9].

In this study gender shows no difference in rise in SCr value. This result is supported by the study conducted by Sweileh WM. in 2009, which concluded that there is no gender difference in susceptibility of hospitalized patients to GM induced nephrotoxicity [10]. Similarly a study conducted by Ali BH et al. in 2001, found that following the GM treatment in intact male and female rats, significant increase in the concentration of plasma creatinine was seen by about 101% and 82% respectively between male and female but there was no gender difference in the histological damage induced by the drug in the cortical proximal tubules [11]. The mechanisms underlying gender differences in aminoglycosides induced nephrotoxicity are difficult to explain. Binding affinity of aminoglycoside and aminoglycoside nephrotoxicity have been cited including the greater binding affinity in male versus female rats. However, more investigation is needed to study the impact of gender on aminoglycoside induced nephrotoxicity.

Age shows positive correlation with rise in SCr value which mean rise in SCr value after GM therapy was increased with advanced age. The pharmacokinetics of GM is extremely variable. Changes in renal function can alter the rate and extent of aminoglycoside elimination with an increase in risk of toxicity. Since renal function tends to decline with increasing age, it is important to establish an individualized dosage regimen [12]. Advanced age has been associated with an increased incidence of aminoglycosides induced nephrotoxicity. Subclinical evidence of impaired renal function was also demonstrated in human. Studies done on risk factors for aminoglycoside induced nephrotoxicity in humans concluded age as a strong risk factor.[3]Result of this research was supported by a study conducted by Sweileh WM. in 2009 which concluded that younger patients on GM showed delayed elevation in SCr suggesting that elderly patients are more susceptible to aminoglycoside induced nephrotoxicity. Advanced age has long been held to be an important risk factor in the development of aminoglycoside-related toxicity [3].

CONCLUSION

GM remains important in the treatment of serious and often life-threatening gram-negative bacterial infections inspite of the introduction of many new antibiotics. Nephrotoxicity receives the most attention, perhaps because of easier documentation of reduced renal function, though it is usually reversible. In most clinical trials, aminoglycosides induced nephrotoxicity has been defined by an elevation of SCr, so periodic monitoring of SCr concentrations is essential.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

Not commissioned; externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.