UTILITY OF SERUM GENTAMICIN LEVELS IN THERAPY OF URINARY TRACT INFECTION

by

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SUMMARY

This study included 48 cases of urinary tract infection, 34 patients had normal renal function (Group A), while 14 had features of impaired renal functions (Group B). Diagnosis of urinary tract infection was based on quantitative colony count. The commonest urinary pathogen was E. coli. All organisms were found to be sensitive to gentamicin. Gentamicin was administered to all the patients in doses of 1.5 mg/kg. with increasing time interval vis-a-vis with increasing severity of renal failure in patients with renal failure.

The serum levels (either peak or trough) were too variable to enable any comparison with blood urea, serum creatinine, dose administered and body weight in both the groups. Forty one per cent patients did not achieve the desired serum concentration of 4 ug/ml and treatment failure resulted in majority of these patients.

Introduction

Gentamicin, an aminoglycosidic antibiotic, has excellent results in Gram negative infections. Since it is excreted almost exclusively by renal mechanisms, it is very effective in urinary tract infections. However, its use in patients with impaired renal function results in accumulation and may be associated with ototoxicity and nephrotoxicity. Also, the absorption after intramuscular injection is variable and these call for need to maintain therapeutic but non-toxic levels in the blood. Measurement of serum concentration is considered to be the best guide for adjustment of dosage schedule of gentamicin. In our country not much work has been done on this useful subject.

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Material and Methods

This study included 48 patients of

urinary tract infection. These were divided into two groups. Group A consisted of 34 patients with normal renal function and Group B of 14 cases with varying degrees of renal function impairment. Group B was divided into B_1, B_2 and B_3 depending on serum creatinine level (Table 1). Diagnosis of urinary tract infection was established on the basis of demonstration of organisms in the properly collected urine, positive culture containing a minimum of 10^5 bacterial colony count per ml of urine (Kass *et al* 1965). Following isolation of bacteria in culture, antibiotic sensitivity test was done by the disc diffusion method (Bauer *et al* 1966).

Serum levels were estimated 1 hour after the injection (Peak/Post dose) and just before the next dose (Trough or basal/Pre dose).

Observation

The commonest causative organism grown in culture was *E. coli* (62.5%). This formed the bulk of infections in Group A, this was followed by P. aeruginosa (25%) which was found more frequently (71.5%) in patients with renal failure. No mixed infection was observed. All organisms were found to be sensitive to gentamicin.

In the patients with normal renal functions (Group A), mean daily dose was

TABLE I
Dosage Schedule of Gentamicin

Groups	Serum Creatinine (mg per 100 ml)	Dose of Gentamicin (mg per kg.)	Dose interval (Hours)
A	Less than 2.0	1.5	8
B_1	2.0-4.9	1.5	1236
B_2	5.0-9.9	1.5	36-72
B_3	10.0 and above	1.5	96 and above

After establishing the diagnosis of urinary tract infection and the sensitivity of the organisms to gentamicin, the drug was given intramuscularly for an average period of 7 days. It was given in dosage of 1.5 mg/kg body weight per dose. In patients with normal renal functions, the drug was given at 8 hourly interval, whereas in patients with renal failure the time internal between the two dosage were extended (Johny *et al* 1975), depending upon renal functional status.

Serum gentamicin levels were estimated by bioassay. Microbiological assay was performed using agar diffusion method with standard strain of Pseudomonas aeruginosa (NCTC 10490) (Broughall, 1978).

202.92 mg per day; range being 180-300 mg/day depending on body weight of the patient. The mean peak serum level (1 hour post injection) of gentamicin achieved after a single dose was 4.53 $\pm$ 1.81 ug/ml. It ranged between 1.1 ug/ml to 9.3 ug/ml. Fourteen (41%) out of 34 patients had serum level below 4 ug/ml with lowest level being 1.1 ug/ml. Out of 14 patients with serum gentamicin levels below 4 ug/ml, 10 (71.4%) had treatment failure as evidenced by positive bacteriological culture after 7 days of gentamicin therapy, whereas there was 100% bacteriological cure in rest of the patients with serum levels above 4 ug/ml.

The mean trough serum level was 1.45

± 0.77 ug/ml, range being from less than 0.625 to 2.5 ug/ml.

In Group B, the mean peak serum level was 8.28 ± 2.11 ug/ml (range — 4.0 to more than 10 ug/ml), while their corresponding trough level was 3.06 ± 1.9 ug/ml (range — 1.4 to 7.3 ug/ml) (Table II).

TABLE II

Serum Gentamicin Level in Patients With or Without Impaired Renal Functions

Group	No. of patients	Peak levels (mean ± S.D.)	Range ug/ml	Trough levels (mean ± S.D.)	Range ug/ml
Normal renal functions	34	4.5 ± 1.81	1.1 to 9.3	1.45 ± 0.77	0.625 to 2.5
Impaired renal functions	14	8.2 ± 2.11	4.0 to >10.0	3.06 ± 1.9	1.4 to 7.3

The resulting mean trough and peak (1 hour post injection) serum levels were found to be significantly ($P < 0.001$) higher in Group B than those of Group A patients.

Discussion

Majority of urinary tract infections are caused by a single urinary pathogen (Prabhu *et al* 1979). Bacteriological spectrum of urinary tract infection is much varied. Most of the authors all over the world have reported *E. coli* as the principle urinary pathogen occurring in about 80-90% of domicilliary or hospital infections (Wing, 1970). Similar results were obtained in this study, *E. coli* being commonest followed by P. aeruginosa.

The aerobic gram-negative bacilli vary in their susceptibility to the aminoglycosides. However, most of the common urinary pathogens such as Enterobacteriaceae and P. aeruginosa strains are susceptible to gentamicin. In the present study there was 100% sensitivity *in vitro* by the disc method to isolates in all the 48 patients.

Concentration of gentamicin in blood is representative of the tissue levels throughout the body and this value may be used for therapeutic purposes (Chis-Holmes *et al* 1968). However, gentamicin has a relatively low therapeutic index, i.e. the therapeutic dose and the potential toxic doses are close to each other. Even standard formula and nomograms prepared by incorporating some of the known factors have not been successful in predicting the dose and serum levels. Therefore, actual monitoring of serum level of the drug is most necessary and is a direct way of achieving adequate therapy (Noone *al et* 1974). Adequate gentamicin therapy is considered to be the dosage, which give a peak serum concentration of 4-8 ug/ml (Hewitt, 1971; Noone *et al* 1974 and Sande and Mandell, 1980).

In this study, in patients without renal failure, the mean peak serum concentration was 4.53 ± 1.81 ug/ml. However, a noticeable individual variation was quite apparent and with similar doses an eight fold variation in peak serum level was