

AMINO GLYCOSIDES; TOXICITY OF ONCE A DAY DOSING

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ABSTRACT ... Aminoglycosides are unique protein synthesis inhibitors and are bactericidal. Instead of three times a day, we gave gentamicin 3 mg/kg once a day, to 10 young patients, whose urine culture report showed sensitivity to gentamicin. They have an average age of 27 ± 6.5 years. The youngest patient was 19 years old and oldest was 37 years old, having normal creatinine clearance. There was no significant ($P > 0.05$) change in renal creatinine clearance before and after 7 days of therapy.

Keywords: Amino Glycosides, Once a day, Nephrotoxicity, Gentamicin, Ototoxicity.

INTRODUCTION

Many diseases are caused by infection. The infections occur due to microorganisms. For killing microorganisms, we use chemical substances known as antibiotics. Salvaran was the first antibiotic used in 1910 for treating syphilis¹. The antibiotics which inhibit the growth of bacteria are known as bacteriostatic and these kill the microorganisms known as bactericidal. Another way to classify the antibiotics are the sites at which they act such as bacterial cell wall or ribosomes.

The antibiotic aminoglycosides act as protein synthesis inhibitors²⁻⁸. Those antibiotics which act as protein synthesis inhibitors are usually

bacteriostatic but aminoglycosides instead of bacteriostatic are bactericidal. They bind with 30s ribosomal subunit, disturbing the initiation of protein synthesis and inducing errors in translation of messenger RNA to peptide. These drugs are highly effective against gram - ve bacilli^{9,10}. The aminoglycosides have side effects on kidney as well as on ear. Numerous studies demonstrate that a single dose of aminoglycosides is just as effective and no more toxic (often less toxic than multiple smaller doses).

Therefore, many authorities now recommend that aminoglycosides should be administered as a single daily dose^{11,12}. The rapidly changing renal function may occur in septic shock or in renal failure

provided. These pitfalls may be avoided as once daily dosing is safe and effective. In order to see the effect of aminoglycosides on renal function and toxicity, we took the following study.

SUBJECTS & METHODS

10 young patients (6 males and 4 females) having average age of 27 ± 6.5 years, youngest 19 years and oldest 37 years, whose urine culture and sensitivity report showed sensitivity to gentamicin were enrolled between June 2001 to April 2002 at Surgical Unit-II PMCH Nawabshah. Their blood urea, creatinine clearance and serum potassium (k) were estimated from laboratory. The patients were asked in detail about nausea, vomiting, vertigo, difficult in standing and tinnitus. Patient having any complaint about nausea, vomiting, tinnitus, vertigo were not included in the study. The laboratory reports and symptoms were noted in table before and after 7 days of treatment. Patients were given gentamicin 3 mg/kg once a day. Students t test was

applied to see the effect on creatinine clearance. As creatinine clearance is the most valuable test for kidney function¹³.

RESULTS

The biochemical laboratory investigations done before and after 7 days therapy with Gentamicin injections, were blood urea, creatinine clearance and serum potassium (k) levels and were expressed as mean \pm S.D values.

The comparative results are shown - Table-I. It clearly indicates that there is no significant difference between these parameters before and after the therapy. Moreover, the development of side effects were evaluated by the findings like, nausea, vomiting, difficulty in standing, tinnitus and vertigo etc. It was clear from the data that no such effect was seen after 7 days treatment with gentamicin injection in both male and female patients. Only two patients complained of nausea.

Table-I. Laboratory Findings before and after Gentamicin Therapy

Patients	Blood Urea (mg%)		Creatinine Clearance (ml/min)		Serum K. (mmol/l)	
	Before	After	Before	After	Before	After
1	40	21	105	120	3.9	3.5
2	33	39	109	115	4.8	2.9
3	29	28	108	119	2.9	4.8
4	37	36	105	104	3.5	3.6
5	27	24	120	118	4.9	4.9
6.	22	20	119	115	3.8	3.7
7.	36	35	120	118	2.9	3.9
8.	29	27	108	111	3.5	3.1
9.	37	33	111	102	4.4	4.5
10.	20	21	107	109	4.6	3.8
Mean	31	28.4	111.2	103.2	3.92	3.87
SD	6.7	6.9	6.1	6.2	.7	.6

DISCUSSION

The aminoglycosids are considered to be potentially

toxic drugs. They are particularly toxic for kidney and vestibulocochlear nerve. These toxicities occur only when this drug is used for a prolonged period and when the plasma concentration remain above toxic level for longer time. With normal renal function, the 24 hours duration is sufficient time for clearing the drug and toxicity usually does not occur. The renal toxicity caused by amino glycosides is reversible. The ototoxicity first effects the higher waves, which can be detected by audiometer.

Our patients did not develop any gross urinary malfunction. The creatinine clearance before therapy was average 111.2 ± 6.1 ml/minute and after treatment, it was average 113.3 ± 6.2 ml/minute ($P > 0.05$). The serum potassium was average 3.92 ± 0.7 mmol/l and after seven days average 3.87 ± 0.6 mmol/l. The urea before the therapy was average 31 ± 6.7 mg/dl and after therapy it was average 28.4 ± 6.9 mg/dl. Our patients did not develop toxicities regarding vestibulocochlear nerve such as headache, vertigo, vomiting or difficulty in standing. Only our two patients complained about nausea, which were probably due to dietary reasons. Even patients with impaired renal function are given amino glycosides but it should be given with longer interval between doses. Our patients with normal renal function did not develop any gross malfunction relating to kidney or ear after 7 days of once a day therapy with amino glycosides, as 24 hours period is sufficient to wash out the drug.

CONCLUSION

Short term (7 days) therapy with gentamicin (Amino Glycosides) once a day instead of 3 times a day, does not effect the renal or ear function of the patients significantly.

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