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Original Article

Every Other Day Gentamicin Injection in Experimental Pyelonephritis in Rats: Risk of Scar Formation

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Abstract

Background: Urinary tract infection in children may cause renal scar formation, which can be prevented by early and appropriate treatment. Recent studies showed that single daily injection of gentamycin can produce best effect without increasing the side effects. The aim of this study was to evaluate the rate of renal scar formation when new regime (every other day gentamicin injection) used for treatment of urinary tract infection.

Methods: Forty eight Sprague Dawley rats were infected by inoculation of 0.1 ml Uropathogenic E.coli suspension (10^9/ml) to their left kidneys. The rats were divided into four groups after 24 hours. Gentamicin was administrated intraperitoneally at dosages of 10mg/kg (daily), 10mg/kg every other day or 20mg/kg every other day to the first three groups. The fourth group did not receive any antibiotic. Renal scar formation was evaluated by histology and responses were evaluated by counting colony forming units (CFU)/ml of homogenized kidney tissue and percentage of sterile kidneys.

Results: Evaluation of all sections showed that 0-30% of interstitial tissues had scar formation. The results showed no significant difference in scar formation between the first three groups, but showed mild to moderate scar formation in the fourth group.

Conclusion: It was concluded that 10mg/kg or 20mg/kg of gentamicin usage in every other day interval dose did not increase the risk of renal scar formation while it had appropriate efficiency.

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Keywords ● Urinary tract infection ● gentamicin ● scar

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Introduction

Urinary tract infection (UTI) in children may cause renal scar formation, which can lead to hypertension and renal failure. About half of the children with acute pyelonephritis develop renal scar.[1] The scars in older children might be the result of unrecognized infection.[2] Therefore, it is logical to prescribe appropriate antibiotics after collecting a diagnostic urine sample.[3,4] Many classes of antibiotics are used for the management of UTI. Among which aminoglycosides are one of the most commonly prescribed. A problem in the use of aminoglycosides is the frequency of injection such as three times a day. Moreover, their use is associated

with renal toxicity. A recent study showed that single daily injection can produce best effect without increasing the adverse effects.[5] The objective of the present study was to examine whether every other day administration of gentamicin might be the cause of renal damage because of delayed microbial eradication.

Materials and methods

Forty eight adult male Sprague Dawley rats (200-250 g) were obtained from Animal Breeding Center, Shiraz University of Medical Sciences. Uropathogenic E. coli was isolated from the patients with proven urinary tract infection, and tested for gentamicin sensitivity. A suspension of the organism with a concentration of 10^9/ml was prepared. The animals were anesthetized with Ketamine (35 mg/kg) and Xylazin (5 mg/kg), and under aseptic condition an oblique incision was made on the left flanks to expose the left kidneys. Afterwards, bacterial suspension (0.1 ml) was injected into both poles of the left kidneys as described by Miller and Robinson.[6]

Twenty four hours later, the rats were divided into four groups. Group one received gentamicin at 10mg/kg/day, group two received gentamicin 10mg/kg every other day, group 3 received gentamicin 20 mg/kg every other day, and group 4 received no antibiotic. The drugs were administered intraperitoneally, and continued for one week.

At the end of the treatment, half of the animals were killed by decapitation, and the left kidneys were excised in sterile conditions. The kidneys were sent for microbiologic study. The percentage of sterile kidneys and CFU/ml of homogenized kidney tissues were considered as indices of the effectiveness of the treatment. The rest of the animals were killed after 8 weeks. Their kidneys were sent for evaluation of long term complications, scar formation, as well as microbiologic study.

Histopathologic study was done by light microscope on sections stained with hematoxylin and eosin. Cortex and medulla including glomeruli, tubules, vessels, and interstitium were examined. Renal scaring was defined as tubulointerstitial fibrosis that characterized by fibroblastic proliferation and excessive matrix accumulation.[7] Severity and extrusion of scar formation were also evaluated by a pathologist who was blind to the study, and classified as mild (<10%), moderate (11-20%), and severe (>20%).

SPSS software version 11.5 was used for statistical analysis. Data were analyzed using Chi-square or analysis of variance (ANOVA). In cases of significant findings with ANOVA, pairwise comparisons were made by Duncan's Multiple Range test. A P value of ≤0.05 was considered statistically significant.

Results

The rates of sterile kidneys in the groups that received gentamicin were 60%, 90.9%, and 60%, respectively. There was no significant difference among groups 1, 2, and 3 in terms of the percentage of sterile kidneys. There was also no significant difference in colony counts among such groups. The fourth group had no sterile kidney.

Pathologic study showed intact glomeruli and vessels. There was 0-30% scar formation in the fourth group. Maximum scar formation (30% of the interstitium) was seen in one case of this group (figure 1). On he average, there was mild to moderate scar formation in the fourth group (table 1), but no scar formation was found in the other groups.

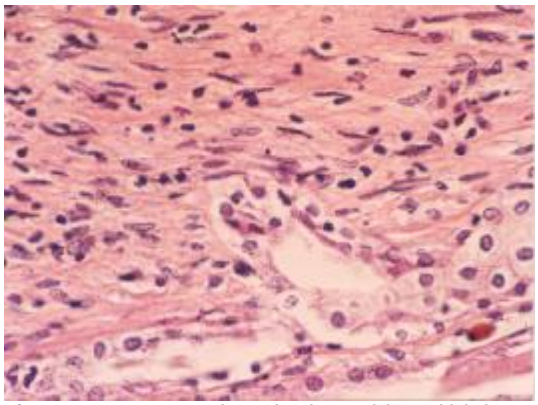

Figure 1: Severe scar formation in renal interstitial tissue of rats 8 weeks after bacterial inoculation in group without treatment (H&E x400).

Table 1: Degree of scar formation in the fourth group

Case number	Degree of scar formation
43	15%
44	20%
45	30%
46	10%
47	5%
48	0%

Discussion

Acute pyelonephritis may produce permanent renal damage, which can subsequently lead to diverse complications including hypertension and loss of renal function.[8] Pyelonephritis accounts for approximately 20% of all renal transplantation.[9] Many factors contribute to the risk of scar formation such as age of patients, febrile UTI, repeated UTI, and presence of vesicourethral reflux.[10,11] Benador and coworkers showed that the risk of scar formation

might not be diminished by age, but all children would benefit from early measures to prevent the renal damage.[12] Active management is worthwhile because it prevents the sequels.[3]

One of the problems in management of UTI is the compliance of patient for parenteral drug usage. Aminoglycosides are one of the most common antibiotics used for the treatment of UTI. They are concentrated in the kidneys and have long effects in urine. According to long post administration effects, gentamicin is suitable for single daily dose with fewer side effects instead of three times a day.[13,14] The present study showed that every other day gentamicin injection had the same efficiency as single daily one. It also showed that every other day gentamicin injection did not have serious side effects, and did not increase the rate of scar formation.

Repeated injections are painful and stressful for children, therefore, reducing the number of injections would add to their compliance. The findings of the present study might be taken as evidence that it might be possible to reduce the number of gentamicin injections to every other day regimen without increasing the risk of renal scar formation.

Conclusion

In conclusion, the findings of the present study suggest that every other day administration of gentamicin can be as effective as every day injection in treating UTI without increasing the chance of renal interstitial scar formation.

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