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Effects of Gentamicin on Iron and Copper Contents of Kidney Tissue

Dear Sir,

Gentamicin is an aminoglycoside antibiotic, which is widely used in the treatment of gram-negative infections. There are however several reports indicating that gentamicin is nephrotoxic [1, 2]. Mechanisms relating to its nephrotoxicity have not yet been fully clarified. Several researchers suggest that toxicity mainly arises from increased lipid peroxidation due to changed free radical metabolism [2–5]. Concerning this subject, Walker and Shah [2] suggested that deferoxamine, an iron chelator, prevented gentamicin-induced renal failure. They concluded that the primary radical responsible for the gentamicin-induced lipid peroxidation was the hydroxyl radical (OH), which was formed from the superoxide radical and hydrogen peroxide by the Haber-Weiss reaction. In this kind of reaction, the primary catalyst is iron. For this reasons, researchers proposed that tissue iron concentrations might be of importance in the hydroxyl radical formation process [2]. They assume that reactive oxygen metabolites might play a role in the release of iron from ferritin into tissue and an additional possible source of iron for the generation of hydroxyl radical might be the enhanced uptake of iron by tissue. In fact, altered trace metal metabolism with increased concentrations of iron in kidney have previously been reported in some diseases [6]. However, it has been pointed out that the precise source of iron and how it gets mobilized to participate in the generation of hydroxyl radical in gentamicin-induced acute renal failure remains unknown.

In our opinion, one must first elucidate the tissue iron status in such a state before making hypothetical evaluations. To test this hypothesis, we treated 10 guinea pigs (2 months old, weight 450 g approximately) with gentamicin (200 mg/kg/day) for 10 days. As control group we used another 10 guinea pigs injected with only physiologic serum solution during this period. Then the animals were killed by cervical dislocation and the kidneys were removed. After they had been homogenized, protein concentration was measured by using Lowry's method [8]. Copper and iron concentrations of the homogenates were determined with an atomic absorption spectrophotometer (Varian Techtron, model AA6, AAS). In the analysis, a standard addition technique was used [8]. Results were shown in table 1. As seen from table 1, there were no differences between the content of the elements in the groups.

Table 1. Element contents of kidney tissues (μg/g protein) from gentamicin-treated and control guinea pigs

	Iron ($p > 0.05$)	Copper ($p > 0.05$)
Control group (n = 10)	330.7 ± 80.9	119.1 ± 57.8
Gentamicin group (n = 10)	334.0 ± 67.7	114.6 ± 39.7

Statistical significance was evaluated with the Student t test.

The results suggest that gentamicin does not cause any changes in copper and iron concentrations of the kidney tissues. Our data do not support the hypothesis of Walker and Shah that increased tissue iron concentration plays a part in the increased hydroxyl radical production via the Haber-Weiss reaction. Since copper concentrations are also determined to be unchanged in the kidney tissues from gentamicin-treated animals, we think that the accelerated Fenton reaction (with copper as catalyst) is not an additional factor.

It seems that there must be some other factors responsible for the gentamicin-induced nephrotoxicity and a possible role of these metals seems unlikely.

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