

Effect of Curcumin in Gentamicin Induced Ototoxicity

M. Abirami*, M. J. Raja, R. Madheswaran, P. Mekala and P. Visha

Department of Veterinary Pharmacology and Toxicology
Veterinary College and Research Institute - Namakkal

*Corresponding Author E-mail: abirami029@gmail.com

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ABSTRACT

Gentamicin is an antibiotic that exhibits a broad spectrum of (Gram –ve) activity and is particularly valuable in several sepsis in animals and humans. Nephrotoxicity and ototoxicity has been recognized as a major complication of aminoglycoside antibiotics for many years. Gentamicin causes reversible renal impairment. The incidence of renal failure is 10-15 % (Naidu et al., 2000) and 10-20 % (Silan et al., 2007) of therapeutic courses. Antibiotics in the aminoglycoside class, such as gentamicin and tobramycin, may produce cochlea toxicity through a poorly understood mechanism (Dobie et al., 2006). The present study aims at studying the ototoxic effect of gentamicin at one high dose (40 mg/kg). The 24 Wistar Albino rats were divided into 4 equal groups (Control, Gentamicin group, curcumin at low and high dose group). The histopathological alterations reveal that the curcumin has reversible effect in gentamicin induced ototoxicity.

Keyword: Gentamicin, Ototoxicity, Curcumin

INTRODUCTION

Gentamicin, an aminoglycoside antibiotic is widely used against a wide range of bacterial infections, mostly Gram-negative bacteria including *Pseudomonas*, *Proteus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Serratia* and Gram-positive *Staphylococcus*. Gentamicin is used commonly in the treatment of respiratory, urinary tract infections, blood, bone and soft tissues infections in human and animals. Aminoglycoside antibiotics are prototype drugs having nephrotoxicity as major side effect. The mechanism of gentamicin induced

nephrotoxicity is not completely understood. However, oxidative stress is implicated as central mechanism of the gentamicin-induced renal cell injury (Walker et al., 1999).

MATERIALS AND METHODS

Chemicals

Gentamicin Sulphate -40mg/ml and curcumin were used in this study.

Animals

Twenty four adult Wistar albino rats weighing approximately 150-200g and aged were used in this experimental study.

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Rats were provided form LAM (Laboratory Animal Medicine) unit, Madhavaram. The rats were housed in plastic cages and fed with *ad libitum* feed and water throughout the experiment.

Experimental design

Rats were divided randomly into 4 equal groups including six animals each.

Group I

Control group: NS (same volume of GS) S/C for 15 days

Group II

Gentamicin sulphate: GS (40 mg/kg) S/C for 15 days

Group III

Curcumin at 50 mg/kg body weight oral for 15 days

Group IV

Curcumin at 100 mg/kg body weight oral for 15 days

Sample Collection

All the animals were fasted overnight before sacrifice. At the end of the study the animals

were sacrificed humanely under deep ether anaesthesia. For histopathological investigation representative samples of cochlea was collected and fixed in 10 per cent buffered neutral formalin solution. Samples were cut at 5 micron thickness and stained with Hematoxylin and Eosin and examined microscopically

Histopathological alterations

In control (T_1), histopathological analysis of cochlea showed normal cochlea showing striated epithelium (Fig. 1). Histopathology of the cochlea showed multiple layers of lining epithelium and severe mononuclear cell infiltration in negative control (T_2) group (Fig. 2). At low dose of curcumin (T_3) histopathology of the cochlea showed moderate thickening of lining epithelium and mild mononuclear cell infiltration (Fig. 3). At high dose of curcumin (T_4) histopathology of the cochlea showed degeneration and mononuclear cell infiltration in lining epithelium (Fig. 4).

Histopathological alterations

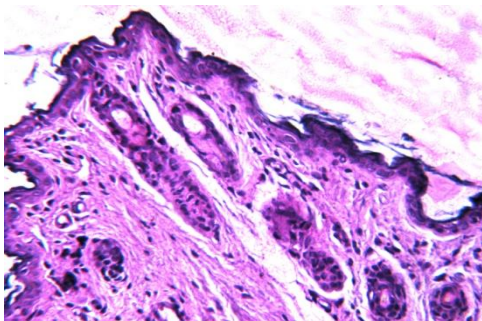


Fig. 1: Cochlea showing striated epithelium. H&E: 40x

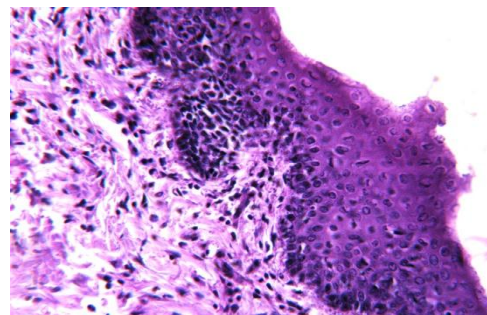


Fig. 2: Cochlea showing multiple layers of lining epithelium and severe mononuclear cell infiltration. H&E : 40x

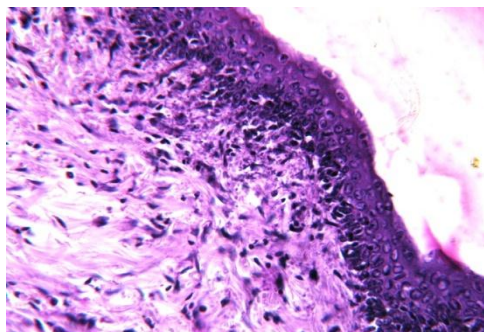


Fig. 3: Cochlea showing moderate thickening of lining epithelium and mild mononuclear cell infiltration. H&E: 40x

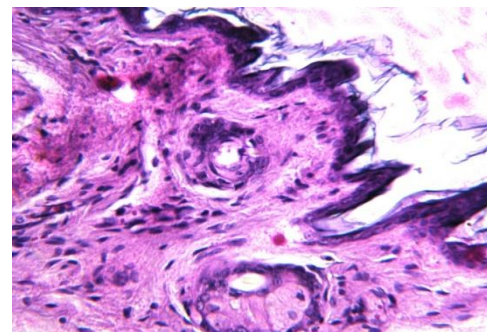


Fig. 4: Cochlea showing degeneration and mononuclear cell infiltration in the lining epithelium. H&E : 40x

RESULT AND DISCUSSION

Bucak et al. (2015) studied and reported that the curcumin had protective role in paclitaxel induced ear damage in rats and has the ability to significantly protect the cochlear morphology and functions

Antibiotics in the aminoglycoside class, such as gentamicin and tobramycin, may produce cochlea toxicity through a poorly understood mechanism (Dobie et al., 2006). It may result from antibiotic binding to NMDA receptors in the cochlea and damaging neurons through excitotoxicity (Basile et al., 1996). In this study, an attempt was made to explore the ototoxic effect of gentamicin and ameliorating property of curcumin and nanocurcumin in rats. The ototoxic effect of gentamicin with marked negative alterations in histomorphological features showed multiple layers of lining epithelium and severe mononuclear cell infiltration of cochlea in rats. Aminoglycoside induced production of reactive oxygen species may be the reason for cell injury of cochlea (Wu et al., 2002).

During treatment, dose dependent response was noticed in groups treated with curcumin. Low and high dose of curcumin showed moderate thickening of lining epithelium with mild mononuclear cell infiltration and degeneration with mononuclear cell infiltration in lining epithelium respectively. The results of the study are in accordance with the study of Bucak et al. (2015) was in the protective role of curcumin in Paclitaxel induced ear damage in rats was reported. These confirm the ability of curcumin in protecting cochlear morphology and functions.

Histopathological alterations

In control (T₁), histopathological analysis of cochlea showed normal cochlea showing striated epithelium. Histopathology of the cochlea showed multiple layers of lining epithelium and severe mononuclear cell infiltration in negative control (T₂) group. At low dose of curcumin (T₃) histopathology of the cochlea showed moderate thickening of

lining epithelium and mild mononuclear cell infiltration. At high dose of curcumin (T₄) histopathology of the cochlea showed degeneration and mononuclear cell infiltration in lining epithelium.

CONCLUSION

According to this study the clinical observations, histopathological changes reveal that curcumin induces the gentamicin induced ototoxicity. The use of aminoglycosides antibiotics must be regulated by administering it for specifically required cases after doing ABST or MIC. The unwanted usage of aminoglycoside antibiotics must be avoided or may be used by combining it with some herbal medicine like curcumin which may reduce the ototoxicity.

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