

OTOTOXICITY OF STREPTOMYCIN AND GENTAMICIN IN IRAQI RAMS

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SUMMARY

The aim of this research was to investigate the ototoxic effects of two different aminoglycoside antibiotics, namely streptomycin and gentamicin on Iraqi rams.

These antibiotics were injected intramuscularly using the therapeutic and double doses of each. The data showed no clear differences in their effects on both vestibular and cochlear structures of inner ear as they showed similar histological changes but in different intensities.

INTRODUCTION

The ototoxic damage caused by drugs has been the subject of interest for many years and has become more important after the discovery of aminoglycoside antibiotics. It has been demonstrated by many workers that aminoglycoside antibiotics are retained in the ear fluid^(1,2,3,4) In this way the delicate structures of the inner ear are directly exposed for long time to concentrations of these antibiotics. Workers in this field has shown that ototoxicity depends on many factors such, the type of aminoglycoside used^(5,6), duration of exposure and the amount of dosage used^(7,8,9,10,11,12).

In the present work an attempt was made to study the histological ototoxic damage of two different doses of two different aminoglycoside antibiotics.

MATERIALS AND METHODS

Twenty-five healthy adult male Iraqi rams with a body weight of 40-50Kg, aging 1-1.5 years were used in this study. The animals were randomly divided into five equal groups.

Groups I and II were injected intramuscularly with a therapeutic dose of 10mg/kg and a double dose of 20mg/kg B.W. daily of streptomycin sulfate for seven days. Groups III and IV were injected intramuscularly with a therapeutic dose of 5mg/kg and a double dose of 10mg/kg B.W. daily of gentamicin sulfate also for seven days. Group V animals served as control. Three animals from each group were sacrificed at the end of the first period, while the remaining two were re-injected with the two doses of the two antibiotics for other seven days, then were sacrificed at the end of the second period.

The structures of inner ear were dissected out, fixed in 10% formal saline and 1.5% osmium tetroxide, processed in a series of graded ethanol, embedded in paraffin. Sections were cut at six micrometers thickness and stained with Harris hematoxylin and eosin, while those fixed in osmium tetroxide were examined without staining using a light microscope.

RESULTS

There was no clear differences in the effect of the two antibiotics used in this study, therefore, it can be generally stated that both antibiotics used caused the same histological changes but in different intensities in comparison with control animals (Fig.1). In the therapeutic dose of streptomycin (10mg/kg B.W.), the effect was shown mostly in cochlear neuroepithelium, however, damage to vestibular structures, semicircular canals and spiral ganglion which is not severe (Fig. 2, A). Slight degenerative changes particularly pyknosis of the outer sensory hair cells and Hensen's cells but were remarkable in Corti organ (Fig. 3, A). At the double dose (20mg/kg B.W.) the nuclei of outer sensory hair cells and outer phalangeal cells were pyknotic and sometimes completely necrotic, this was also obvious in Hensen's cells (Fig.3, B). Some neurons of spinal ganglion showed different degree of necrosis that corresponded to the duration of injected dose (Fig. 4, A & B).

Gentamicin was found to affect the sensory and supporting cells of Corti organ. Changes were more pronounced by this antibiotic than by streptomycin. The outer sensory hair cells and Hensen's were more affected than the inner sensory hair cells were more affected than the other types of supporting cells. These changes became more pronounced in the double dose of gentamicin (Fig. 3, C). Gentamicin affected the neural epithelium of the vestibular structures and semicircular canals especially the of macula sacculi and superior crista ampullaris (Fig. 2, B). The degenerative changes of this antibiotic in spiral ganglion were similar to that of streptomycin. At the double dose of gentamicin, the eighth nerve showed myelin degeneration in many fasciculi (Fig. 5).

DISCUSSION

The ototoxic effects of streptomycin on the cochlea, Corti organ and the outer sensory hair cells are evident. Results of this study revealed that this antibiotic has damaging effect by the two different doses used (10mg/kg & 20mg/kg B.W.). Similar degenerative changes to those induced by this antibiotic were also noticed earlier^(13,14). *Voldrich*⁽²⁾ injected intramuscularly streptomycin and other aminoglycosides in guinea pigs. He

observed ototoxic effect in the inner ear. The degree of this ototoxicity depended on the dose of the antibiotic used and elimination rate from the inner ear.

Our observations are in agreement with the findings of *Cawthorne* and *Ranger*⁽¹⁵⁾ that the degenerative changes after injecting streptomycin were especially pronounced in the cochlear structures, whilst the vestibular structures appeared normal.

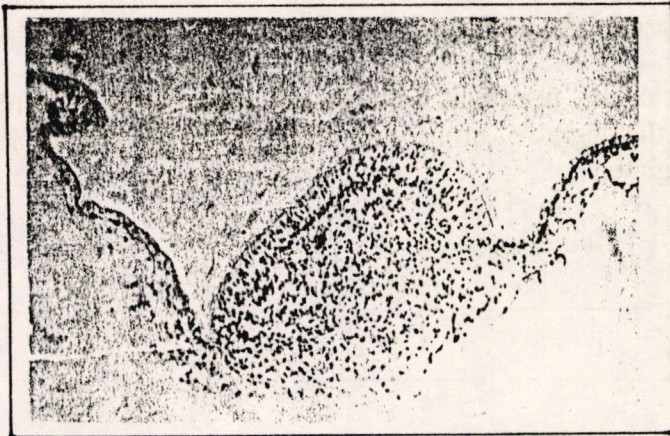
The ototoxicity of gentamicin was more pronounced in both cochlear and vestibular structures in the two doses used (5mg/kg and 10mg/kg B.W.) in comparison with that of streptomycin. This feature of gentamicin effect was mentioned earlier^(10,16,17).

In the present work the degenerative changes in the inner ear of local breed rams are in agreement with the findings in guinea pigs⁽¹⁰⁾ and in squirrel monkeys⁽⁹⁾.

In conclusion, histological studies of aminoglycoside antibiotics effects showed that the degree of ototoxicity depended on the type of antibiotic used, the dosage regimen.



(A)



(B)

Fig.1 : Ampulla and macula of semicircular canal of a control Iraqi rams, H & E, X200.
A-Crista ampullaris, B-Macula sacculi, Note the normal neuroepithelium.

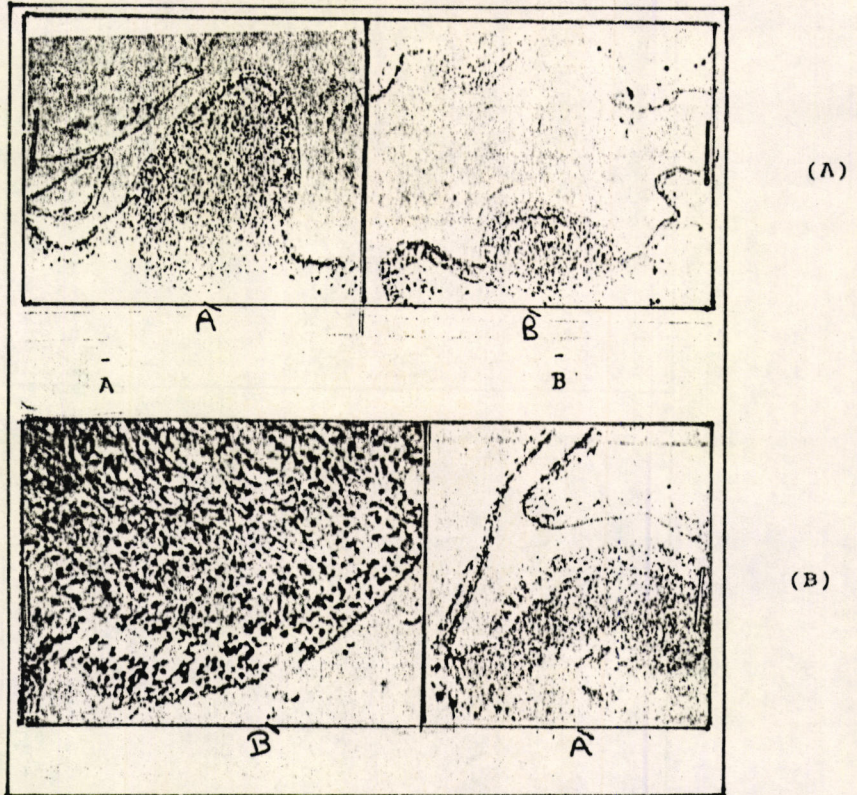
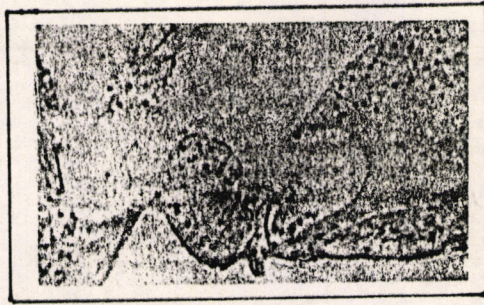


Fig.2 : Ampulla and macula of semicircular canal of Iraqi rams injected intramuscularly with streptomycin and gentamicin.

A : Note slight degenerative changes in neuroepithelium of crista ampullaris (A) and macula sacculi (B) after injection with streptomycin, H & E, X100.

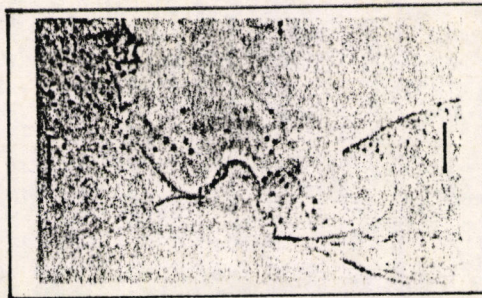
B : Showing more degenerative changes in neuroepithelium after injection with gentamicin, H & E, X250.



(A)

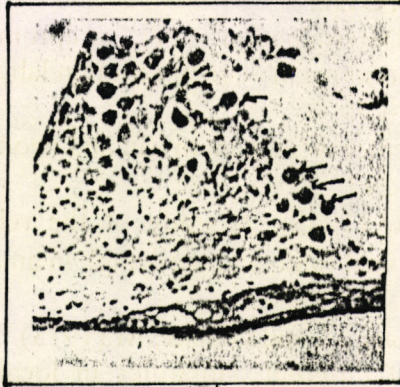


(B)

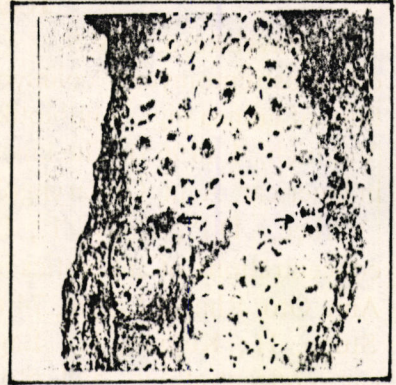


(C)

Fig.3 : Corti organ of injected Iraqi rams.
A : Therapeutic dose of streptomycin : Note pyknosis of the outer sensory cells and Hensen's cells, H & E, X200.
B : Double dose of streptomycin showing pyknosis of the outer sensory cells and outer phalangeal cells, some of them were completely necrotic, H & E, X312.
C : Double dose of gentamicin showing extensive degenerative changes in sensory cells and supporting cells, H & E, X200.



(B)



(A)

Fig.4 : Spiral ganglion of Iraqi ram injected with streptomycin showing necrosis in some neurons, H & E, X250.

A : Therapeutic dose (10mg/kg b.w.).

B : Double dose (20mg/kg b.w.).

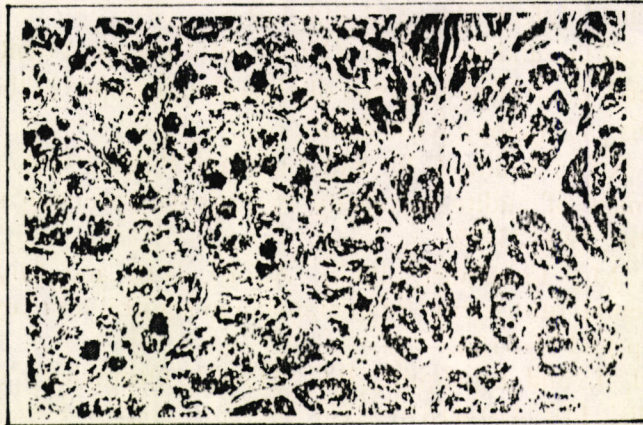


Fig.5 : Eight nerve of Iraqi ram injected with double dose of gentamicin (10mg/kg b.w.), osmium tetroxide, X250, showing myelin degeneration.

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التأثيرات السمية للمضادين الحيويين (الستربتومايسين والجنتاميسين) على الأغنام العراقية

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الخلاصة

يهدف البحث الى معرفة التغيرات النسيجية في الأذن الداخلية للأكباش العراقية بعد استعمال مضادين حيويين من مجموعة الأمينوكليكويزات هما الستربتومايسين والجنتاميسين .
استعمل 25 من الأكباش البالغة قسمت الى خمس مجاميع احداها بمجموعة سيطرة والمجاميع الأربعة الأخرى حقنت عضلياً بالمضادين وبجرعتين احداها جرعة علاجية والأخرى جرعة مضاعفة .

اظهرت النتائج بأن التأثيرات النسيجية لكلا المضادين متشابهة ولكن شدتها مختلفة حيث انحصرت تأثير الستربتومايسين في الجزء القوقعي للتيه الغشائي بينما كان تأثير الجنتاميسين على الجزء الدهليزي والقوقعي للتيه الغشائي .