Original Article

ISSN (0): 2455-5274; ISSN (P): 2617-5207

Diameters of Perikarya in Different Regions of Rat Central Nervous System after Streptomycin and Kanamycin Intoxication

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Abstract

Introduction: Streptomycin and Kanamycin, an aminoglycosidic antibiotic, is known to destroy the ventral cochlear nuclei of brainstem in man. Ototoxicity is well known side effect of kanamycin, the effect on central nervous system in general and central auditory pathway in particular is still unclear. **Subjects and Methods**: Thirty albino rats were divided into three groups I, II and III of ten animals each. Group III was control. Group I and II received Streptomycin (30mg/Kg body weight) and kanamycin (400mg/kg body weight) intramuscular injections, daily for 3 weeks. Paraffin embedded sections of cerebellum, spinal cord, dorsal cochlear nucleus, inferior colliculus nucleus and auditory cortex were stained with haematoxylin and eosin stains and perikarya measured using slide and ocular micrometres. **Results:** Size of cerebellar Purkinje cells increased significantly in control rats for streptomycin and kanamycin intoxicated animals respectively. Ventral horn cells of spinal cord are affected highly significantly only by streptomycin. Vestibular nucleus also showed similar results i.e. neuronal body. Neurons of dorsal cochlear nucleus is affected significantly by both the drugs i.e. streptomycin and kanamycin. **Conclusion:** Streptomycin causes an increase in diameter of auditory cortical cells on other hand kanamycin led to highly significant decrement in size of cells of same region. Preferential affinity and differential effects were noticed. The latter throws some clues about mechanism of action.

Keywords: Histomorphometry, kanamycin, neurotoxicity, perikarya, streptomycin.

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Received: March 2019
Accepted: March 2019

Introduction

Streptomycin, an aminoglycosidic antibiotic, is known to destroy the ventral cochlear nuclei of brainstem in man.[1] Kanamycin, another member of same group was introduced by Umezava to supplement streptomycin and dihydrostreptomycin.[2] Although ototoxicity is well known side effect of kanamycin, the effect on central nervous system in general and central auditory pathway in particular is still unclear.[1] Both the drugs are antitubercular, but the kanacmycin is often used intramuscularly in resistant cases of septicaemia due to Escherichia coli and Proteus.[3] Toxicities of both the drugs have been explored at multiple levels of organzations i.e.biochemical,[4,5] histochemical and neurohistological.[6-8] Unfortunately the mechanism of action is yet to be ascertained. The differential and preferential effects of the two drugs on CNS have further generated interest in such studies.[9,10] The authors have analysed an unpublished restropective histomorphometric results of neuronal perikarya of rat central nervous system intoxicated with streptomycin and kanamycin. Looking into the study with different angle might provide some clue to mechanism of action.

Subjects and Methods

Thirty male albino rats weighing, about 180±10g were divided into three groups of ten animals each. They were fed gram ad libitum with ready access to tap water. The first group of rats received streptomycin sulphate (ambystrin, Sarabhai) in a dose of 30mg/kg body weight, IM, daily for 21 days. Second group of animals received kanamycin sulphate (kancin, Alembic) IM (400mg/Kg body weight daily) for 3 weeks. Physiological saline was injected into the third group IM daily for same period. Doses of antibiotics were decided on the basis of previous literature.[9,10] All the rats were anaesthetised with sodium pentobarbitone 30mg/kg body weight intraperitoneally on day 22 and perfused through heart with 10% neutral formalin. Paraffin embedded sections of different parts of CNS were stained with 1% thionin. Perikarya of different regions of CNS were measured by using slide and ocular micrometers in both control and experimental groups. Results were analysed by using Student's 't' test.

Result

[Table 1] shows effect of streptomycin and kanamycin intoxication on the size of perikarya of neurons in selected regions of central, auditory and vestibular pathways. Size of cerebellar Purkinje cells is increased significantly from 13.08 µm in control rats to 15.14µm and 16.65µm for streptomycin and kanamycin intoxicated animals respectively. Ventral horn cells of spinal cord are affected highly significantly only by streptomycin in which size increased from 19.19 µm to 27.30 µm. Vestibular nucleus also showed similar results i.e. neuronal body showed a significant increase (from 22.30 µm to 24.76 µm) in streptomycin treated animals. The control value of 11.95 µm neurons of dorsal cochlear nucleus is affected significantly by both the drugs i.e. streptomycin and kanamycin but the former caused increased in the value to 14.49 µm and latter resultant decreased in the measurement to 10.38 µm. Effects of drugs were observed in both medium and small sized cells of inferior colliculus. Although both the cell types show swelling by both the drugs but effect was produced more by kanamycin compared to styreptomycin in terms of percentile changes. There was 30% and 10% increase in size by kanamycin in medium and small sized cells respectively while only 19% and 9% increase in two cell types respectively by streptomycin. Streptomycin causes an increase in diameter of auditory cortical cells from 12.49 µm in control rat to 13.01µm in experimental one but this difference is not highly significant. On the other hand kanamycin led to highly significant decrement in size of cells of same region. The size was found to be 10.97 µm in experimental rats compared to 12.49µm in control ones.

Table 1: Diameters of perikarya in different regions of rat-CNS after streptomycin and kanamycin

Regions		Control	Streptomycin	Kanamycin
Purkinje cells of cerebellum		13.08±0.27	15.14±0.31*(↑16 %)	16.65±0.28*(↑27 %)
Ventral horn cells of spinal cord		19.19±0.75	27.30±1.11*(↑42 %)	22.75±1.37*** (19%)
Vestibular nucleus		22.30±0.72	24.76±0.70*(↑11 %)	22.43±1.02 NS
Dorsal cochlear nucleus		11.95±0.24	14.49±0.45*(↑21 %)	10.38±0.26 * (↓13%)
Inferior Colliculus	Medium sized cells	15.30±0.45	18.81±0.67*(↑19 %)	19.92±0.59*(↑30 %)
	Small cells	10.23±0.22	11.19±0.32** (↑9%)	11.24±0.29*(↑10 %)
Auditory cortex		12.49±0.32	13.01±0.23** (↑6%)	10.97±0.27*(↓12 %)

*P<0.001, **P<0.01, ***p<0.02, NS Not Significant,(Per cent change, ↑increased,↓decreased)

Discussion

Aminoglycosides are known to bring about changes in central auditory pathway.[6,11,12] Present study considers more regions in central nervous system to rule out a generalised effect. Degeneration in central nervous system is slow compared to peripheral ones therefore an alteration in it at microscopic level due to drug toxicity makes it a serious issue.[13] Spinal cord and vestibular nucleus is affected exclusively by streptomycin. Such preferential effect on spinal cord by streptomycin has been reported earlier.[9]

Preferential toxicity of streptomycin on both spinal cord and cerebellum was noticed by Faruqi et al.[10]

Cerebellar toxicity was noticed in our study also but equally affected by streptomycin and kanamycin. Interestingly kanamycin showed its effect mainly on dorsal cochlear nucleus, inferior colliculus and auditory cortex.

So, we can say that streptomycin is more toxic to vestibular pathway and kanamycin is more damaging to auditory pathway with some overlapping. Such effects are long established.[14] Although in most of the cases there was an increase in size of perikarya but kanamycin specifically caused reduction in sizes of cells in dorsal cochlear nucleus and auditory cortex. Most common cause of increased size is osmotic swelling due to ATP depletions leading to failure of ATP dependent Na+/K+ pump and Ca2+ pump. This leads to influx of Na+ and Ca2+ and in turn logging of water inside the cell.[15] An extension of study at molecular level is needed to ascertain the exact mechanism of toxicity.

Conclusion

Streptomycin causes an increase in diameter of auditory cortical cells on other hand kanamycin led to highly significant decrement in size of cells of same region. Preferential affinity and differential effects were noticed. The latter throws some clues about mechanism of action.

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How to cite this article: Tandon R, Gupta P, Syed M, Faruqi NA. Diameters of Perikarya in Different Regions of Rat Central Nervous System after Streptomycin and Kanamycin Intoxication. Acad. Anat. Int. 2019;5(1):59-61.
DOI: dx.doi.org/10.21276/aanat.2019.5.1.13

Source of Support: Nil, **Conflict of Interest:** None declared.