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**EVALUATION OF GENTAMICIN SULFATE IN AQUEOUS HUMOR
OF DONKEYS FOLLOWING ITS ADMINISTRATION**
(With 2 Table and 1 Figure)

By

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تعيين تركيز سلفات الجنتاميسين في السائل المائي للعين في الحمار

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تم في هذا البحث استخدام سلفات الجنتاميسين في ٢٠ حمار بالغ طبيعي العين من الناحية الاكلينيكية . قسمت الحيوانات إلى خمس مجموعات : في المجموعة الأولى تم الحقن في الوريد وفي الثانية تم الحقن تحت ملتحة العين وفي الثالثة كان الحقن في الوريد مع التنقيط الموضعي على العين وفي المجموعة الرابعة تم الحقن تحت الملتحة للعين مع التنقيط الموضعي على العين بينما في المجموعة الخامسة استخدم التنقيط الموضعي فقط . أخذت عينات من السائل المائي للعين لمدة ٢٤ ساعة ثم تم تعيين تركيز سلفات الجنتاميسين بكتريولوجيا (معمليا) . أوضحت النتائج أنه للحصول على تركيز عالي من المضاد الحيوي داخل العين يفضل الحقن في الوريد أو الحقن تحت ملحمة العين . بينما الاستخدام الموضعي لا يعطي نتائج فعالة خاصة في الحيوانات .

SUMMARY

The concentration of gentamicin sulfate inside the aqueous humor of twenty normal adult donkeys was measured periodically after its administration by five different routes. Samples were collected from aqueous humor after instilling a few drops of a novesin as a topical conjunctival anesthesia. Gentamicin sulfate was assayed bacteriologically by the standard agar-cup diffusion method. Gentamicin sulfate concentration in the aqueous humor after intravenous or subconjunctival was greater than that achieved by topical application alone.

INTRODUCTION

Gentamicin is a patent broad spectrum antibiotics and it is very effective in the treatment and prevention of simple and mixed bacterial infections of the eye including the conjunctiva, cornea and eye lids (PEYMAN, 1974).

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ENGLISH and WITHY (1959); BENSON (1974); ELLERHORST *et al.* (1975) and BROWN *et al.* (1984) mentioned that the penetration of gentamicin into the normal cornea may be limited and markedly increased in the presence of keratitis and corneal ulceration. Diseases of the episclera, sclera, lacrimal gland, uvea, anterior and posterior segments and orbit require parenteral therapy, which can be supplemented by topical and subconjunctival administration (PAVAN-TANGSTON and FOSTER, 1977).

The same authors mentioned that eye lids, superficial corneal, conjunctival and nasolacrimal diseases may be managed with topical and subconjunctival medications.

Subconjunctival injection of gentamicin may be indicated for acute anterior uveitis, panophthalmitis, episcleritis, initial control of chronic superficial keratitis and infectious keratitis (BENSON, 1974).

Intravenous or intramuscular injection of antibiotics were utilized to treat diseases of the posterior and anterior segments of the eye, orbit, sclera, eye lids and optic nerve (BISTNER *et al.*, 1969; PEMAN, 1974 and TRUEBLOOD, 1975). Gentamicin sulfate which was occasionally given by continuous intravenous infusion induced prolonged high intraocular drug concentration in severe infections (SPRODBROW, 1963 and ROWLEY & RUBIN, 1969; SISODIA, 1980 and RAPHEL, 1983).

The aim of this work was to determine the most suitable method of administration of gentamicin sulfate to obtain the high level of penetration and concentration of this antibiotic into aqueous humor for ocular treatment.

MATERIAL and METHODS

Twenty adult donkeys with clinically normal eyes weighing 50 to 70 Kg were used. The animals were divided into 5 groups each of 4 donkeys and gentamicin was administered once by different routes as shown in Table (1).

Table,(1):Methods of administration of gentamicin in aqueous humor of donkeys.

Group	Route of administration	dose
Group 1	intravenous injection (Kentlloyed <i>et al.</i> 1988).	2.2mg/kg b.wt
Group 2	subconjunctival injection (Gelatt,1967)	40mg
Group 3	intravenous injection and topical (Kentlloyed <i>et al.</i> ,1988).	2.2mg/kg b.wt & repeated eye drop
Group 4	subconjunctival injection and topical	40mg & repeated eye drops.
Group 5	topical only.	repeated eye drops

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Samples of aqueous humor (one eye was used) were collected after 1,2,3,5,6,12 & 24 hours. A few drops of a novesin was instilled into the conjunctival sac as a topical conjunctival anesthesia after washing the eye with normal saline and after 2 to 3 minutes, this application was repeated. Anterior chamber paracentesis was performed at the lembus using a 25 gauge needle with a 1 ml (tuberculin) syringe. All the specimens of the aqueous humor were kept each in a plastic tube, and were frozen at -20C until tested.

Bacteriological estimation of gentamicin

Gentamicin sulfate was assayed bacteriologically by the standard agar-cup diffusion method (BENNEH and BRODIE, 1966), using two reference strains; Staphylococcus aureus ATCC25923 and E.coli ATCC25923, as tested organisms.

RESULTS

The results of the examined samples are summarized in Table 2 and Fig. 1.

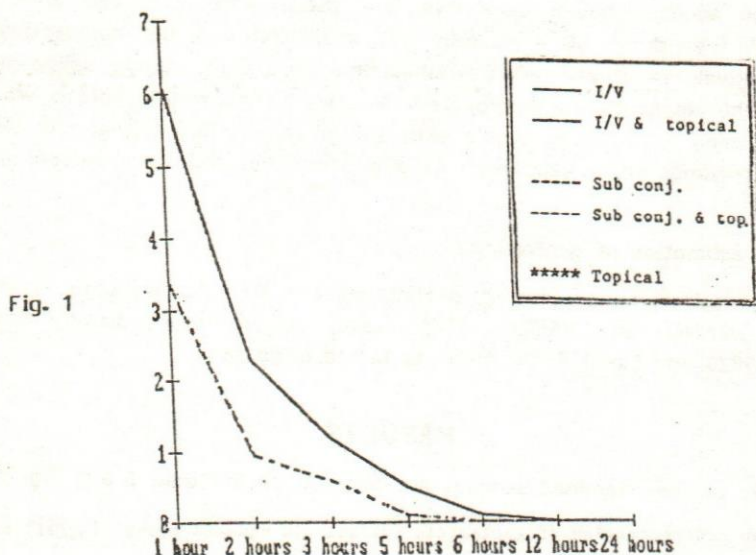
Table (2): Mean concentration of gentamicin sulfate in aqueous humor (ug/ml) after different routes of administration.

Route of administration	time of sampling after						
	1 hr	2 hrs	3 hrs	5 hrs	6 hrs	12 hrs	24 hrs
I/V	6.10	2.30	1.20	0.50	0.10	---	---
Subconjunctiva	3.40	0.95	0.60	0.10	0.10	---	---
I/V & topical	6.10	2.30	1.20	0.50	0.10	---	---
Subconj. & top.	3.40	0.95	0.60	0.10	0.10	---	---
Topical	0.01	---	---	---	---	---	---

DISCUSSION

The proper choice of the route of administration is related to an understanding of the specific ocular disease and knowledge of ocular barriers as well as the drug characteristic. Excellent ocular absorption and concentration of most drugs occurs by intravenous then subconjunctival injection when compared with topical administration as recorded by PEYMAN (1974) and ELLERHORST *et al.* (1975). Similar findings were obtained experimentally with gentamicin sulfate in this study.

Topical application especially in animals suffering from ocular disease is not effective in the treatment and needs to be repeated for several time as reported by several authors (SPRODBRAW, 1968; BENSON, 1974; ROWLEY & RUBIN, 1969; BEASLEY *et al.*,

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1975 and ELLERHORST *et al.*, 1975).

The present study revealed that the intravenous injection of gentamicin sulfate gave good results for the achievement of prolonged concentration of the drug in aqueous humor and it may be necessary to repeat another injection after six hours to obtain the least therapeutic level (0.10 ug/ml). The same findings were stated by BISTNER *et al.* (1969); PEYMAN (1974); TRUEBLOOD (1975) and ADAMSON *et al.* (1985).

In this investigation subconjunctival injection of gentamycin sulfate gave a high concentration in aqueous humor; the same result was obtained by LAVACH (1990) who stated that subconjunctival injection of antibiotics allowed greater diffusion into the eye. So this route of injection can be used for reaching the therapeutic levels of antibiotic and may be also repeated after six hours according to the severity of ocular infection. The effect of topical therapy is proportionally related to the frequency of drug administration. ROBINSON (1983) mentioned that the most common method of topical application of antibiotics was giving it periodically for a long time till recover would occur.

CONCLUSION

Evaluation of our findings suggests that the topical application of gentamicin sulfate in animals does not induce a high intraocular concentration. Intravenous injection has a highly intraocular penetration and concentration of gentamicin inside aqueous humor. Subconjunctival injection could also produce a prolonged high penetration and concentration

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but to a lesser degree. Accordingly, it is more advantageous to use gentamicin injections either intravenous or subconjunctival or even both together in case of severe infections of the eye.

REFERENCES

- Adamson, P.J.; Wilson, W.D. and Hirsh, D.C. (1985): Susceptibility of equine bacterial isolates to antimicrobial agent. *Am.J.Vet.Res.*, 46: 447-450.
- Beasley, H.; Baltralik, J.J. and Baldwin, J.A. (1975): Chloramphenicol in aqueous humor after topical application. *Arch. Ophthalmol.*, 93: 184-189.
- Benneh, J.V. and Brodie, J.L. (1966): Simplified accurate method for antibiotic assay of clinical specimens. *Appl. Microbiol* 14: 170-177.
- Benson, H. (1974): Permeability of the cornea to topically applied drugs. *Arch. Ophthalmol.*, 91: 313-315.
- Bistner, S.I.; Roberts, S.R. and Anderson, R.P. (1969): Conjunctival bacteria: Clinical appearance can be deceiving. *Mod. Vet. Pract.*, 50: 45.
- Brown, N.P.; Kelly, R.H. and Gronwall, R.R. (1984): Chloramphenicol sodium succinate in the horse. Serum, synovial, peritoneal and urine concentration after single dose of intravenous administration. *Am. J. Vet. Res.*, 45: 578-580.
- Ellerhorst, B.; Golden, B. and Jerudi, N. (1975): Ocular penetration of topically applied gentamicin. *Arch. Ophthalmol.*, 93: 371-372.
- English, P.B. and Withy, D. (1959): Serum, urine and tissue levels of chloramphenicol in the horse. *Aust. Vet. J.*, 35: 193-198.
- Gelatt, K.N. (1967): Postoperative subpalpebral medications in horses and dogs. *Vet. Med. Small Anim. Clin.*, 62: 1165-1171.
- Kentlloyed, K.C.; Stovae, S.N. and Pascae, J.R. (1988): Plasma and synovial fluid concentration of gentamicin in horse. *Am.J.Vet.Res.*, 49: 644-649.
- Lavach, D.J. (1990): *Large Animal Ophthalmology*. The C.V.Mosby Company. Baltimore, Philadelphia, Toronto.
- Pavan-Langston, D. and Foster, C.S. (1977): Trifluorothymidine and idoxuridine therapy of ocular herpes. *Am. J. Ophthalmol.*, 84: 818-823.
- Peyman, G.A. (1974): Intraocular injection of gentamicin. *Arch. Ophthalmol.*, 92: 42-51.
- Raphel, C.F. (1983): Bacteraemia. In: Robinson, N.E. ed. *Current therapy in equine medicine*, Philadelphia, W.B. Saunders Co.
- Robinson, N.E. (1983): *Current Therapy in Equine Medicine*, Philadelphia, W.B. Saunders Company.
- Rowley, R.A. and Rubin, L.F. (1969): Penetration of penicillin into the aqueous humor of the dog. *Am.J.Vet.Res.*, 30: 1945-1956.
- Sisodia, C.S. (1980): Pharmacotherapeutics of chloramphenicol in veterinary medicine. *J.Am.Vet.Assoc.*, 176: 1069-1071.
- Sprodbrow, P. (1968): The bacterial flora of ovine conjunctival sac. *Aust. Vet. J.*, 44: 117-122.
- Trueblood, J.H. (1975): Corneal contact times of ophthalmic vehicles. *Arch. Ophthalmol.*, 93: 127-130.