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**DETERMINATION OF GENTAMICIN SULFATE IN PLASMA  
AND SYNOVIAL FLUID OF DONKEYS  
FOLLOWING ITS ADMINISTRATION**  
(With 3 Table & 2 Figures)

By

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تعيين تركيز سلفات الجنتاميسين في البلازما والسائل الزلالي  
للمفصل في الحبيسر

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تم في هذا البحث حقن سلفات الجنتاميسين في ٢١ حمار بالغ طبيعي المفصل من الناحية الإكلينيكية . قسمت الحيوانات إلى ثلاث مجموعات وتم الحقن في الوريد وفي المجموعة الثانية تم الحقن في المفصل بينما في المجموعة الثالثة تم الحقن في الوريد والمفصل معاً . أخذت عينات من الدم والسائل الزلالي للمفصل لمدة ٢٤ ساعة ثم تم تعيين تركيز سلفات الجنتاميسين بكتريولوجيا ( معمليا ) . أوضحت النتائج أن للحصول على تركيز عالي من المضاد الحيوي في المصل يفضل الحقن داخل المفصل فقط أو مضاف إليه الحقن في الوريد .

**SUMMARY**

The concentrations of gentamicin sulfate in plasma and synovial fluid of clinically healthy adult donkeys were measured periodically for 24 hours on twenty one donkeys after the intravenous and/or the intra-articular administration of the drug. Synovial fluid samples were obtained via a catheter placed into the hock joint capsule and the blood was collected from the jugular vein. Gentamicin was assayed bacteriologically by the standard agar-cup diffusion method. Gentamicin sulfate concentration achieved in the synovial fluid after intra-articular administration with or without simultaneous intravenous injection, was greater than that achieved by intravenous injection alone. Although only traces of the drug was detected in the synovia after the intravenous administration of the drug, its concentration was markedly increased when the intravenous route was used in addition to the intra-articular injection in contract with the last route alone. The mean plasma concentration of gentamicin sulfate after intravenous administration was significantly greater than of all other routes of administration.

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## INTRODUCTION

Gentamicin sulfate is a broad spectrum bactericidal aminoglycoside effective mainly against gram-negative and some gram-positive bacteria (KAELLEL, 1970; TOBIN, 1979 and BURROWS, 1980). Gentamicin has a highly polar action which is not absorbed readily after oral administration or does not cross the blood brain barrier (CONZELMAN, 1980).

A single dose of gentamicin (3 ml [50 mg/ml]) given intra-articularly would be considered effective for the treatment of septic arthritis against 90% of coagulase-positive *Staphylococcus* spp., and against 90% of *Escherichia coli* and *Actinobacillus* spp. and 50% of *Salmonella* spp. (ADAMSON *et al.*, 1985 and VAN PELL & RILEY, 1969).

Gentamicin sulfate was administered intra-articularly alone and in combination with hyaluronic acid and corticosteroids prophylactically for prevention of joint infection in horses. (ROSE and FRAUENFELDER, 1982; AUER *et al.*, 1980).

Gentamicin sulfate was used to treat bacterial and idiopathic septic arthritis and was given concurrently with arthrocentesis (AUER *et al.*, 1980 and MORRIS, 1980).

Systemic administration of gentamicin sulfate is advocated for use in equine infectious arthritis. The concentration of an antibiotic within the joint capsule and synovial fluid is important for effective elimination of a susceptible bacterial pathogen (STOVER and POOL, 1985; LEITCH, 1979 and AUER *et al.*, 1980).

The aim of the work was to investigate the level of gentamicin sulfate in the joint synovial fluid after its intra-articular administration alone or with intravenous injection in comparison with that following the intravenous use of the drug.

## MATERIAL and METHODS

Twenty one mature clinically healthy donkeys with clinically normal hock joints weighting 70 to 100 Kg were divided randomly into 3 equal groups which were injected as shown in table 1. The hock joint of one of the hind limbs was chosen for the aseptic intra-articular administration of the drug and/or collection of the synovial fluid samples using a catheter (2.5 cm long, 0.8 mm in diameter). This catheter was removed after 24 hours.

Table 1: Doses and Routes of administration of gentamicin sulfate in donkeys.

Group	Route of administration	Dose
Group 1	Intravenous injection (Stover & Pool, 1985)	2.2mg/kg b.wt.
Group 2	Intra-articular injection (Kent Lloyd <i>et al.</i> , 1988)	3ml [50mg/ml]
Group 3	Intravenous and intra-articular	2.2mg/kg b.wt & 3ml [50mg/ml]

## GENTAMICIN

After the drug administration, blood samples (3 ml) were collected from the jugular vein into tubes containing sodium heparin at post injection 1,6,12 & 24 hours. The plasma was separated by centrifugation and was placed into a plastic specimen tube, which was frozen at  $-20^{\circ}\text{C}$ .

Specimens of the synovial fluid (0.4 ml) were obtained through the catheter, using a 1 ml tuberculin syringe and a 2.5 cm long & 0.8 mm in diameter hypodermic needle also at 1,6,12 and 24 hours. These specimens were placed each in a plastic tube and frozen at  $-20^{\circ}\text{C}$ .

## Bacteriological estimation of gentamicin

Gentamicin was assayed bacteriologically by the standard agar-cup diffusion method (BENNEH and BRODIE, 1966) using two reference strains: Staphylococcus aureus ATCC 25923 and E.coli ATCC 25922, as test organisms.

## RESULTS

The results of the examined samples are summarized in (Table 2 & 3 and Fig. 1 & 2).

Table (2): Mean concentration of gentamicin sulfate in the synovia (ug/ml) after different routes of injection.

Route of injection	1 hr.	Time of sampling		
		6 hrs.	12 hrs.	24 hrs.
Intra-articular	270.00	49.00	18.00	11.00
Intravenous	0.70	0.14	0.00	0.00
Intra-articular and intravenous	287.00	61.00	28.00	18.00

Table (3): Mean concentration of gentamicin sulfate in the plasma (ug/ml)

Route of injection	1 hr.	Time of sampling		
		6 hrs.	12 hrs.	24 hrs.
Intra-articular	0.27	0.00	0.00	0.00
Intravenous	5.60	3.10	1.00	0.00
Intra-articular and intravenous	6.20	4.10	1.60	0.00



SAMIA M. SELEIM et al.**DISCUSSION**

The causative infective organisms commonly isolated from pyoarthritis, viz Escherichia coli, Staphylococcus aureus, Streptococcus zooepidemicus and Actinobacillus spp. are often susceptible to gentamicin, which is therefore used routinely for treatment (LEITCH, 1979; MORRIS, 1980 and ADAMSON et al., 1985).

STOVER and POOL (1985) and KENT LLOYD et al. (1988) proved that the supported out gentamicin sulfate concentration achieved in the synovial fluid after intra articular injection was greater than that achieved after intravenous administration alone.

Our investigation revealed that the concentration of gentamicin sulfate attained in synovial fluid inside the joint in case of intravenous injection was less than achieved following the intra-articular injection along the whole period of experiment; the same result was recorded before (LEITCH, 1979; STOVER & POOL, 1985 and KENT LLOYD et al., 1988).

The mean plasma gentamicin sulfate concentration after intravenous administration, was significantly greater than that after intra articular administration; this result is nearly in agreement with that reported by some authors (BEECH et al., 1977; BROWN et al., 1982 and KENT LLOYD et al., 1988).

The present work showed that the mean synovial fluid concentration of gentamicin sulfate after both intra-articular and intravenous injection was the highest one attained in donkeys receiving the antibiotic by a method other than that mentioned. Similar results were recorded by BROWN et al. (1982) and KENT LLOYD et al. (1988). The intra-articular injection of gentamicin sulfate gave good results but to obtain prolonged concentration of antibiotic inside the joint and it may be necessary to repeat the injection after 24 hrs. to reach the least therapeutic level (11 ug/ml); the same result was obtained by other workers (STOVER & POOL, 1985 and KENT LLOYD et al., 1988).

**CONCLUSION**

To obtain high concentration of the antibiotic in the plasma, the intravenous route is the best method, while to achieve a high concentration of the drug inside the joint the intra-articular and/or intravenous should be used.

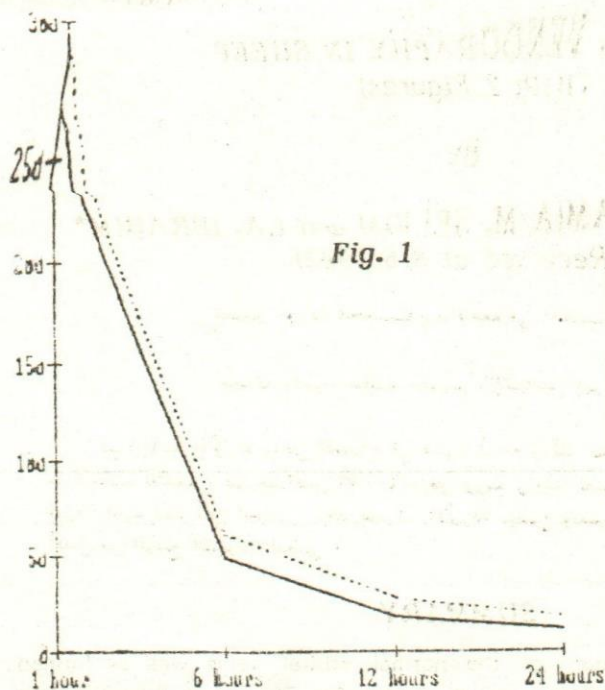
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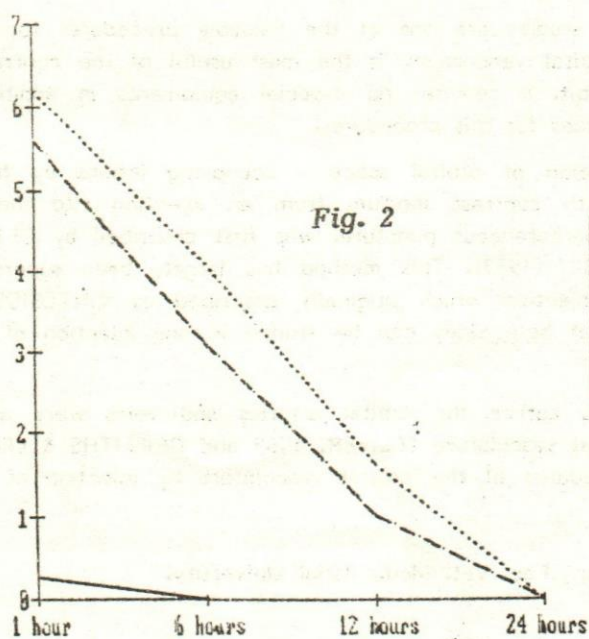
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Mean concentration of Gentamicin sulfate in the synovia (mg/ml) after different route of injection.



Mean concentration of Gentamicin sulfate in the plasma (ug/ml) after different route of injection.