A Study of the Potency of Certain Aminoglycoside Antibiotics against some Local Clinical Isolates

Pages with reference to book, From 7 To 15

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Abstract

The inhibitory activity of Kanamycin, Gentamicin, Tobramycin and Sisomicin was studied against some of the common local clinical isolates by disc diffusion technique. On a section of the isolated strains susceptible to gentamicin, tobramycin and sisomicin, MIC of the three drugs was determined and correlated with the size of the zones of inhibitions.

For three of the isoiates studied, Sisomicin, Tobramycin and Gentamicin gave the sanie percentage of susceptible strains, however the sizes of the zones of inhibition were variable. Escherichia coli and Pseudomonas aeruginosa were found equally susceç tible to sisomicin and tobramycin, but to a lesser extent to gentamicin; again the distribution pattern of zone sizes of the suscertible strains was variable. Streptococcus pyogenes least effective against some strains and ineffective or nearly so, against the others.

It was considered that the differences observed could be attributed to the possibility of existence of inherently resistant strains and geograaphical differences in the susceptibilities of the strains. In case of the older aminoglycosides the declining effectivity could be attributed to their being in use or rather indiscriminate and improper use for a length of time.

The part of the study on correlation of the mean MIC and the mean zone of inhibition, revealed lesser MIC and larger zone of inhibition for sisomicin in general (JPMA 33:7, 1983).

Introduction

Aminoglycosides, structurally interrelated group of bacteriocidal antibiotics, which have a common mode of action viz the loss of initiation of Protein Synthesis at the ribosome level. Erythromycirz and chioramphenicol also affect Protein Synthesis but are only bacteriostatic (Girdwood, 1976).

Structural differences of various members of the group are supposed to account for the differences in their properties, for example Streptomycin in addition to affecting Protein Synthesis also impairs cell respiration and interferes with cell membrane permeability. Gentamicin differs in number of methyl groups, Kanamycins in the presence or absence of hydroxyl or amino groups. Sisomicin differs from Gentamicin c 1 a in possessing a double bond in one of amino sugar rings which is believed to be the reason for unique properties of Sisomicin (Waltz and Miller, 1980). Lias and Letourneu (1980) reported more rapid and higher uptake of Sisomicin, by the bacterial cells as compared with gentamicin, and attributed this for the superior microbiological potency of Sisoniicin in susceptible bacterial strains.

With the discovery of new members of arninoglycoside gioup of antibiotics, as a natural sequence, their antimicrobial activity has been compared with similar antibiotics. The differences en countered have been mainly atti ibuted to tee differences in the chemical structure. Both standard and locally isolated strains from clinical specimens have been employed in such studies.

Waitz et al. (1972) comparing activity of sisomicin, gentamicin, kanamycin, and to bramycin, reported the overall ranking of in vitro activity of these antibiotics against isolated bacterial strains. Hyams (1973) in his study on the in vitro bactericidal effectiveness of four aminoglycoside antibiotics against clinical isolates observed an equal activity of tobramycin and sisomicin against Pseudomonas aeruginosa but sisomicin was more effective as compared to tobramycin and gentamicin against

Klebsiella, Escherichia coli, Proteus and Streptococcus Pyogenes. Young and Hewitt (1973) found Sisomicin more consistently active as compared to Amikacin, tobramycin, gentamicin and butirosin against gram negative bacilli and Staphylococcus aureus. Waitz and Miller (1980) in their in vitro study with clinical isolates found Sisomicin to be as active as tobramycin against Pseudomonas and equal to or superior to gentamicin, tobramycin and amikacin against other gram negative bacteria and Staphylococcus.

Weinstein (1975) in his study on the correlation o" drc diffusion activity and broth mininrim in ibitorsr concentration of Siso omicin, found that strains sew itive to 4 mcg per ml or less, gave 14 mm or larger zones by the disc diffusion technique.

In discussion following the paper of Wtitz and Miller (1980), in the International round table diFcussion on Si omicin, Noone pointed out the pos ;ibility of geographical differences in the susceptibilities of thç microorganisms to the antibiotics, as observed regarding activity of Sisomicin against strains from U.S.A. and U.K.

Geographical differences in susceptibilities of the microorganisms could be attributeu to the inherent genetic characters in the strains of an area, evolved by mutation and selection. With the introduction of Sisomicin, it was thought to be an opportune time to study the possibility of geographical differences in sus ceptibilities of strains of this area to a new antibiotic, since theoretically resistance by adaptation could evolve later when the drug is in use or rather not proper use, for a length of time

A study of inhibitory activity of kanamycin, gentamicin, tobramycin and sisomicin against some of the common local clinical isolates was undertaken using disc diffusion technique. The correlation between the size of zone of inhibition produced by gentamicin, tobramycin and sisomicin and their minimum ithibitory concentration, on a section of the isolated strains was determined.

Material and Methods

Twenty five strains each of Pseudomonas aeruginosa, Klebsiella aerogenes, Escherichia coli, Proteus mirabilis, Staphylococcus aureus and Streptococcus pyogenes were isolated from clinical specimens arriving in our laboratory from Central Hospital, Maternity and Children Hospital, Mahjar Hospital and King's Hospital in jeddah. The clinical specimens comprised swabs from the upper respiratory tract, ear swabs, mid stream urine, pus swabs, swabs from umbilicus and swab from genital region (Table-I).

Table I

Types of Isolated Strains According to Site.

Specimen Site	*Number of specimens*	*Staphylo* coccus*	*Pseudomo* nas*	*Klebsiella*	*Proteus*	*E. coli*	*Streptococcus*
Ear	16	5	6	1	4	—	—
Throat	56	9	10	9	2	1	25
Wound	14	6	2	1	5	—	—
Urethra	1	1	—	—	—	—	—
Umbilical	7	—	2	1	2	2	—
Vagina	3	—	—	—	2	1	—
Nasal	3	2	—	1	—	—	—
Urine	50	2	5	12	10	21	—
Total:	150	25	25	25	25	25	25

Isolation and identification of the bacterial species from thc clinical specimens was carried according to the technique described by Cruickshank et al. (1973) and Finegold et al. (1978). Primary cultures from the clinical specimens, were obtained on blood agar and eosin methylene blue agar. Pure isolates obtained by subculture were subjected to biochemical characterisation and identification. Each isolatcd strain was subjectcd to inhibitory activity of four of the aminoglycoside antibiotice viz kanamycin, gentamicin, tobramycin and sisomicin by the Bauer and Kirby, agar disc diffu ion technique as described by Bauer et al. (1974).

Five strains each found significantly susceptible by the disc diffusion technique were selected from Pseudomonas, Klebsiella, Proteus, Escher-. ichia coli anu Stanhylococcus species and were employed for determination of the minimum inhibitory concentration of gentamisin, tobnmycin and sisomicin against them; for the correlation of the finding with the zones of inhibition.

Oxoid brand Mueller-Hinton agar was used as the sensitivity test medium for the disc diffusion technique, and oxoid brand trypticase soy broth for the preparation of the standard inoculum for both the disc diffusion technique and MIC determination.

Potent sensitivity discs (Table-II)

Table II Sensititre Plate-3 (Schering).

Row	Gentamicin ug / ml	Tobramycin ug / ml	Sisomicin ug /ml	Control
A	16	16	16	–
B	8	8	8	–
C	4	4	4	–
D	2	2	2	–
E	1	1	1	–
F	0.5	0.5	0.5	–
G	0.25	0.25	0.25	–
H	0.12	0.12	0.12	–

of the four aminoglycoside antibiotics were used for the determination of the zone of inhibition.
Sensititre Packs Plate- (Table-III)

Table III
Sensitivity Discs Employed in the Disk Diffusion Sensitivity Testing.

Drug	Disc Potency	Manufactured By	Sensitivity	Zone
Kanamycin	30 mcg	Becton Dickinson		usual 18 mm
			Staph. aureus	19–26 mm
			E. coli	17–25 mm
Gentamicin	10 mcg	Becton Dickinson		usual 13 mm
			Pseudomonas	16–21 mm
			Staph. aureus	19–27 mm
			E. coli	19–26 mm
Tobramycin	10 mcg	Becton Dickinson		usual 14 mm
			Pseudomonas	19–25 mm
			Staph. aureus	19–29 mm
			E. coli	18–26 mm
Sisomicin	10 mcg	Becton Dickinson		usual 14 mm

(Seward Laboratory, U.K.) was employed in the determination of the minimum inhibitory

concentration of gentamicin, tobramycin and sisomicin.
The standard inoculum was prepared by inoculating three to five colonies from the pure isolated strain, on to 5 ml of trypticase soy broth, incubating the inoculated medium at 37°C and comparing the opacity of the growth suspension everyl 30 minutes with that of 5 ml of the Barium Sulfate standard in a similar test tube. The Barium Sulfate standard was prepared by the addition of 0.5 ml of 1.17% Barium chloride (0.36 N) and kept in the refrigerator.
In case the growth suspension was lighter than Barium Sulfate standard, it was reincuba- ted for another 30 minutes, until matching. In case it became denser, then the growth suspension was diluted with sterile trypticasc soy broth, with aseptic precautions until the opacity matched to that of the Barium Sulfate.
Standardised growth suspension was used within fifteen minutes of its preparation, in either case for the disc diffusion technique and for the minimum inhibitory concentration determination.
For determination of susceptibility by disc diffusion, sterile cotton swab was soaked in the standardised growth suspension, excess fluid was drained along the side of the tube and the swab was rubbed uniformly on the surface of a 4 mm thick Mueller-Hinton agar plate. Duplicate plates were inoculated to obtain a mean value for the zone of inhibition.
After the inoculum dried on the surface of the plate in three to five minutes, sensitivity discs were placed on the surface of inoculated medium, approximately equidistant from each other, with the help of a flamed and then cooled forceps, and the discs were gently pressed down on to the surface of the medium. The plates were then incubated at 37°C for 18 hours. After incubation the diameters of the zones of inhibition, including the 6 mm disc, were measured from the back of the plate with the help of a ruler and mean of the two values of the zones of inhibition was recorded.
For the determination of the minimum inhibitory concentration 50 microliters of the standardised growth suspension was added with the help of sterile pipets to each well of the sensititre plate, in the rows for gentamicin, tobramycin, sisomicin and control. The plate was then sealed with the transparent adhessive seal, gently rotated for a while, and incubated at 37°C for 18 hours. After incubation the plate was read on a viewer displaying the undersides of the wells in a mirror and the lowest concentration of the antibiotic inhibiting viEible growth, in comparison with the control, was recorded as the MIC (Table II).

Results

Susceptibility of a strain to the drug was established according to the size of the zone of inhibition, as indicated in Table-II. An 18 mm or more zone of inhibition by kanamycin for Proteus, Kiebsiella, Pseudomonas and Streptococcus species, 17 mm for Escherichia coli and 19 mm or more for Staphylococcus, was considered as sensitive zone. In case of gentamicin and tobramycin the size of zone of inhibition indicating susceptibility was 16 mm or more and 19 mm or more respectively for Pseudomonas; 19 mm. or more and 18 mm or more respectively for Escherichia coli; 13 mm or more and 14 mm or more respectively for Klebsieila, Proteus and Streptococcus pyogenes; and 19 mm or more in both for staphylococcus aureus. In case of Sisomicin 14 mm or more zone size was considered as indicative of susceptibility for all species.
The percentage of the individual aminoglycoside-susceptible strains, out of the clinical isolates studied, is shown in Table-II; also presented is the mean zone of inhibition+ standard deviation, calculated for each species from the zones of inhibition of susceptible strains in each case. The table also reveals the number of strains in each species that were resistant to certain aminoglycoside but were sensitive to the others. All twenty five strains of Pseudomonas aeruginosa were foand resistant to kanamycin, 16 of these were resistant to gentamicin but sensitive both to tobramycin and sisomicin. One strain was found also resistant to tooramycin and sisomicin as well; while the rest (96%) were sensitive to both. The

mean of zones of inhibition of Pseudomonas strains susceptible to tobramycin was larger than that of the sisomicin, likewise the mean of zone of inhibition for sisomicin was larger than that for gentamicin. Only one strain of Streptococcus pyogenes was susceptible to Kanamyciii (4%), 22 (88%) to gentamicin and 21 (84%) to tobramycin while all (100%) were sensitive to sisomicin; here the mean figure of zone size in descend.ing order was better for sisomicin, followed by gentamicin, tobramycin and kanamycin.

Table IV

Percentage of Aminoglycoside—Susceptible Strains and Mean ± S.D. of Zone of Inhibition.

Species	*Kanamycin*			*Gentamicin*			*Tobramycin*			*Sisomicin*		
	No. of S.S.	*% of S.S.*	$\bar{X}$ ± *S.D. of Z.I.*	*No. of S.S.*	*% of S.S.*	$\bar{X}$ ± *S.D. of Z.I.*	*No. of S.S.*	*% of S.S.*	$\bar{X}$ ± *S.D. of Z.I.*	*No. of S.S.*	*% of S.S.*	$\bar{X}$ ± *S.D. of Z.I.*
Staph.	16	64.0%	21.1±1.86	25	100.0%	21.48±1.75	25	100.0%	23.92±1.69	25	100.0%	24.0 ±1.79
Pseudo.	—	—	—	8	32.0%	17.75±1.61	24	96.0%	24.29±2.67	24	96.0%	22.75±2.02
Kleb.	10	40.0%	19.2±1.33	25	100.0%	20.2 ±1.84	25	100.0%	21.76±1.73	25	100.0%	23.0 ±1.83
Proteus	15	60.0%	20.2±1.51	25	100.0%	19.64±1.58	25	100.0%	22.92±1.69	25	100.0%	23.6 ±1.75
E. coli	15	60.0%	19.2±1.68	19	76.0%	20.89±1.45	25	100.0%	22.64±1.89	25	100.0%	23.52±1.54
Strept.	1	4.0%	18.0±0.0	22	88.0%	20.36±1.85	21	84.0%	19.0 ±2.20	25	100.0%	22.52±2.18

S.S. = Sensitive strains

Z.I. = Zone of inhibition

Kiebsiella, Proteus and Staphylococcus aureus were susceptible to kanamycin 40%, 60%, and 64% respectively, while 100% of the strains of all the three species were susceptible to gentamicin, tobramycin and sisomicin. However the mean zone size of the susceptible strains was better in order for sisomicin, tobramycin and gentamicin; kanamycin was next to gentamicin in case of zone sizes of Klebsiella and Staphylococcus, but gave slightly larger mean zone size than gentamicin against Proteus.

Strains of Escherichia coli sensitive to kanamycin weie 50%. Four of the kanamycin resistant E. Coli strains were sensitive to gentamicin making the percentage of susceptible strains to gentamicin as 76%; while all (100%) were susceptible to tobramycin and sisomicin. Here again sisomicin produced larger nv an zone size, next being in, order tobramycin, gentamicin and kanamycin.

Table V

Pattern of Zones of Inhibition.

Species	*Agent*	*Zone of Inhibition (m.m.) and number of strains presenting that zone*									
		13—	15—	17—	19—	21—	23—	25—	27—	29—	31—
Staph.	Kanamycin	—	—	—	10	4	1	—	—	1	—
	Gentamicin	—	—	—	12	10	2	—	—	—	1
	Tobramycin	—	—	—	—	5	16	3	—	—	1
	Sisomicin	—	—	—	—	5	14	4	1	—	1
Pseudo.	Kanamycin	—	—	—	—	—	—	—	—	—	—
	Gentamicin	—	4	1	2	1	—	—	—	—	—
	Tobramycin	—	—	—	4	—	8	6	5	1	—
	Sisomicin	—	—	2	4	4	9	3	2	—	—
Klebsiella	Kanamycin	—	—	3	5	2	—	—	—	—	—
	Gentamicin	—	1	6	4	13	1	—	—	—	—
	Tobramycin	—	—	—	8	9	7	1	—	—	—
	Sisomicin	—	—	—	5	5	8	7	—	—	—
Proteus	Kanamycin	—	—	3	8	2	2	—	—	—	—
	Gentamicin	—	—	7	14	1	3	—	—	—	—
	Tobramycin	—	—	—	1	13	8	2	—	1	—
	Sisomicin	—	—	—	1	8	10	5	1	—	—
E. coli	Kanamycin	—	—	7	4	4	—	—	—	—	—
	Gentamicin	—	—	—	9	9	—	1	—	—	—
	Tobramycin	—	—	1	3	9	8	4	—	—	—
	Sisomicin	—	—	—	—	8	12	4	1	—	—
StrePt.	Kanamycin	—	—	1	—	—	—	—	—	—	—
	Gentamicin	—	—	5	8	6	3	—	—	—	—
	Tobramycin	2	2	6	7	—	4	—	—	—	—
	Sisomicin	—	1	—	7	8	2	6	1	—	—

Table-V shows the overall patterns of zone sizes of the susceptible strains to the four aminoglycosides. The pattern of zone sizes against Pseudomonas was better by tobrarnycin, next in order was sisomicin and gentamicin. In case of Streptococcus pyogenes, sisomicin presented better distribution pattern of zone sizes of inhibition, next in order being gentamicin, tobramycin and kanamycin. In case of Kiebsiella, Proteus, Staphylococcus and Escherichia coli, likewise the overall pattern of zone sizes was better in order by sisomicin, tobramycin, gentamicin and kanamycin; although the calculated mean value of zone sizes of kanamycin turned out better than gentamicin in the case of Proteus.

The strains of Staphylococcus aureus, Pseudomonas aeruginosa, Kiebsiella aerogenes, Proteus mirabilis and Escherichia coli were found equally susceptible to sisomicin and tobramvcin with regard to the percentage of susceptible strains; but lesser number of strains of Streptococcus pyogenes were susceptible to tobramycin. Gentamicin was similar to siomicin and tobramycin regarding the percentage susceptibility of Staphylococcus, Klebsiella and Proteus; however the number of susceptible strains of Streptococcus, Escheri- chia coli and Pseudomonas towards gentamicin were less than towards robramycin and sisomicin. Kanamycin proved less effective against Staphylococcus, Proteus, Escherichia coli and Klebsiella and ineffective against Pseudomonas and neariy so against Streptococcus.

Mean of the minimum inhibitory concentration of gentamicin, tobramycin and sisomicin, against five susceptible strains of Staphylococcus, Pseudomonas, Klebsiel Ia, Proteus, and Escherichia coli; alongside the mean of their zones of inhibition, is shown in Table-V.

Mean MIG of tobramycin and sisornicin against Pseudomonas was the same viz 1. (6+0. 98 ug per ml but the zone size mean by tobramycin was larger, while gentamicin gave higher MTC and smaller zone

size.
Mean MIC of gentamicin and sisomicin was identical against Klebsieila and Proteus viz 1.8±0.8 ug per ml, but this corresponded with a larger mean zone sizes produced by sisomicin in both species.
To'bramycin presented higher mean MIC in these organisms with mean zone sizes in between the values for the other two drugs.
With Staphylococcus the mean MIC of sisomicin was 0.6±0.50 ug. per ml. corresponding with the mean zone size of 23.8±1.13 mm, next in rank was gentamicin giving mean MIC of 0.8±0.92 ug per ml, the mean MIG value for tobrarnycin being 0.9±0.98 ug per ml. However the mean MIC of tobramycin corresponded to a larger mean zone size than that produced by gentamicin.
In case of Escherichia coli, gentamicin and tobramycin gave identical mean MIC of 1.6±0.98 mcg per ml but the mean zone size of tobramycin was larger, where as sisomicin gave lesser mean MIC than the two corresponding with 26.2±2.9 mm zone size that was larger than the value presented by tobramycin.
In general the MIC of sisomicin was lesser corresponding with a larger zone size, only Pseudomonas and Kiebsiella appeared to present larger zone with tobramycin as compared to sisomicin in these seiected strains, this could be due to the random selection and statistically small number of these strains.

Discussion

The local clinical isolates subjected to the activity of kanamycin, gentamicin, tobramycin and sisomicin were twenty five strains each of Staphylococcus aureus, Pseudomonas aeruginosa, Proteus mirabilis, Escherichia coli and Streptococcus pyogenes.
All strains studied were found susceptible to sisomicin except one strain of Pseudomonas aeruginosa

Table VI

Comparison of MIC and Zone of Inhibition, from Five Aminoglycoside–Susceptible Strains of each Species (Mean ± S.D.).

Species	*Gentamicin*		*Tobramicin*		*Sisomicin*	
	MIC ug/ml	*Z.I. mm*	*MIC ug/ml*	*Z.I. mm*	*MIC ug/ml*	*Z.I. mm*
Staphylococcus	0.8±0.92	21.2±1.70	0.9±0.98	23.6±1.56	0.6±0.56	23.8±1.13
Pseudomonas	2.8±1.44	11.8±2.1	1.6±0.98	24.6±1.96	1.6±0.98	20.8±2.1
Klebsiella	1.8±0.8	21.4±0.98	2.8±1.38	27.0±2.97	1.8±0.8	23.6±1.33
Proteus	1.8±0.8	19.2±1.65	3.6±1.13	28.0±3.1	1.8±0.8	29.0±3.22
E. Coli	1.6±0.98	19.0±1.54	1.6±0.98	26.0±2.82	1.4±0.98	26.2±2.90

(Table-IV which was also found resistant to thc other three aminoglycosides. The evidence though small, points towards the possibility of encountering inherently resistant strains to a new antibiotic introduced in an area.
The result for tobramycin regarding percentage susceptibility were similar to those of sisomicin except in the case of Streptococcus pyogenes, where sisomicin was higher in rank then tobramycin However sic omicin had produced larger zone sizes of inh ibition than tobramvcin in the cases of Staphylococcus, Klcbsella, Proteus, Escherichia coil and Strcptococcus, as evident prom the mean

values of Zone sizes of the susceptibi' strains (Tcbl' JVynd from the over all pattern of zone sizes (T ble V); but in the case of Pseudomonas, tobramvcin presented better zone sizes ble IV and V). The larger inhibition zone again t Pseudomonas by tobramvcin may be due to the possibility that this drug is still behaving more effective against our Pseudomonas strains than sisomicin. While against our Streptococcus pyogenes sisomicin appears to have taken the upper hand; the upper hand of sisomicin also looks logically true regarding the other strains, considering the zone sizes. The larger zones of inhibition produced by Sisomicin could be due to its smaller molecular size, better diffusion, or better effectiveness.

In the mean values calculated on the basis of the five randomly selected strains, we found that the mean zone size of inhibition of tobramycin against Klebsiella though larger than sisomicin (Table IV the mean MIC value of sisomicin was better than tobramycin (Table VI). The mean MIC of sisomicin was also lesser than that of tobramycin in cases of Staphylococcus, Proteus and Escherichia coli but was similar in the case of Pseudomonas. The MIC observations though not meant for this comparison because being statistically small in number, still in general, they were found to support the findings bascu on the disc diffusion technique.

Gentamicin ranked lower than tobrantycin and sisomicin regarding percentage of suscept-ible strains of Pseudomonas, Escherichia coli and Streptococcus, but equal to them in case of Staphylococcus, Klebsiella and Proteus (Table IV). With regard to the over all pattern of zone size (Table V) it ranked lower than the two against all strains except Streptococcus, in which case its position was between gentamicin and sisomicin. The findings reflect upon the fading effectivity of a one time master aminoglycoside antibiotic. Here again, just for mention, the mean MIC values of gentemicin were also higher than tobramycin and sisomicin regarding Pseudomonas, higher than sisomicin but equal or less than tobramycin in cases of Escherichia coli and Staphylococcus, and equal to sisomicin but lower than tobramycin in cases of Klebsiella and Proteus (Table VI). The impression about gentamicin from this small number of observations was comparable to that drawn from the disc diffusion study.

Kanamycin was lower down in the list both regarding percentage of susceptible strains, mean of zones of inhibition and pattern of the zone sizes of inhibition except that it reveakd better mean zone size than gentamicin in the case of Proteus, (20. ±1 . 51) as compared to (l9.6± 08). Thus old has no longer rem..in the gold.

Summing up the findings with regard to the percentage susceptibilities, our strains of Staphylococcus, Klebsiella and Proteus were equally susceptible to sisomicin, tobramycin and gentamicin, however there were differences in the pattern of zone of inhibition and the calculated mean zone sizes. Escherichia coli and Pseudomonas strains were equally susceptible to sisomicin and tobramycin but lesser number of them was susceptible to gentamicin, the differences of pattern of zone sizes and mean zone sizes were there, between sisomicin and tobramycin regarding these strains. Our Streptococcus strains were distinctly more sensitive to sisomicin than the other aminoglycosides both regarding the percentage of susceptible strains and the zone size of inhibition. In general our strains behaved more immune to kanamvcin.

The retreating efièctivity of gentamicin may be considered as reflecting upon its being in use for a long time. Thus having had more chance in causing selection and evolution, of resistont mutants or in causing the theoretical development of resistance by adaptation. This process appears to have got more established, in the case of kanamycin.

Our findings regarding the susceptibility of Pseudomonas and Streptococcus pyogenes are similar to those of Hyams (1973), who in his study found equal activity of tobramycin and sisomicin against Pseudomonas and more effectivity of sisomicin than tobramycin and gentamicin, against Streptococcus pyogenes, Kiebsiella, Escherichia coli and Proteus. But our Kiebsiella, Proteus, and Escherichia coil strains behaved slightly different, the former two being equally susceptible to gentamicin, tobramycin and sisomicin, and the latter equally susceptible to tobramycin and sisomicin, but less susceptible to gentamicin. These findings support the view of the presence of geographical differences in the

susceptibilities of the strains.
Likewise strains of gram negative bacilli and Staphylococcus aureus studied by Young and Hewitt (1973) were reported to be consistently more susceptible to sisomicin compared to tobramycin and gentamicin, while in the present study Staphylococcus stra ins were found susceptible in equal percentage to sisomicin, tobramycin and gentamicin. Crowe and Sanders (1973) found sisomicin more active than tobramycin and gentamicin against Proteus, while in our study the percentage of susceptible strains of Proteus, to these drugs was equal. W4itz and Miller (1980) with their clinical isolates, also found sieomicin to be as active as tobramycin against Pseudomonas; and equal to or superior to gentamicin and tobramycin against other gram negative bacteria and Staphylococcus; their findings are comparable to those of Hyams (1973).
Although the studies of those workers were based on MIC values, and we have not accounted our MIC values in this comparison because of statistically small number, still in our opinion the differences observed could be attributed to the possibility of the presence of inherently resistant strains towards a new antibiotic, and to the presence of geographical differences in the susceptibilities of the strains. The pattern of resistant presented towards the older aminoglycosides could be the out come of their being in use or rather indiscriminate and improper use for a length of time, giving them more chance for the evolution and selection, of resistant mutants or for the development of resistance by adaptation.
The MIC study on a section of randomly selected strains revealed that in general lesser MIC of sisomicin corresponded with larger zone size. A mean MIC of 1.8±0.8 meg per ml or less of sisomicin corresponded with a mean zone size or 20.8±2. 1 mm/or more, this was found to be in accordance with the finding of Weinstein (1975) who reported that strains sensitive to less than 4 meg per ml of sisomicin presented larger than 14 mm zone of inhibition.

Acknowledgement

We wish to thank Dr. Faisal Jameci Rowaihy, Director of The Regional Laboratory Jeddah and supervisor general of the Labo-. ratories in the Western region, for his hind consent and encouragement for this studv, Mr. Mohammed Zaidan and Mr. Sameh Farrag, representatives of Schering Company in Jeddah for supply of the sensititre plates and Sisomicin discs, Miss Mercy, R. Dayandayan for typing of the manuscript and proof reading and to other colleagues for their cooperation and positive criticism.

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