The antibiotic sensitivity pattern of coagulase negative staphylococci; a major ocular normal flora

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ABSTRACT

Objective: To describe the changing drug sensitivity patterns for Coagulase Negative Staphylococci (CNS), the most commonly isolated bacteria of the conjunctival normal flora

Design: Descriptive retrospective study

Setting: University of Nairobi, Department of Ophthalmology and Kikuyu Eye Unit from January 1994 to December 1997
Subjects: 55 asymptomatic volunteers at KNH and KEU with no signs of ocular infections or ocular surface abnormalities who tested positive for Coagulase negative Staphylococcus (CNS).

Results: There was high resistance to the most commonly used antibiotics like amoxicillin, aminoglycosides, the 1st and 2nd generation flouroquinolones accept ofloxacin and tetracycline whereas chloramphenicol, carbenicillin, polymixin B and cephalexin maintained a high sensitivity.

Conclusion: The percentage of positive finding of CNS of the conjunctival normal flora is comparable to that in other regions of the world. Sensitivity patterns on the newer generation antibiotics which are being used more frequently in the region should be studied in subsequent studies.

INTRODUCTION

Normal ocular flora constitutes those organisms that are present on the eyelid and conjunctiva. These organisms are considered to be saprophytic without causing any diseases but have the potential to become pathogenic when the normal defence mechanisms fail.[1,2] The normal conjunctival flora appears to be derived from the skin and it establishes itself a few weeks after birth forming an equilibrium within the sac. This is protective against the proliferation of pathogenic bacteria.[3]

In conjunctival smears, the bacterial species widely predominate over fungal, parasitic or viral elements. Out of the over sixty-five types of the bacteria of the conjunctiva, gram-positive bacteria predominate. These include coagulase negative Staphylococcus (CNS), Propionibacterium and Corynebacterium species as well as Peptostreptococcus, Streptococcus and Actinomyces families. Gram negatives include Neisseria, Haemophillus and Proteus sp. from the Enterobacteriaceae family.[4]

In a recent study done on the antibiotic susceptibility pattern of bacterial ocular flora of 164 patients prior to undergoing surgery, de Kasper et al isolated bacteria in 162 (98.8%) patients. The commonest bacteria isolated was CNS (76%) with 2% of them resistant to gatifloxacin and moxifloxacin whereas none were susceptible to minocycline or vancomycin. [5]

In a study conducted by Alveranga et al on the aerobic conjunctival flora of diabetic patients, CNS was the most common microorganism isolated, and its identification was more frequent in patients with retinopathy than in those without diabetic retinopathy.[6]

Knowledge of the normal flora of the conjunctiva and the changing resistance and sensitivity patterns is important, as these germs can be responsible for the invasion of the ocular structures when defense mechanisms are compromised. This will assist practicing Ophthalmologists in the region in their choice of appropriate antibiotic treatment prior to culture and sensitivity results, and especially so in regions where laboratory facilities are not widely available. It may also assist in reducing the injudicious use of antibiotics. Our aim was therefore to determine the changing drug sensitivity patterns for CNS, a commonly occurring ocular normal flora in the normal conjunctiva.

METHODOLOGY

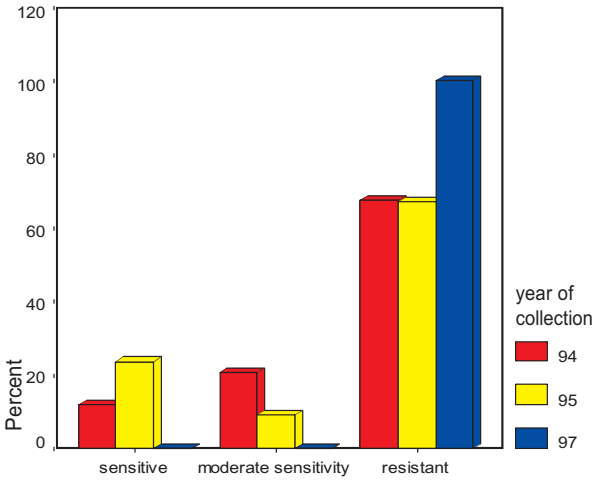
Fifty five asymptomatic volunteers at Kenyatta National Hospital (KNH) and Kikuyu Eye Unit (KEU) with no signs of ocular infections or ocular surface abnormalities from January 1994 to December 1997 were selected. The samples were collected at the microbiology laboratory in the Department of Ophthalmology, University of Nairobi between 1994 to 1997. Other data collected in 1995 was

from preoperative patients without ocular surface disorders who were scheduled for intra ocular surgery at the KEU. An informed verbal consent was taken from all the volunteers prior to sampling. The samples were inoculated immediately on culture plates (Blood Agar, Chocolate Agar, and Thioglycolate Agar). After 24hrs of incubation at 37°C (28°C for fungal cultures), the plates were inspected for colony growth which were then processed for identification. In case of no growth the plates are reincubated for further 24hrs before reporting it as a negative growth. The samples from KEU were transported immediately to the microbiology laboratory at the Department of Ophthalmology of the University of Nairobi, where the plates were incubated and slides were stained for microbiological examination. The Kirby Bauer disc diffusion method of sensitivity testing was applied.[7]

RESULTS

There were 15 cases in 1994, 31 in 1995 and 9 in 1997. There was no data collected in 1996. Not all the cases were tested for the antibiotic senstitivity. The antibiotics tested were amoxicillin, carbenicillin, cephalexin, chloramphenicol, ciprofloxacin, norfloxacin, ofloxacin, gentamicin, tobramycin, tetracycline and polymixin B. The antibiotics chosen were representative of groups of the most commonly used antibiotics in the region.

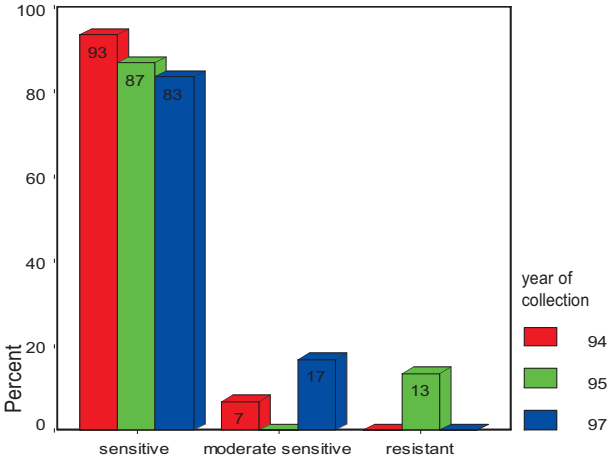
Figure 1: Amoxicillin sensitivity pattern (n=52)



amoxicillin/CNS

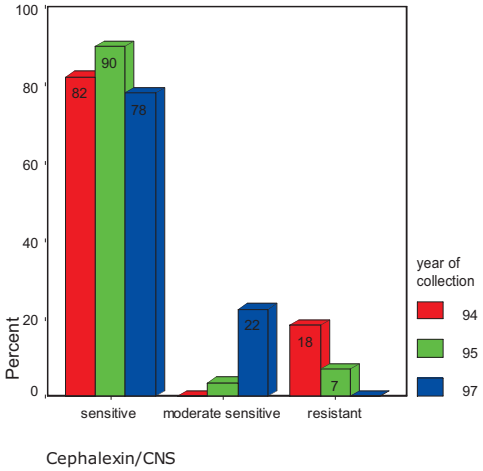
The resistance of amoxicillin increased overall with 100% resistance in 1997 (P=0.324).

Figure 2: Carbenicillin sensitivity pattern (n=51)



The sensitivity to Carbenicillin remained high. Although there is a mild drop in the sensitivity, it is statistically insignificant (P=0.146).

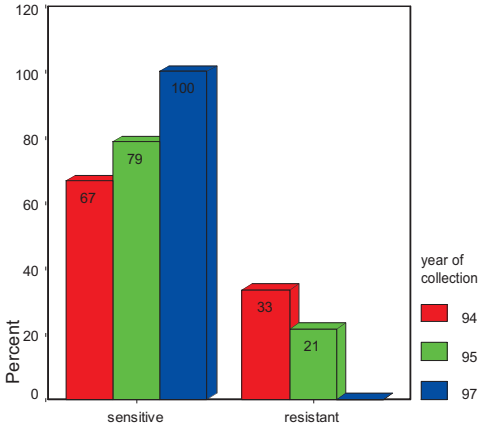
Figure 3: Cephalexin sensitivity pattern (n=49)



Cephalexin/CNS

The sensitivity of Cephalexin remained good overall (P=0.130).

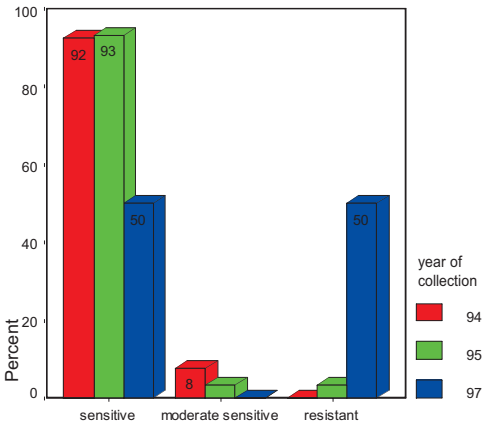
Figure 4: Chloramphenicol sensitivity pattern (n=46)



Chloramphenicol/CNS

There was an overall increase in the sensitivity, with 100% sensitivity in 1997. There were no cases for moderate sensitivity all through (P=0.413)

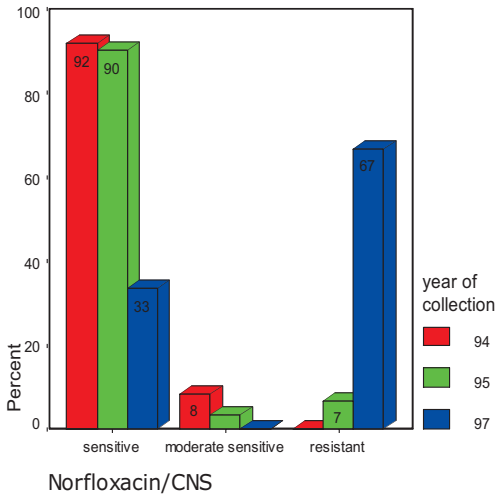
Figure 5: Fiprofloxacin sensitivity pattern (n=44)



Ciprofloxacin/CNS

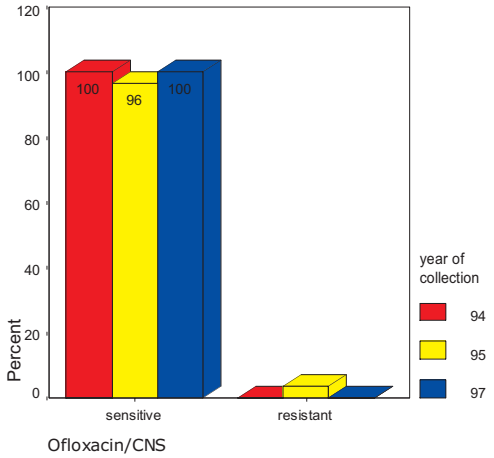
There is an increase in the resistance to ciprofloxacin, the number of cases examined to this day were only 2 in 1997 (P=0.032).

Figure 6: Norfloxacin sensitivity pattern (n=45)



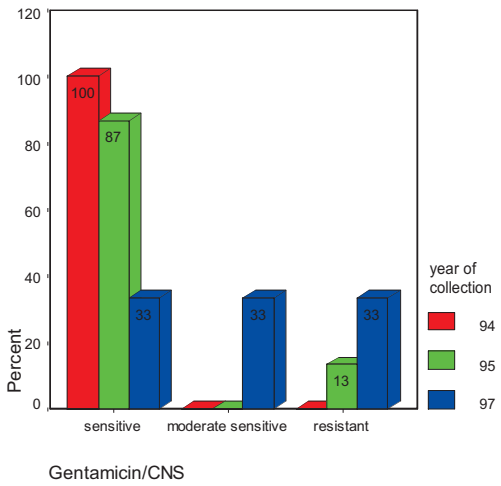
There was a statistically significant increase in the resistance of the antibiotic over the years (P=0.007).

Figure 7: Ofloxacin sensitivity pattern (n=40)



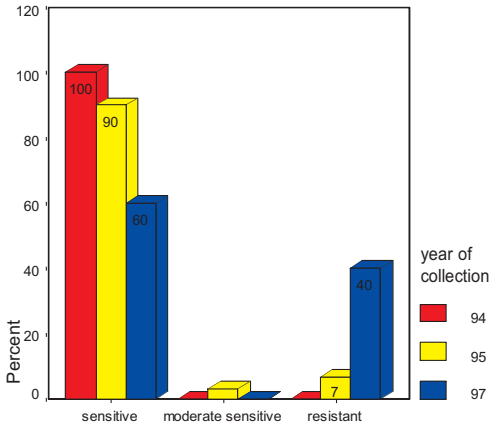
Ofloxacin was highly sensitive to CNS over the years (P=0.803)

Figure 8: Gentamicin sensitivity pattern (n=43)



There is a statistically significant increase in the resistance to gentamicin over the years (P=0.002)

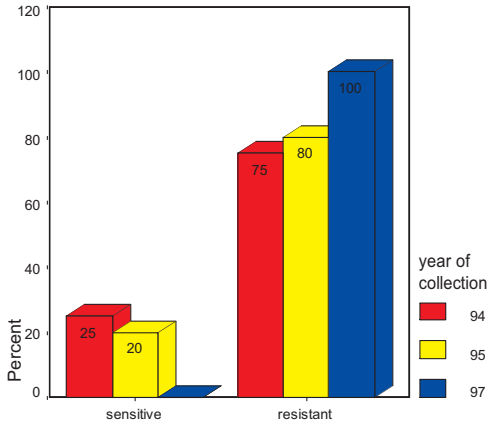
Figure 9: Tobramycin sensitivity pattern (n=47)



Tobramycin/CNS

There was a gradual increase in the resistance of the antibiotic over the years (P=0.086)

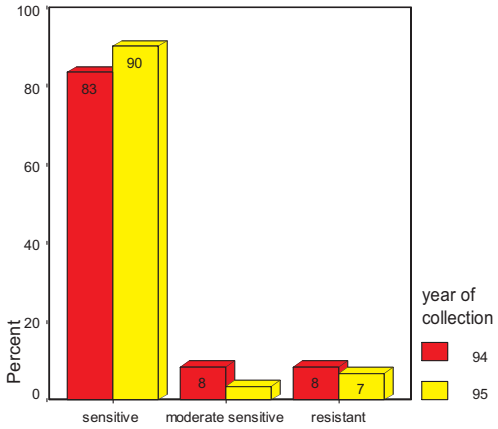
Figure 10: Tetracycline sensitivity pattern (n=43)



Tobramycin/CNS

Tetracycline was highly resistant all through and the resistance steadily increased over the years (P=0.819)

Figure 11: Polymixin b sensitivity pattern (n=42)



Polymixin B/CNS

There was no data collected for 1997. The antibiotic remained highly sensitive overall (P=0.769)

DISCUSSION

Fig 1 shows the sensitivity pattern of amoxicillin, a penicillin with an extended spectrum of activity. CNS has a high level of resistance to this antibiotic over time. In previous studies done by Patel and Gichangi, both have already shown a high level of resistance (Reference?). Although both authors examined pathological cases, we can compare our resistance patterns since the organisms have been shown to share the same genetic pattern from other studies. The same organisms have been shown to be causative agents in some of the infections. [8, 9]

Fig. 2 shows the sensitivity pattern of carbenicillin an antibiotic with anti pseudomonal activity. CNS had good sensitivity all through the years, carbenicillin is an infrequently used antibiotic in this region and this could explain the consistently good sensitivity of the antibiotic over the years. In our study, carbenicillin was not tested specifically against the Pseudomonas spicies.

In previous studies done in the region Mundia found a resistance of 5% of CNS to cephalexin.[9, 10] Fig. 3 shows the sensitivity pattern of cephalexin, a 1st generation cephalosporin whereby the sensitivity of the antibiotic remained good (>80%) overall for against the microbiota. There is also a decrease in resistance from 1994 to 1997 for CNS. In this study the organisms mainly isolated are the gram positive organisms and the 1st generation antibiotics are known to have good sensitivity against the gram positive organisms. cephalexin has generally been a good antibiotic in the region.

In general the results show that the cephalosporins have a good sensitivity pattern to CNS and this may be due to the fact that Cephalosporins are not a commonly used group of antibiotics.

Fig. 4 shows the sensitivity pattern of chloramphenicol, a commonly used topical antibiotic in this region which acts by binding the 50s subunit of the bacterial ribosome and preventing protein synthesis.[11] The sensitivity of chloramphenicol has gradually changed overall from 1994 to 1997 for the microbiota. CNS shows a gradually increasing sensitivity to chloramphenicol. The sample size however was low in 1997 (3 cases). In the study done by Mundia [9], the sensitivity was 13% while Patel[10] found a sensitivity of 25% to chloramphenicol. Our figures for 1994 and 1995 are comparable, although the figures for 1997 show a fall in the resistance. This could be explained by the fact that entamicin was a more commonly used antibiotic and a 1st line during that period, hence chloramphenicol retained a good sensitivity. Secondly chloramphenicol is used more in the pediatric group against suspicion of H. influenza and in adults in meningitis. This may explain the good sensitivity of the antibiotic during that period.

Fig. 5 shows the sensitivity pattern of CNS to ciprofloxacin. The sensitivity has remained good overall though there is a mild increase in the resistance in 1997 although the sample size is relatively low (3 samples). CNS has good sensitivity to norfloxacin from 1994 through to 1997. Due to the low number of cases in 1997, the pattern cannot be interpreted reliably. CNS has remained highly sensitive to ofloxacin all thorough the years. This was the first topical flouroquinolone to be introduced in the market. The emerging resistance to ciprofloxacin and norfloxacin could be due to the increasing systemic and local usage of the two flouroquinolones and the ready availability of the antibiotics in the market. Ofloxacin was not widely used in 1994 and 1997. Our result is similar especially for ciprofloxacin with that of Patel (20%) [9], but higher then that of Gichangi (no resistance) [8] and Mundia (no resistance)[10]. However our figures for norfloxacin and ofloxacin are comparable with these studies. Other studies have shown that there is raising emergence of resistance to the flouroquinolones especially ciprofloxacin. Our results follow suit for ciprofloxacin and norfloxacin but ofloxacin had remained an antibiotics with low resistance.[11, 12, 13]

In Fig. 8, CNS shows a statistically significant increase in its resistance to gentamicin from 1994 to 1997. CNS shows a reduction in the sensitivity of gentamicin from 1994 to 1995. Fig. 9 shows a reducing sensitivity to tobramycin. The overall raise in resistance could be explained by the fact that there may be cross resistance to the antibiotics considering the fact that gentamicin is a very frequently used antibiotic in our setting. The mechanism of cross resistance may most likely be enzymatic modification of the drug which is both inactivated and prevents uptake of the active drug.[11]

Out of the two tetracyclines (doxycycline, tetracycline) studied in this series, results were available only for the resistance pattern of tetracycline. Fig 10 showed a rising resistance to tetracycline from 75% to 80% then to 100% from 1994 through to 1997. This rise was statistically insignificant, considering it was already a highly resistant antibiotic. In previous studies done[8, 9, 10] all have shown a high degree of resistance to the tetracyclines and their figures are comparable to our figures. This high resistance could be attributed to the wide and injudicious use of the tetracyclines in our setup, including use as a lubricant when no other appropriate ophthalmic lubricant is available.

Fig. 11 shows that resistance of CNS to polymixin B remained low all through. This is not a commonly used antibiotic except in combinations with other topical antibiotics or steroids. This antibiotic is not utilized as a systemic antibiotic, and this could possibly explain the low overall resistance .

The study has shown that there is a change in the sensitivity pattern of the antibiotics, especially the commonly ones used in the region like gentamicin, and chloramphenicol. As surgeons adapt and use newer antibiotics with more frequency, we realize there is a gradual increase in the resistance of such antibiotics like ciprofloxacin and norfloxacin, whereas the less commonly used antibiotics such

as carbenicillin and cephalexin maintain a general good sensitivity pattern due to their minimal usage.

Sensitivity patterns on the newer generation antibiotics which are being used more frequently in the region should be studied in subsequent studies to find out the new sensitivity patterns like gatifloxacin, moxifloxacin, levofloxacin and azithromycin.

The above results are laboratory results where the Kirby disc diffusion technique was utilized to test the sensitivity pattern of the antibiotics.[7]The concentrations tested on these discs tests for the blood concentrations achieved by the standard systemic dosages of these antibiotics. To the contrary, the concentrations achieved by the local applications of these antibiotics to the eye are much higher therefore these results give an orientation but the clinical response remains decisive.

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