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Research Article

A PROSPECTIVE STUDY OF THE PATTERN OF TOPICAL ANTIMICROBIAL USE IN SUPERFICIAL OCULAR INFECTIONS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND:Superficial ocular infections can be bacterial, viral or fungal, treated empirically by topical AMAs. The pattern and duration of use depends upon the nature and severity of infections, the likely pathogens, and the antimicrobial spectrum of AMAs. Because of paucity of published reports in the Indian literature regarding the pattern of use, efficacy, safety, tolerability of topical AMAs, the present study was taken up.OBJECTIVES:To study the pattern of use, criteria for selection, efficacy, safety and tolerability of topical AMAs in superficial ocular infections.METHODS:210 properly selected subjects with superficial ocular infections were included for the present study. The topical AMAs were used empirically as monotherapy for 5-21 days, depending upon the treatment response. The treatment outcome was assessed on 5th and 14th day. Tolerability and patient compliance for the prescribed medications were also assessed during the follow up visits.RESULTS:Moxifloxacin was the most commonly used topical AMA for bacterial infections, acyclovir and ganciclovir for viral infections, and natamycin for fungal corneal ulcer. Most of the subjects showed complete resolution of infection by 14 days, and only a few subjects with chronic viral keratitis needed continued therapy for 21 days. INTERPRETATION AND CONCLUSION:The superficial ocular infections can be effectively treated by empirical use of topical AMAs. Moxifloxacin can be considered as the primary option for bacterial infections. The viral infections respond very well to acyclovir and ganciclovir and the fungal infections to natamycin.

KEY WORDS:Superficial ocular infections, Topical AMAs.

INTRODUCTION

Ocular infections are caused by a variety of microorganisms like bacteria, viruses, fungi and protozoa. Though some of the infections may be self-limiting, the severe, chronic or recurrent infections if not treated promptly and effectively, may lead to impairment or loss of vision.

Superficial ocular infections like conjunctivitis, keratitis, corneal ulcer and anterior uvetitis, are usually treated with topical antimicrobial agents (AMAs) in the form of eye drops or ointments, whereas infections involving deeper, intraocular/periocular structures or posterior segment, may require systemic or intralesional/intrabulbar administration like subconjunctival, intracameral and intravitreous injections.

The topical application is a very convenient and noninvasive procedure ensuring high local concentration of AMAs, minimizing systemic adverse effects and also not requiring any medical assistance or supervision, and hence usually undertaken on outpatient basis. The efficacy of topical AMAs depends upon the susceptibility of the pathogens, duration of contact, the local

pharmacokinetics of the agent and the ability to penetrate into deeper layers. The topical AMAs if used in appropriate formulation, adequate concentration, adequate frequency and duration, effectively control the superficial ocular infections. However, indiscriminate and irrational use of topical AMAs may cause irritation, sensitization, histological and ultra structural changes in conjunctiva, sometimes delaying the healing process and also super infections. In addition, the emergence of antimicrobial resistance is a growing problem in ocular therapeutics.

There is a wide range of topical AMAs including the antibiotics and the synthetic AMAs, which differ in their spectrum, mechanism of action, ocular pharmacokinetics and tolerability. The selection of topical AMAs is usually empirical, depending upon the clinical pattern of infections, predisposing factors, the likely causative organisms and their anticipated susceptibility / resistance pattern and the local pharmacokinetics of the agents. Bacteriological studies like culture and sensitivity are usually not undertaken except for chronic, recurrent or complicated infections. However, considering the efficacy, tolerability, pharmacokinetics and pharmaceutical feasibility, there are relatively few and limited options in choosing the suitable topical AMAs.

Though topical AMAs are used routinely and extensively in ophthalmic practice, there are few systematic studies reported in the Indian literature regarding the clinical pattern of their use, the evaluation of their efficacy, safety, tolerability and clinical outcome. Hence, the present study was taken up to generate some valid and clinically useful data.

In this study, the pattern of use of topical AMAs for superficial ocular infections, the criteria for their selection, their safety, tolerability and clinical outcome, was assessed in the ophthalmology outpatient department of a tertiary care teaching hospital.

METHODOLOGY

1. Study subjects

Outpatients attending the Department of Ophthalmology, KIMS Hospital and Research Centre, Bangalore.

2. Study period

This study was carried out from 01-01-2011 to 30-06-2012 (18 months)

1.1 Sampling

Purposive sampling, involving 210 patients with superficial ocular infections receiving topical antimicrobial therapy.

1.2 Inclusion criteria

a. Patients from all age groups of either gender with superficial ocular infections i.e., conjunctivitis and keratitis who received topical AMAs.
b. Willingness to give written informed consent and comply with study procedure and available for follow up, if any.

1.3 Exclusion criteria

a. Patients with deep ocular or periocular infections requiring or receiving systemic or topical antimicrobial therapy like blepharitis, dacryoadenitis, dacryocystitis, uveitis, endophthalmitis, etc.
b. Patients or their legal representatives not willing to give written informed consent, comply with study procedure or available for follow up.

2. Study procedure

After obtaining approval and clearance from the **Institutional Ethics Committee**, **210** consecutive patients from all age groups of either sex, who presented with superficial

ocular infections **(conjunctivitis or keratitis)** and required topical AMAs, were included for the study.

3. **Laboratory investigations (baseline)**
    a. Bacteriological – gram staining and culture, done in selected cases
    b. KOH preparation for suspected fungal infections
    c. Fluorescein staining for viral infections
4. **Follow up**

    Follow examination to assess the outcome of treatment was done on 5th and 14th day after initiating the AMA therapy.
5. **Statistical analysis**

    The data collected was analyzed statistically using descriptive statistics namely mean, median and standard deviation for quantitative variables. Results were also depicted in the form of tables and graphs.

RESULTS

A. DEMOGRAPHIC DATA

Table 1: Age distribution (n=210)

Age group	Number of patients	Percentage
0-18	56	26.67%
19-25	37	17.61%
26-35	49	23.33%
36-45	35	16.67%
46-55	11	5.24%
>56	22	10.48%
Total	210	100%

Table 2: Gender distribution* (n=210)[a]

Gender	Frequency	Percent
Female	99	47.1
Male	111	52.9
Total	210	100

OBJECTIVE PARAMETERS (SIGNS) AT BASE LINE (VISIT – 0)

Table 3a: Conjunctival congestion (n=210)

Grading*	Left eye	Right eye	Bilateral
0	–	–	–
1	3	3	45
2	20	19	98
3	6	7	9
Total	29	29	152

*****Conjunctival congestion was graded as Grade 0 (Nil), Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe)

Table 3b: Ciliary congestion (n=33)

Grade*	Left eye	Right eye	Bilateral
0	-	-	-
1	4	4	6
2	5	6	5
3	1	2	0
Total	10	12	11

***** Grade 0 (Nil), Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe)[25]

Table 3c: Corneal edema (n=4)

Grade*	Left eye	Right eye	Bilateral
0	-	-	-
1	2	0	2
2	0	0	0
3	0	0	0
Total	2	0	2

*****Corneal edema was graded as Grade 0 (absent), Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe)[25]

Table 3d: Number of patients showing corneal ulcer* (n=11)

Eye	No. of patients
Left eye	4
Right eye	4
Bilateral	3

*****Assessed by clinical examination

Table 3e: Conjunctival discharge# (n=198)

Grading*	Left eye	Right eye	Bilateral
0	-	-	-
1	17	13	85
2	9	10	64
Total	26	23	149

* 0 = no discharge, 1= watery discharge; 2= mucopurulent discharge
#Twelve subjects did not have any discharge

Table 4: Laboratory tests/investigations*

Tests	No. of patients	Outcome
Gram staining	14	Positive in 5 patients
Conjunctival swabbing for bacterial culture	4	Staphylococcal growth in 2 patients
KOH preparation for fungal staining	5	Positive in all 5 patients@
HIV test#	1	Positive
RBS$	10	>120 mg/dl
Total	32	

* Only in selected patients; all tests were done at base line
#For confirmation, since the patient gave history of HIV positivity
$ For patients with history of diabetes mellitus
@ Probably aspergellosis: further tests for confirmation not done

Table 5: Total number of patients treated with each AMA

AMAs*	No. of patients	Percentage (%)
Moxifloxacin	108	51.43
Gatifloxacin	13	6.19
Ofloxacin	5	2.38
Ciprofloxacin	1	0.48
Azithromycin	8	3.81
Tobramycin	41	19.52
Chloramphenicol	16	7.62
Acyclovir	7	3.33
Ganciclovir	6	2.86
Natamycin	5	2.38
Total	210	100%

*All the AMAs were used as monotherapy, combinations not used in any patient.

Table 6: Change of AMAs

Initial drug	Substitute drug	Reason for change	No. of patients	Percentage (n=210)
Moxifloxacin	Tobramycin	Inadequate clinical response*	4	01.90%
Chloramphenicol	Moxifloxacin	Inadequate clinical response	1	0.47%
Total			5	02.38%

*Subjective and objective features of infection not resolving after initial therapy for 5 days (at visit-1)

Table 7: Outcome of therapy at visit-1 (5 days)

AMAs	Patients initially treated (N)	Patients with adequate resolution of infection* (N)	Percentage (%)
Moxifloxacin	108	71	65.74
Gatifloxacin	13	9	69.23
Ofloxacin	5	2	40
Ciprofloxacin	1	1	100
Azithromycin	8	2	25
Tobramycin	41	26	63.41
Chloramphenicol	16	12	75
Acyclovir	7	1@	14.28
Ganciclovir	6	3	50
Natamycin	5	0	0
Total	210	127	60.47

*Hence discontinued after first visit
@ Though resolution was adequate in the patient with acute viral conjunctivitis, the treatment was continued for 2 more days

Table 8: Outcome of therapy on visit-2 (14 days)

AMAs	Patients with treatment extended up to visit-2 (N)	Patients with adequate resolution of infection (N)	%
Moxifloxacin*	34	34	100.00
Gatifloxacin	4	4	100.00
Ofloxacin	3	3	100.00
Ciprofloxacin#	--	--	--
Azithromycin	6	6	100.00
Tobramycin	19	19	100.00
Chloramphenicol	4	4	100.00
Acyclovir@	6	4	66.66
Ganciclovir	3	3	100.00
Natamycin$	5	5	100.00
Total	84	82	97.61

*In four patients, moxifloxacin was substituted by tobramycin, and one patient was changed from chloramphenicol to moxifloxacin because of inadequate clinical response
[#] Ciprofloxacin which was initially used in only one patient was stopped after 5 days because of the complete resolution of the infection
[@] Only 4 patients showed complete resolution of infection and the other 2 patients with chronic viral keratitis required continuation of the treatment upto 21 days for complete resolution
[$] Stopped after 14 days as the regression of the ulcer and epithelization was complete

Table 9: Overall outcome of therapy[*]

Outcome of therapy	Number of patients	Percentage (%)
Infection completely resolved[#]	205	97.62
Infection resolved with change of AMAs[$]	5	02.38
Total	210	100%

* As assessed clinically at the end of the ultimate follow up observation after 21 days
[#] Without any sequleae or complications
[$] At visit-1

Table 10: Outcome of therapy based on clinical diagnosis*

Diagnosis	Infection resolved completely with initial treatment (n)	Infection resolved completely with change of AMA (n)	Total
Acute bacterial conjunctivitis	174	4	178
Chronic bacterial conjunctivitis	10	1	11
Acute viral conjunctivitis	1	0	1
Acute bacterial keratitis	1	0	1
Chronic bacterial keratitis	2	0	2
Chronic viral keratitis	12	0	12
Fungal corneal ulcer	5	0	5
Total	**205**	**5**	**210**
Pearson Chi-Square 2.657[a]; df 6; Asymp. Sig. (2-sided) 0.851			

* At the end of the observation period

a. 11 cells (78.6%) have expected count less than 5. The minimum expected count is .02.

DISCUSSION

In the present study, the pattern of use of topical AMAs for superficial ocular infections, the criteria for their selection, their safety, tolerability and clinical outcome, was assessed in patients attending the ophthalmology outpatient department in KIMS Hospital and Research Centre, a tertiary care teaching hospital.

The age distribution of the study subjects is shown in **Table 1**. Majority of the patients (~ 68%) were under 35 years of age, and only 10.48% of subjects above 55 years. There was no significant difference in gender distribution as shown in **Table 2**.

The objective parameters or clinical signs at base line (visit-0) have been summarized in **Tables 3a to 3e**. **Table 3a** shows the grading of conjunctival congestion. Conjunctival congestion was present in all the subjects and it was bilateral in majority of the subjects (n=152). In 137 subjects, the conjunctival congestion was of grade 2 (moderate), and severe congestion (grade 3) was present in only 22 subjects (9 bilateral+13 unilateral). Ciliary congestion which was present only in 33 subjects, has been graded in **Table 3b** Most of the patients (n=30) had grade 1 or grade 2 congestion (unilateral or bilateral), and only in 3 subjects had grade 3 congestion which was unilateral. Only 4 subjects had grade 1 (mild) corneal edema, 2 bilateral and 2 unilateral, (**Table 3c)**. Corneal ulcers were present in 11 subjects, 8 unilateral and 3 bilateral (**Table 3d)**.Conjunctival discharge was present in majority of the subjects (n=198) and it was bilateral (n=149) and unilateral (n=49). Most of the subjects had watery discharge (n=115), and mucopulurent discharge was seen in 83 subjects **(Table 3e)**.

The laboratory tests and investigations to confirm the diagnosis were done in selected patients, at baseline **(Table 4).** Gram staining of the conjunctival secretions was done in 14 randomly selected patients with mucopurulent discharge, and was positive in 5 patients. Bacterial culture of the conjunctival swabbing was done in 4 subjects with chronic bacterial conjunctivitis, and staphylococcal growth was observed in 2 patients. Fungal staining was positive in all the 5 subjects with fungal corneal ulcer.

The total number of subjects treated with each topical AMAs is summarized in **Table5**. Moxifloxacin was the most commonly used topical AMAs (n=108, 51.43%), followed by tobramycin (n=41, 19.52%). The overall number of subjects treated with fluoroquinolone group of AMAs was 127 (60.47%), reflecting the fact that they are widely preferred topical AMAs for bacterial ocular infections. However, gentamicin, another widely used topical aminoglycoside, was not used in any of the patients.

Table 6 shows the change of AMAs which was done only in 5 subjects because of inadequate resolution or control of infection after initial therapy for 5 days. 4 subjects were changed from moxifloxacin to tobramycin, and one subject from choramphenicol to moxifloxacin. These changes were considered and effected during visit-1.

The outcome of therapy with various topical AMAs as assessed at visit-1 (5 days) is tabulated in **Table7**. The rate of resolution of infection was almost comparable with moxifloxacin, gatifloxacin, tobramycin and chloramphenicol, though the no. of subjects treated with the individual antibacterial agents varied significantly. The treatment was discontinued is those subjects with adequate resolution of infection i.e., subjective and objective features of infection. Among the 7 subjects treated with acyclovir, complete resolution occurred in the patient with acute viral conjunctivitis (n=1), however the treatment was continued for 2 more days. In chronic viral keratitis treated with ganciclovir, adequate resolution was seen in 3 subjects and hence the treatment was discontinued. In other 3 pateints with inadequate resolution, the treatment was further continued up to 2 weeks. None of the patients with fungal

corneal ulcer treated with natamycin showed adequate regression at visit-1. The rate of resolution of the bacterial infections at visit-1 was 64.06% (n=123/192), and the overall rate of adequate resolution was 60.47% (n=127/210).

The outcome of treatment assessed at visit-2 (14 days) is summarized in **Table8.** There was complete resolution in all the subjects with bacterial infections treated with various antibacterial agents and hence the treatment was discontinued. Only 2 subjects with chronic viral keratitis treated with acyclovir showed inadequate resolution of the infection and treatment was continued up to 21 days for complete resolution. In all subjects with fungal corneal ulcer (n=5) treated with natamycin complete regression of ulcer with epithelialization had occurred, and hence the treatment was discontinued. The rate of resolution was 100% with bacterial infections, with the overall rate of resolution been 97.61%. Thus in all the study subjects (n=210) complete resolution of all infections had occurred at the end of the ultimate follow up observation after 21 days, of which 97.62% of the subjects (n=205) showed complete resolution with the initial therapy and other 5 subjects showed resolution of infection with the change of AMAs at visit-1 **(Table9).** The outcome of treatment based on the clinical diagnosis is shown in **Table 10**.

In the present study, the pattern of use of topical AMAs in superficial ocular infections was considered, excluding deep ocular, periocular infections and infections involving the adenexa, which may require supplementation with systemic AMAs therapy. The superficial ocular infections include the bacterial, viral and fungal infections of conjunctiva and cornea. The bacterial and viral infections may be acute or chronic, whereas the fungal infections usually chronic. The commonest pathogens involved in acute bacterial conjunctivitis are *S. aureus, H. influenzae,H. aegyptius*and, *N. gonorrhoeae,* which may produce purulent or mucopurulent infections. Though acute bacterial conjunctivitis is generally self-limiting and resolving within 1-2 weeks, the use of AMAs significantly improves clinical and microbiological remission, shortens the duration of symptoms and decreases the contagious spread of infection. Chronic bacterial conjunctivitis usually involves staphylococci, trachoma and inclusion conjunctivitis, often occurring due to incomplete resolution of acute conjunctivitis, and hence appropriate topical AMA therapy for appropriate duration is very essential to ensure adequate resolution. Recurrent and resistant infections may require bacteriological studies for optimizing antimicrobial therapy. Bacterial keratitis is less common, usually developing when the normal ocular defense mechanisms are compromised due to trauma, prolonged use of topical steroids, dry eyes, entropion with trichiasis, lagopthalmos, wearing of contact lenses, bullous keratopathy, diabetes, vitamin A deficiency and poor local hygiene. The most common pathogens are *P. aeruginosa, S. aureus, S. pyogenes, S. pneumoniae, N. gonorrhoeae, E. coli,* etc. Since bacterial keratitis is a vision-threatening infection causing loss of vision due to corneal opacity or corneal destruction, intensive AMA therapy is required to eradicate the infection and to prevent corneal scarring and perforation. The viral infections affecting the superficial ocular tissues include acute viral conjunctivitis, chronic viral keratitis and keratoconjunctivitis. Acute viral conjunctivitis is usually due to adenovirus, and it is self-limiting requiring only symptomatic treatment. Herpes simplex conjunctivitis requires topical antiviral therapy to hasten resolution and to prevent the possible corneal involvement. Viral keratitis is usually due to herpes group of virus and requires treatment with topical antiviral agents to prevent the sequelae and the complications.

Fungal conjunctivitis and keratitis are commonly due to *Aspergillus, Fusarium or Candida albicans,* andmay occur due to trauma, preexisting chronic ocular surface disease/epithelial defects, immunocompromized individuals, diabetes and people using hydrophilic contact lenses. Because of the chronic nature of the infection, prolonged therapy

with topical antifungal agents is required for several weeks to ensure adequate regression and resolution of the infection.

In the present study, the most common superficial ocular infection observed was acute bacterial conjunctivitis (84.76%). Other studies have reported a lower prevalence of bacterial conjunctivitis (35-50%) and higher prevalence of bacterial keratitis and corneal ulcer.[26, 27]The bacteriological studies were done routinely in all cases to isolate the causative organisms.[15.] In our study bacteriological tests were done only in randomly selected patients at baseline, and not repeated further because of good clinical response with the topical AMAs. However, bacterial cultures were done only for chronic bacterial conjunctivitis. For bacterial infections the topical AMAs were chosen empirically at the clinical discretion of the prescribers, whereas in other studies, the choice of AMAs was mainly based on bacterial culture and sensitivity tests.[28,29] The most commonly used AMAs for bacterial infections were fluoroquinolones (66.14%), and aminoglycosides (19.52%). Among the fluoroqunolones, moxifloxacin was the most widely used drug (n=108). Tobramycin was the only aminoglycoside used in the present study. The other AMAs like ofloxacin, gatifloxacin, ciprofloxacin, azithromycin and chloramphenicol were used less frequently. All the AMAs were used as monotherapy and no combinations were used. Change of therapy was needed only in 5 subjects because of incomplete resolution on day 5. Complete resolution of all bacterial infections occurred by 14 days. In other studies, the topical AMAs used were ciprofloxacin, gentamicin, chloramphenicol, cefazolin, neomycin, bacitracin, polymyxin and norfloxacin were the AMAs used.[18,26,28] Hence, the pattern of selection and use of AMAs may vary from centre to centre depending upon the pattern and prevalence of infections and the prescribing trend of the clinicians.

Moxifloxacin is a newer fluoroqunolone having a wide antimicrobial spectrum with a highly potent and rapid bactericidal action against most of the pathogens involved in superficial ocular infections. It has a good penetrating ability achieving a very high and sustained residual concentration in the superficial ocular tissues and hence effective by thrice daily instillation. In addition, it has excellent tolerability because of its near neutral pH (6.8) as topical solution, and it is self-preserved not requiring any preservative. Development of resistance to moxifloxacin is extremely rare and unusual. Most of the superficial ocular infections generally respond with a short course of topical therapy for 3-7 days.[30,31] However for deep ocular infections like endopthalmitis, systemic administration may be required.[16] Considering its distinct advantages, moxifloxacin is generally preferred for empirical therapy of acute and chronic bacterial infections of the eye and also to prevent post-operative and post-traumatic infections. Tobramycin, the only aminoglycoside used in the present study, has potent bactericidal action mainly against aerobic gram negative organisms with some activity against streptoccoi, and effective against gentamicin resistant oraganisms like *Pseudomonas.*[16] However, because of its low lipid solubility, it has limited penetrating ability requiring frequent instillation every 4-6 hours.[4]

The viral infections observed in the present study included acute viral conjunctivitis (n=1) and chronic viral keratitis (n=12), suspected to be herpetic, and were treated by topical acyclovir and ganciclovir which have good activity against herpes virus. The duration of administration for chronic viral keratitis ranged from 5-21 days depending upon the time required for complete resolution. The rate of resolution in chronic viral keratitis appears to be faster with ganciclovir. Ganciclovir has good penetrating ability producing faster resolution

compared to acyclovir, and found to be effective even in acyclovir resistant cases, and also showed good tolerability.[32]

In the present study, only 5 subjects had fungal infection presenting as fungal corneal ulcer suspected to be due to aspergillosis, unilateral in all the subjects, and treated with natamycin suspension for 8-14 days depending upon the rate of resolution, and complete resolution occurred in all the 5 subjects after 2 weeks. None of these patients had predisposing risk factors. Other studies have reported similar pattern of fungal infection presenting as fungal corneal ulcer and the causative organisms were *Aspergillus, Candida* and *Fusarium,* and the topical antifungal agents used were natamycin, ketoconazole, amphotericin B, fluconazole and voriconazole. All these topical agents had comparable efficacy and cost-effectiveness and voriconazole was reserved in refractory cases.[33,34]However, in one study, topical terbinafine was found to be superior to natamycin.[35]Natamycin is the only topical ophthalmic antifungal agent currently available, and the other antifungal agents are extemporaneously compounded and formulated for topical administration. Natamycin is a polyene antifungal, antibiotic with good activity against *Aspergillus, Candida* and *Fusarium*and it is predominantly fungicidal, attaining effective concentration in the stroma.[36]Hence, natamycin can be considered as the primary option for superficial fungal infections of the eye for keratitis, blepharitis, corneal ulcers, etc.

Thus, it was observed in the present study that most common superficial ocular infection was acute bacterial conjunctivitis which was treated empirically with various topical AMAs. The most commonly employed topical AMA for bacterial infections was moxifloxacin because of its distinct advantages like wider antimicrobial spectrum, potent bactericidal action and good tolerability. The viral infections suspected to be due to herpes virus, were treated with topical antiviral agents such as acyclovir and ganciclovir because of their good activity and established efficacy against herpes virus. The fungal corneal ulcers which occurred in only few patients were treated with topical natamycin, the only available topical antifungal agent. The treatment response was assessed on day 5 and 14. Most of the ocular infections completely resolved by day 14, but only a few cases of chronic viral keratitis required continued administration for 21 days to ensure complete resolution. There was no residual visual impairment in any of the subjects. All the topical AMAs used in the present study showed good tolerability with only mild local reactions which were self-limiting. Patient compliance for the prescribed medications was excellent (100%).

In conclusion, it can be postulated that, the superficial ocular infections can be effectively treated empirically by various topical AMAs as monotherapy. Moxifloxacin can be considered as the mainstay or primary option for most of the bacterial infections and other AMAs like tobramycin, chloramphenicol and azithromycin can be considered as reserve options. Acyclovir and ganciclovir are very suitable for herpetic viral infections, and natamycin the only option for fungal infections. The duration of administration depends upon the nature of infection, the possible causative organism and the treatment response.

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