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Research Article

Pathogens and Antibacterial Therapy in Pediatric Bacterial Conjunctivitis, Dacryocystitis and Chalazion

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Abstract

This paper studies the spectrum of pathogens and the antibacterial therapeutic results of using azithromycin 1.5% eye drops in pediatric bacterial conjunctivitis, dacryocystitis, and chalazion. *Staphylococcus epidermidis* and *Staphylococcus aureus* proved to be the most frequently occurring pathogens, with rates of 58.5% and 24.5%, respectively. Mixed infections were discovered in 61.7% of cases. During the first year of life in children with congenital dacryocystitis, *Staphylococcus epidermidis* was detected most frequently (40.9%), followed by *Staphylococcus aureus* and *Staphylococcus haemolyticus*, with rates of 22.7% and 9.0%, respectively. In chalazions and in bacterial conjunctivitis, *Staphylococcus epidermidis* was also the most frequent, with rates of 68.3% and 62.3%, while *Staphylococcus aureus* was less frequent and identified in 10.5%. and 30.2% of cases, respectively.

Azithromycin was found to have high efficacy (98.9%) despite the fact that pathogens' sensitivity to it is not sufficiently high (45.7%). Azithromycin 1.5%, administered in a convenient dosage regimen of one drop twice daily for three days, leads to rapid resolution of the main signs of pediatric purulent eye diseases. This improved convenience makes it easier to follow the treatment regimen and reduces the burden of the disease on and parents.

Keywords: *Bacterial Conjunctivitis; Dacryocystitis; Chalazion; Pathogens; Azithromycin; Children*

Introduction

The problem of the rational use of antibiotics in clinical practice, and particularly - in the treatment of ophthalmic diseases, remains relevant and has even become more acute in recent years due to the large number of antibacterial agents, the lack of clear indications, and insufficient control over their use. Many studies on topical antibiotics in ophthalmic practice have focused on adults and adolescents, while the use of such antibiotics in young children has not been sufficiently considered [1-4].

Among the most common pediatric eye diseases caused by bacterial pathogens are bacterial conjunctivitis, dacryocystitis of newborns, and eyelid chalazion. Bacterial conjunctivitis is observed in 50 - 80% of all conjunctivitis cases in children. Dacryocystitis occurs in the event of lacrimal tract obstruction in infants [5-7]. The prevalence of pyogenic inflammatory eye diseases in children necessitates the identification of the most effective treatment program, which can be achieved by studying the spectrum of the existing pathogenic microflora.

Purpose of the Study

The purpose of this study is to determine the microbiological spectrum of causative agents in pediatric patients with purulent eye diseases and to assess the efficacy of azithromycin 1.5% eyedrops for treating pediatric conjunctivitis, dacryocystitis and chalazion.

Materials and Methods

Study design and patients

The study was carried out at the Pediatric ophthalmology department of the SI "The Filatov Institute of Eye Diseases and Tissue Therapy of NAMS of Ukraine", from January to December 2021.

In total, 94 children with the purulent diseases of the conjunctiva, eyelids, and lacrimal duct were enrolled in the study. The patients' ages ranged from two weeks to fifteen years. The study included the following groups: i) 22 children, aged from two weeks to three years (average, 1.8 ± 1.2 years), with congenital dacryocystitis due to lacrimal duct obstruction; ii) 19 children, aged from 2 to 12 years (average 6.8 ± 4.9 years), with chalazion in the infiltration and abscessed stages; and iii) 53 children, aged from 3 to 15 years (average, 8.2 ± 5.3 years), with conjunctivitis.

Dosing regimen and assessments

All children received azithromycin 1.5% eye drops, in a regimen of one drop twice daily for three days. On initial admission and after 3 days of azithromycin treatment (on the 7 - 9 day after prescription), the children underwent clinical examination to determine the severity of inflammatory signs, as well as a microbiological study.

Discharge from the conjunctival cavity in cases of chalazion and conjunctivitis and from the lacrimal sac in cases of dacryocystitis was studied microbiologically to determine the microbiological spectrum of the causative agents and their sensitivity to antibiotics.

Clinical assessments

The inflammatory signs, such as eyelids and conjunctiva hyperemia, edema, and photophobia, as well as the nature and amount of discharge, were analyzed before and after azithromycin treatment.

Pathogen determination

Bacteriological studies of the discharge from the conjunctiva in chalazion and conjunctivitis and from the lacrimal sac in dacryocystitis were performed to isolate and identify etiologically significant bacteria and to determine their antibiotic sensitivity.

A dry, sterile cotton swab was used to collect the discharge from each patient's eye. A smear was taken in the morning and patients were advised not to perform an "eye wash" before the procedure. Biomaterial was obtained from the inner surface of the lower eyelid by moving towards the inner corner of the palpebral fissure. It was important to prevent eyelashes from touching the swab when blinking. The swab was placed into a sterile test tube. Thus, the sample was collected under aseptic conditions.

At the laboratory, the swabbed samples were seeded on Petri dishes with 5% blood agar and with a "sterility control medium" (a meat-peptone broth with the addition of 0.2% glucose, i.e. an accumulation medium).

The temperature was maintained at 37°C during the holding period using a thermostat.

On day 2, when growth appeared in the accumulation medium, we studied the growth patterns and performed Gram staining. Depending on the morphology of the micro-organisms, plating on elective nutrient media was performed in order to isolate pure cultures, followed by identification and sensitivity testing. In the presence of growth on 5% blood agar, the tinctorial properties of the grown colonies were studied morphologically by bacterioscopy with Gram staining. The bacterial growth was assessed qualitatively and quantitatively. Individual colonies were isolated on elective media for identification and sensitivity testing.

When no growth occurred during the first day, the seeds were left in a thermostat and checked daily. If growth was detected, appropriate separations were made. The final answer of "no growth" was given after three days.

Antibiotic sensitivity testing

Sensitivity to antibiotics was determined according to the disc-diffusion method, using standardized nutrient media and standardized antibiotic discs [8].

When collecting the data, zones of growth suppression were measured. Thus, a zone that was detectable to the naked eye when the dish was placed at a distance of approximately 30 cm from the eyes was considered a zone of total (or complete) bacterial growth suppression. Rotating the cup at a 45° angle to the workplace made it easier to record results when the edge of the zone was difficult to distinguish. A Petri dish with Müller-Hinton (MH) agar was covered with a lid and placed bottom up over a dark surface in reflected light. A ruler was used to measure the growth suppression zones. The diameters of the growth suppression zones were interpreted according to the sensitivity categories using the borderline values presented in the EUCAST values tables.

Results

The detection rates of pathogenic flora in purulent diseases of the lacrimal ducts, eyelids, and conjunctiva, as well as their sensitivity rates to azithromycin, are shown in table 1.

Pathogen	*Staph. Epidermidis*		*Staph. aureus*		*Staph. haemolyticus*		*Escherichia coli*		*Strept. haemolyticus*		*Enterococcus*		*Klebsiella*		*Pseudomonas aeruginosa*		Mixt
Dacryocystitis n = 22/100%	9 (40.9%)		5 (22.7%)		2 (9.0%)		1 (4.6%)		1 (4.6%)		1 (4.6%)		1 (4.6%)		2 (9.0%)		17 (77.3%)
Sensitive (S) Resistant (R)	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	
	3	6	2	3	2	-	-	1	-	1	-	1	-	1	-	2	
	Sensitive = 7 (31.8%) / Resistant = 15 (68.2%)																
Chalazion n = 19/100%	13 (68.3%)		2 (10.5%)		1 (5.3%)				2 10.5%		1 5.3%						10 (52.6%)
Sensitive (S) Resistant (R)	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	
	9	4	2	-	1	-	-	-	2	-	1	-	-	-	-	-	
	Sensitive = 15 (78.9%) / Resistant = 4 (21.1%)																
Conjunctivitis n = 53/100%	33 (62.3%)		16 (30.2%)		1 (1.9%)						3 (5.6%)						31 (58.5%)
Sensitive (S) Resistant (R)	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	
	14	19	14	2		1	-	-	-	-	1	2	-	-	-	-	
			Sensitive = 29 (54.7%) / Resistant = 24 (45.3%)														
Total n = 94/100%	55 (58.5%)		23 (24.5%)		4 (4.2%)		1 (1.1%)		3 (3.2%)		5 (5.3%)		1 (1.1%)		2 (2.1%)		58 (61.7%)
Sensitive (S) Resistant (R)	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	
	26	29	18	5	3	1	-	1	2	1	2	3	-	1	-	2	
	Sensitive = 51 (54.3%) / Resistant = 43 (45.7%)																

Table 1: *Detection rates of various pathogenic flora in purulent diseases of the lacrimal duct, eyelids, conjunctiva and pathogen sensitivity to azithromycin.*

The conjunctival flora varied in children with purulent diseases of the lacrimal duct, eyelids, and conjunctiva.

In children in their first year of life with congenital dacryocystitis, *Staphylococcus epidermidis* was detected most frequently (40.9%), followed by *Staphylococcus aureus* and *Staphylococcus haemolyticus*, with rates of 22.7% and 9.0%, respectively. At the same time, there were single cases of diverse pathogenic flora: *E. coli, Streptococcus haemolyticus, Enterococcus, Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*. Mixed forms, with a combination of different pathogens, were detected in the majority (77.3%) of cases.

In chalazions in the infiltration and abscessed stages, *Staphylococcus epidermidis* was also the most frequent, at 68.3%. Meanwhile, *Staphylococcus aureus* was less frequent, with a rate of 10.5%, and there were single cases of *Staphylococcus haemolyticus, Streptococcus haemolyticus,* and *Enterococcus*, accounting for 5.3%. Mixed forms were detected in nearly half of cases (52.6%).

In bacterial conjunctivitis, *Staphylococcus epidermidis, Staphylococcus aureus, Enterococcus,* and *Staph. haemolyticus* were detected in 62.3%, 30.2%, 5.6%, and 1.9% of cases, respectively, with Staphylococcus epidermidis as the most and *Staph. haemolyticus* as the least frequently revealed. Mixed forms were rather frequent (58.5%).

The identified flora were studied microbiologically to determine their sensitivity to azithromycin. For congenital dacryocystitis, of 22 cases, only 7 (31.8%) showed sensitivity to azithromycin, while 15 (68.2%) showed no sensitivity (Figure 1). For chalazions, sensitivity and no sensitivity to azithromycin were detected in 15 (78.9%) and 4 (21.1%) cases, respectively. For conjunctivitis, of 53 cases, sensitivity and no sensitivity to azithromycin were detected in 29 (54.7%) and 24 (45.3%) cases, respectively (Figure 2).

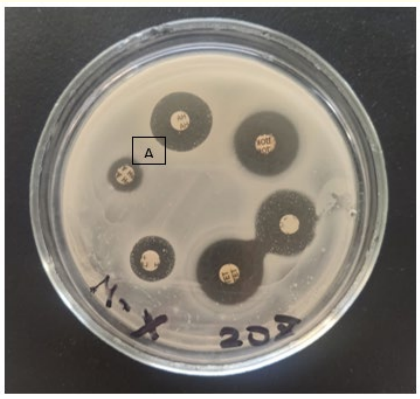

Figure 1: *Antibiotic sensitivity testing by the disc-diffusion method on standardised nutrient media with standardised antibiotic discs. ARN-disc (A) with azithromycin 15 μg; 3 mm zones of growth suppression is an azithromycin-resistant strain.*

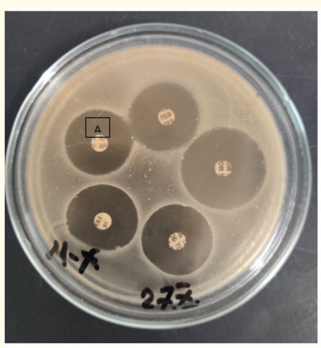

Figure 2: *Antibiotic sensitivity testing by the disc-diffusion method on standardised nutrient media with standardised antibiotic discs. APH-disc (A) with azithromycin 15 μg; 25 mm zones of growth suppression is an azithromycin-resistant strain.*

Treatment using azithromycin 1.5% eyedrops was administered according to a regimen of one drop twice a day for three days in all cases, and was started before the preliminary microbiological results were available.

The three-day treatment with azithromycin 1.5% eyedrops in congenital dacryocystitis made it possible to reduce the symptoms of purulent inflammation, and to reduce the amount and change the nature of the discharge. On repeated microbiological examination, an absence of pathogenic flora growth was found in all cases (100%) of congenital dacryocystitis, which allowed for a surgical intervention by probing to restore the lacrimal duct patency.

In chalazion, after a three-day course of azithromycin 1.5% eyedrops twice daily, a significant reduction in inflammatory signs and eyelid tissue infiltration was observed. The repeated seeding of the conjunctival flora revealed the absence of pathogenic agents in all cases (100%), which allowed for the surgical removal of chalazion.

In children with bacterial conjunctivitis, the resolution of signs of inflammation - hyperemia, conjunctival and eyelid edema - was observed after treatment in most cases (98.1%); there was no discharge. The growth of pathogenic flora (*Enterococcus*) with persistent insensitivity to azithromycin was observed in one case and there was no clinical stabilization of the inflammatory process.

Overall, after treating children with purulent diseases of the lacrimal duct, eyelids, and conjunctiva according to the conventional regimen of azithromycin 1.5% eyedrops twice daily for three days, a positive clinical result was obtained in 98.9% of cases.

Discussion

There is a pressing need to develop recommendations for the optimal treatment of pediatric bacterial eye diseases, such as bacterial conjunctivitis and chalazion, as well as dacryocystitis in newborns. This need has arisen because antibacterial therapy of these diseases during the initial stages is prescribed empirically [9]. Moreover, the modern health care system requires that children with such problems visit a pediatrician or family doctor who treats such "simple" eye pathologies. However, antibacterial drops are quite often prescribed according to a template without a clear understanding of the specifics of their mechanisms of action.

Comparing the data obtained in our previous studies on the nature of bacteriological pathogens in cases of conjunctivitis and dacryocystitis [10] with those obtained in this study shows the presence of the same palette of coccal flora. Comparing our microbiological findings with those in the literature, the different spectrum of microflora isolated from the conjunctival cavity should be noted. Blondeau., *et al*. [11] reported *Haemophilus influenzae, Streptococcus pneumoniae, Staphylococcus,* and *Streptococcus mitis* to be most common microflora in children with both polybacterial and monobacterial eye infections. Meanwhile, in our study, the most common were *Staphylococcus epidermidis* (58.5%) and *Staphylococcus aureus* (24.5%). This confirms the opinion of some authors that the nature of bacterial contamination of the conjunctiva depends on the region studied and on other factors [12].

An important trend revealed by comparing our previous and recent findings on pathogens in pyogenic eye diseases is that the number of mixed-infection cases has increased. In children with purulent eye diseases, a combination of several pathogens was observed in 36.9% of cases in 2011 [10], but this figure reached 61.7% in 2022.

The largest increase in the frequency of mixed microflora was observed in cases of newborn dacryocystitis, with rates of up to 77.3%. Lower rates were observed in cases of conjunctivitis and chalazion, with values of 58.5% and 52.6%, respectively. It should be noted that the rates of mixed infections in our study were significantly higher than those of other authors, who report that 23.6% of pediatric subjects with culture-confirmed conjunctivitis had polybacterial infections [11]. The increased prevalence of mixed microflora as a causative agent of purulent eye diseases in pediatric practice emphasizes the need to use broad-spectrum antibiotics for antibacterial empiric therapies.

The microflora cultured from the conjunctiva were found to be most sensitive to azithromycin in chalazion and conjunctivitis in older children (2 to 15 years), with rates of 78.9% and 54.7%, respectively, whereas no sensitivity was noted in 68.2% of children with dacryocystitis in their first year of life. Nevertheless, the clinical picture quickly improved in all cases when using azithromycin in the treatment of conjunctivitis, and the effective sanitation of the conjunctival cavity in cases of neonatal dacryocystitis and chalazion was objectively confirmed during preoperative preparations. This requires determining the clinical activity of azithromycin even in cases where the sensitivity of a particular pathogen to it is not determined in the laboratory. The phenomenon of high clinical efficacy against the background of the insufficiently high susceptibility of pathogens to azithromycin can probably be explained by its properties. Azithromycin circulates into intracellular compartments, undergoes rapid and extensive distribution, and remains highly concentrated in anterior eye tissues, as has been shown in clinical studies on pharmacokinetics and the mechanisms of antimicrobial action [13,14].

D. Bremon-Ginac., *et al*. reported the findings of one of the largest studies on the use of azithromycin 1.5% eye drops in children [7,18]. An international, multicenter, randomized clinical trial determined the efficacy of azithromycin 1.5%, administered as one drop twice daily for three days, and tobramycin 0.3%, administered as one drop every two hours for two days, then four times daily for five days. They demonstrated the sufficient efficacy of both drugs. However, the azithromycin regimen provided a more rapid resolution of conjunctival purulent discharge and bulbar conjunctival hyperemia and required less frequent administration during the day and a shorter duration of treatment, which implies its higher efficacy. Moreover, the parents of children enrolled in the study completed a standardized questionnaire and noted the ease of the azithromycin regimen, suggesting its advantages over tobramycin.

Azithromycin eyedrops allow for the achievement of clinical and bactericidal effects with shorter treatment durations and less frequent administration, as compared with other antibacterial eyedrops. These factors accurately reflect the current trends in the use of topical antibiotics [3,7] and produce a convenient regimen that children's parents can easily follow.

Antibiotic resistance remains a significant problem due to many factors, including the uncontrolled use of antibiotics without clear indications, and the use of antibiotics in agriculture with the possibility of their ingestion into the human body through food. In this respect, the studies of Asbell P.A. and DeCory H.H [16] showed a significant decrease in resistance rates among *S. aureus* to azithromycin over an eight-year study period, which confirms the relevance of using this antibacterial agent in the first-line treatment of bacterial eye diseases.

Conclusion

The spectrum of pathogens in pediatric bacterial conjunctivitis, dacryocystitis, and chalazion has remained almost unchanged in Ukraine over the last ten years. This spectrum includes *Staph. Epidermidis, Staph. aureus, Staph. haemolyticus, E. coli, Strept. haemolyticus, Enterococcus, Pseudomonas aeruginosa* and *Klebsiella pneumoniae*, with *Staphylococcus epidermidis* and *Staphylococcus aureus* being the most frequently detected, with rates of 58.5% and 24.5%, respectively. However, the frequency of mixed infections has increased significantly to 61.7%.

Azithromycin was found to have high efficacy (98.9%), despite the fact that pathogens do not have sufficiently high sensitivity to this treatment (45.7%).

Azithromycin 1.5%, administered in a convenient dosage regimen of one drop twice daily for three days, provides rapid resolution of the main signs of pediatric purulent eye diseases. This improved convenience makes it easier to follow the treatment regimen and reduces the burden of the disease on both children and parents.

Author Contributions

Conceptualization, B.N.F.; methodology, B.N.F and M.A.L.; formal analysis, M.A.L., D.G.M. and T.S.A.; investigation, B.N.F, M.A.L., D.G.M., T.S.A and D.O.D.; data curation, M.A.L. and D.G.M.; writing - review and editing, all authors; visualization, M.A.L. and D.O.D. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of SI "The Filatov Institute of Eye Diseases and Tissue Therapy of NAMS of Ukraine" (Protocol № 1; 01.03. 2023).

Informed Consent Statement

Informed consent was obtained from one parent of all children involved in the study.

Data Availability Statement

The data are not publicly available due to privacy concerns given the small sample size. However, the data presented in this study are available upon request from the corresponding author.

Conflicts of Interest

The authors declare no conflict of interest.

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