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Original Research Article

Proportion of ophthalmia neonatorum following prophylaxis with azithromycin eye ointment in newborns at a tertiary care centre in Central Kerala

Najeeba Chamban Mammooty, Madhu George, Jino Joseph, Abdul Tawab*

Department of Neonatology, Rajagiri Hospital, Ernakulam, Kerala, India

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***Correspondence:**
Dr. Abdul Tawab,
E-mail: abdultawab03@gmail.com

ABSTRACT

Background: The objective was to evaluate the proportion of ophthalmia neonatorum among 425 hospital born newborns who had received antibiotic eye prophylaxis within one hour of birth at a tertiary care centre in Central Kerala and to detect their causative organisms.
Methods: The study design was an observational study done for a period of 10 months. A total of 425 term well newborn babies were included in the study. At delivery after the normal routine newborn care, babies were received azithromycin 1% eye ointment as prophylaxis for neonatal conjunctivitis in both eyes within one hour of birth. Babies were observed routinely during every vital monitoring for developing signs of neonatal conjunctivitis for the first 72 hours of life at hospital. During outpatient follow ups, 7 to 14 days and 14 to 28 days, these babies were examined for the presence of neonatal conjunctivitis. Babies having neonatal conjunctivitis were treated empirically with the same topical 1% azithromycin eye ointment after taking eye swab for culture and sensitivity in both eyes. The treatment has been modified based on the culture reports. Proportions were compared using Chi-square test with significance at $p<0.05$.
Results: A total 15 (3.5%) of the 425 babies developed ophthalmia neonatorum. The most common isolate was *Staphylococcus aureus* which was 4 (26.7%) of all positive cultures followed by *Escherichia coli* 13.3%, *Klebsiella pneumoniae* 6.7%, *Serracia marcescens* 6.7%. None of the risk factors were found to be having association with conjunctivitis.
Conclusions: This study concludes that a high proportion of neonatal conjunctivitis present despite eye antibiotic prophylaxis, though a greater reduction in cases has been shown when compared with no prophylaxis at our centre during the previous year. *S. aureus* was the most common causative organism isolated.

Keywords: Ophthalmia neonatorum, Antibiotic eye prophylaxis, Newborn eyes

INTRODUCTION

Neonatal conjunctivitis often known as ophthalmia neonatorum (ON), which is defined as conjunctivitis occurring in newborn during the first month of life with clinical signs of erythema, oedema of the eyelids and palpebral conjunctivae, purulent eye discharge.[1] It was described in 1750 and is the most common infection occurring in the first month of life. Ophthalmia neonatorum leads to blindness in approximately 10,000 babies annually worldwide.[2]

It is a worldwide problem with incidence varying from 2-23% in different countries. In India, the reported incidence was 0.5-33%.[3]

The predisposing risk factors for conjunctivitis include maternal vaginitis, presence of meconium at birth, premature rupture of membranes, prolonged labour,

untrained birth attendant interference, low levels of lysozymes and immunoglobulins in neonatal conjunctiva, unhygienic practices and non-sterile environment.[4]

The infectious pathogens which cause neonatal conjunctivitis differs in various parts of the world, which depends upon the prevalence of prenatal maternal care and the use of prophylactic treatment to prevent infections in the pregnant mother and the newborn infant.[5]

The ON may be due to infectious or non-infectious (chemical) causes. *Chlamydia trachomatis* and *Neisseria gonorrhoea* are the commonest bacterial organisms implicated. However in developing countries the most frequent organism reported is *S. aureus*.[6] The known causes of neonatal conjunctivitis have continued to expand and now includes *E. coli*, *Klebsiella spp*, *P. aeroginosa*, herpes virus and chemical conjunctivitis.[6]

Microbiological workup with cytology and cultures is mandatory as the clinical presentations of conjunctivitis are not diagnostic of the cause. The treatment of ON has to be adequate because systemic complication and visual loss can occur particularly with *C. trachomatis* and *N. gonorrhoea* which are the leading causes of sexually transmitted diseases. To avoid these complications, routine prophylaxis with antimicrobial eye drops or ointments is practiced in many countries.[7]

Prophylactic treatment to reduce the incidence of neonatal infectious conjunctivitis began with the use of silver nitrate proposed by Crede in 1881.[8]

He used silver nitrate to prevent infection with *N. gonorrhoea*. However, silver nitrate caused a transient mild conjunctival inflammation in over 90% of treated eyes, characterized by redness and tearing that resolved within 24-48 hours. Hence more recently, prophylactic treatment has shifted to the use of erythromycin, which was well tolerated. Povidone-iodine solution was also increasingly used as prophylaxis because of its easy availability.[9] Macrolide antibiotics such as azithromycin, clarithromicin and roxithromicin may be more effective against chlamydial infections but have not been well studied in neonatal chlamydial conjunctivitis.[7] No much data is available from India regarding this important disease and there is no routine eye prophylaxis practiced immediately after birth.

The experience from our centre showed that 12.5% of babies born in the year 2018 over a period of 10 months developed signs of ON without giving any antibiotic prophylaxis at birth. This data was collected from previous case records.

We have been using azithromycin eye ointment as treatment for neonatal conjunctivitis for the last 3 years without any side effects and good cure rate.

This study was to evaluate the proportion of newborns developing ON following prophylaxis with azithromycin eye ointment and to identify the organisms prevalent in neonatal conjunctivitis based on culture of eye discharge.

This study had been undertaken to evaluate the proportion of newborns developing ophthalmia neonatorum despite prophylaxis with azithromycin (1%) eye ointment and to identify the organisms prevalent in neonatal conjunctivitis based on culture of eye discharge.

METHODS

A total of 425 term well newborn babies born at Rajagiri hospital, a tertiary care referral centre in Aluva from April 2019 to January 2020 were included for the study. At delivery after the normal routine newborn care, babies were received 1% azithromycin eye ointment as prophylaxis for neonatal conjunctivitis in both eyes within one hour of birth.

Inclusion criteria

Well newborn babies more than 37 weeks were included in the study.

Exclusion criteria

Babies with ocular malformations and babies requiring resuscitation or neonatal intensive unit care were excluded from the study.

Method of instillation of eye ointment

Both eyelids were gently wiped with a cotton gauze soaked in normal saline from inner to outer canthus. Each eyelid was wiped across 2-3 times. Lower eyelid was gently pulled downward and 0.5-1 cm ribbon of 1% azithromycin eye ointment was instilled into each conjunctival sac and closed eyelids were gently massaged to spread the ointment. After one minute excess ointment was wiped away with gauze. Hand hygiene was performed as and when required.

Babies were observed routinely during every vital monitoring for developing signs of neonatal conjunctivitis or any side effects related to the prophylaxis for the first 48 hours of life at hospital. Babies having eye discharge with redness and eyelid oedema was classified as neonatal conjunctivitis.

Routine newborn care was continued and babies were discharged as per the clinical status of the baby. During outpatient follow ups, 7 to 14 days and 14 to 28 days, these babies were examined for the presence of neonatal conjunctivitis. Babies having neonatal conjunctivitis were treated empirically with the same topical 1% azithromycin eye ointment every 8 hourly after taking eye swab for culture and sensitivity in both eyes. The treatment has been modified based on the culture reports.

Sample size

With reference to a study conducted by Zamani et al the proportion of ophthalmia neonatorum following prophylaxis with 0.5% erythromycin eye ointment was 18.4%.[9] Assuming that 95% confidence interval and 20% relative precision, based on the 18.4% prevalence, p value of 0.05 was significant, the required minimum sample size was 425, using the formula,

$$n=\frac{(Z1-\alpha/2)^2\times p\,(1-p)}{d^2},$$

where,

Z1-α/2: significance level,

d: relative precession,

p: prevalence.

Statistical methods

The statistical analysis was performed by IBM SPSS 25. Qualitative variables are expressed as frequency and percentages and quantitative variables as mean and standard deviation. Association between various factors were assessed using Chi-square test for categorical variable. P value of <0.05 was considered to be statistically significant.

Ethical considerations

No extra invasive techniques were required. Ethical committee clearance was obtained prior to the commencement of study.

RESULTS

A total of 425 hospital born newborns who were received prophylaxis (azithromycin 1% eye ointment) within one hour of birth at Rajagiri hospital were enrolled in the study. A total of 425 neonates were enrolled in the study.

212 (49.9%) were males and 213 (50.1%) were females. Mean birth weight of 425 newborns enrolled in the study was 3.08±0.35 kgs. The mean gestational age of the newborns were 38.79±0.7 weeks. There were 310 (72.9%) neonates delivered by vaginal delivery and 115 (27.1%) were delivered by caesarean section. All the 425 newborns who were enrolled in the study received prophylaxis within one hour of birth. There were no adverse effects reported following the prophylaxis.

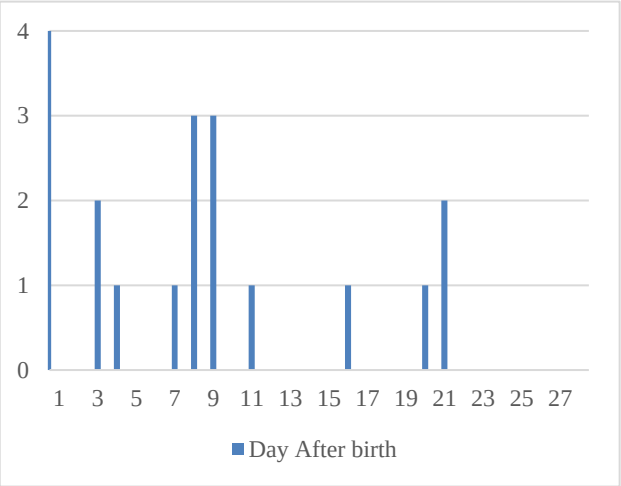

Figure 1: Day of presentation of neonatal conjunctivitis after birth (n=425).

Table 1: Distribution of baseline characteristics included in the study (n=425).

Characteristics		N (%)	Mean ±SD
Gender	Male	212 (49.9)	
	Female	213 (50.1)	
Birth weight			3.08±0.35
Gestational age			38.79±0.7
Mode of delivery	Normal	310 (72.9)	
	LSCS	115 (27.1)	
Maternal risk factors (n=39)	Fever	21 (53.8)	
	PROM	17 (43.6)	
	Meconium stained liquor	1 (2.6)	

Table 2: Proportion of babies having clinical signs of conjunctivitis despite prophylaxis (n=425).

Clinical signs	Total	Right eye	Left eye	Both eyes
	N (%)	N (%)	N (%)	N (%)
Conjunctivitis present	15 (3.5)	7 (46.7)	7 (46.7%)	1 (6.6%)
Conjunctivitis absent	410 (96.5)			

Table 3: Association of conjunctivitis with maternal risk factors (n=425).

Association with risk		Conjunctivitis positive	Conjunctivitis negative
		N (%)	N (%)
Risk factors present	n=39	1 (2.6%)	38 (97.4)
Risk factors absent	n=386	14 (3.6%)	372(96.4)
P=0.753			

Of the 425 newborns, 15 (3.5%) babies developed clinical signs of conjunctivitis in the form of purulent eye discharge and redness. Of the 15 (3.5%) babies, 46.7% had involvement of right eye, 46.7% had involvement of left eye and only 1 baby, 6.6% had involvement of both eyes.

Of the 425 newborns, 39 (9.2%) babies had maternal risk factors. Of the 39 (9.2%) babies who had maternal risk factors, only 1 (2.6%) baby had developed signs of conjunctivitis. 1 (2.6%) baby who developed signs of conjunctivitis, the maternal risk factor present was fever prior to delivery. None of the babies whose mothers with prolonged rupture of membranes and meconium stained liquor developed signs of conjunctivitis.

Of the 386 (90.8%) babies who does not had maternal risk factors, 14 (3.6%) babies had developed signs of conjunctivitis.

Day of appearance of conjunctivitis

The day of appearance of signs of conjunctivitis in the newborns is shown in Figure 1.

The mean age at the time of conjunctivitis was 10th day of life with a range of 3-21 days. Of the 15 babies with signs of conjunctivitis, 2 (13.3%) babies developed conjunctivitis during the 1st 3 days of life prior to discharge from the hospital, 2 (13.35) more babies developed conjunctivitis by 7th day of life, 7 (46.6%) babies developed conjunctivitis during the 2nd week of life and 4 (26.6%) babies developed conjunctivitis during the 3rd week of life.

Table 4: Bacteria isolated on culture of eye swabs.

Micro-organisms	N (%)
E. coli	2 (13.3)
Methicillin sensitive *S. aureus*	3 (20)
Methicillin resistant *S. aureus*	1 (6.7)
K. pneumoniae	1 (6.7)
S. marcescens	1 (6.7)
No organisms (culturesterile)	7 (46.6)

Eye swab culture and sensitivity were sent for all 15 (3.5%) babies with clinical conjunctivitis, Out of them, 8 (53.3%) cultures were positive.

Among the important pathogenic bacterial conjunctivitis, there were 2 cases of *E. coli*, 3 cases of methicillin sensitive *S. aureus*, 1 case of methicillin resistant *S. aureus*, 1 case of *K. pneumonia* and 1 case of *S. marcescens.*

The most common isolate was *S. aureus* which was 4 (26.7%) of all positive cultures followed by *E. coli* 13.3%, *K. pneumoniae* 6.7%, *S. marcescens* 6.7%.

DISCUSSION

Conjunctivitis or purulent eye discharge from one or both eyes is the commonest infection during the neonatal period.

The proportion of conjunctivitis in the first month of life among hospital born newborns at Rajagiri hospital was calculated to be 3.5% out of total 425 newborns in this study with eye antibiotic prophylaxis at birth.

In a published study by Syeda et al in 2010 in Pakistan, the frequency of ophthalmia neonatorum was 17% of all live births with no eye prophylaxis after birth.[10] A study published by Verma et al in 1994 India, Vellore, the incidence of conjunctivitis 7.2% of all live births with no prophylaxis.[11] A another study published by Zamani et al in 2007 the proportion of neonatal chlamydial conjuctivitis in the betadine eye drops, erythromycin and no prophylaxis were 9%, 18.4%, 22.4% respectively.[9]

The relative low incidence in the present study may be due to azithromycin eye ointment, which was a good prophylactic antibiotic.

The demographic data of 15 babies with conjunctivitis in this study had 49.9% females and 50.1% males which was in similar to a study published by Zamani et al in 2007.[9] In India, the proportion between male and female was 1.1:1.[10]

Risk factors for conjunctivitis were evaluated in this study. The association with the presence of known maternal risk factors like prolonged rupture of membranes, fever, meconium stained liquor and absence of risk factors were not found to be significant in this study which was in contrast to data from other places.[11]

Unilateral conjunctivitis was more common in this study which was in similar to a study published by Zamani et al in 2007.[9]

The earliest time at which conjunctivitis occurred was on the 3rd day of life which was in accordance with similar studies.[10]

Pathogens responsible for conjunctivitis vary geographically due to difference in socioeconomic conditions, standard of maternal health care, prophylactic programme, hygienic conditions during labour and postnatal exposure to micro-organisms. In the present study, the most common microbial agent was *S. aureus* which was known to be acquired after birth. This was in line with the studies from different countries like Hong Kong 34%, Argentina 27.6%, Nigeria 67.9%.[12-14] Other organisms were *E. coli*, *Klebsiella*, *S. marsescens*. All babies with conjunctivitis recovered completely with the use of azithromicin eye ointment.

In the present study, 46.6% of the conjunctival cultures did not reveal any growth. In other studies the range was between 50-55%, like Iran had 48% negative cultures despite positive signs of conjunctivitis.[10] In UK, no organism was grown in 53.5%cultures.[15]

In a study group from India, bacteria could not be isolated in 50% newborns.[16] The fact that most cultures were negative could be due to infections by viruses or anaerobes.

CONCLUSION

This study concludes that a high proportion of neonatal conjunctivitis present despite eye antibiotic prophylaxis, though a greater reduction in cases has been shown when compared with no prophylaxis at our centre during the previous year. *S. aureus* was the most common causative organism isolated.

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