

Treatment of Neonatal Conjunctivitis

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● The effect of different treatment regimens on clinical and microbiologic cures of neonatal conjunctivitis was evaluated during a 32-day observation period. In 84 infants with mild to moderate conjunctivitis and no signs of dacryocystitis, clinical cures were achieved in more than 50% of the cases with lid hygiene only. *Staphylococcus aureus* was the most common organism (48%) isolated from these infants. *Chlamydia trachomatis* could not be isolated from eyes with mild to moderate conjunctivitis. Forty-four infants with severe conjunctivitis, with or without dacryocystitis, were randomly assigned to treatment with either topical chloramphenicol or oral erythromycin for 14 days. *Chlamydia trachomatis* was isolated from 19 (43%) of these infants. All infants with chlamydial conjunctivitis who were treated with 25 mg/kg of oral erythromycin ethylsuccinate twice daily for 14 days were clinically and microbiologically cured. In contrast, all treatment of chlamydial conjunctivitis with topical chloramphenicol failed clinically as well as microbiologically. Dacryocystitis was a common complication in neonatal conjunctivitis (17%). The clinical failures in neonatal nonchlamydial conjunctivitis were associated with persistent obstruction of the nasolacrimal duct.

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Conjunctivitis is the most common infection during the first month of life.¹ Microorganisms such as *Staphylococcus aureus*, *Streptococcus*

pneumoniae, *Haemophilus*, *Streptococcus viridans*, and enterococci have been implicated in neonatal conjunctivitis.^{2,3} These organisms are most likely transmitted nosocomially to the infant. Conjunctivitis due to these organisms is often uncomplicated, and the recommended treatment is lid hygiene, with or without topical antibiotics.

Chlamydia trachomatis is the most common sexually transmitted organism isolated in neonatal conjunctivitis.^{2,8} Untreated, acute conjunctivitis will develop into a chronic follicular conjunctivitis that resolves spontaneously within eight to 12 months. Late sequelae with micropannus formation and scarring of the tarsal conjunctiva have been reported.⁹ Chlamydial conjunctivitis is often the only early clinical manifestation of a potential systemic disease in the newborn, with pneumonia and otitis as complications.^{5,10,11} Topical antibiotics have failed to eradicate chlamydial infection from the eye and from the nasopharynx.^{5,7,8} Oral erythromycin at a dosage of 30 mg/kg/d for 14 days has also failed to eradicate chlamydial infection.⁵ In contrast, a dosage of 50 mg/kg/d for 14 days has been reported to eradicate chlamydial infection effectively from the eye and the nasopharynx.⁸

Erythromycin has a low toxicity, and has been used in pediatric practice for many decades. The absorption of erythromycin ethylsuccinate is increased when administered with milk.^{12,13}

A congenital nasolacrimal obstruction is frequently seen in the newborn. The usual cause of occlusion is an imperforate membrane at the distal end of the nasolacrimal duct. In neonatal conjunctivitis, dacryocystitis is a common complication, with an inci-

dence of 1.75% to 5%.^{14,15} Topical antibiotics combined with massage of the lacrimal sac is the traditional primary management of this disorder.¹⁵⁻¹⁹

The aims of the present study were to follow the natural course of mild to moderate neonatal purulent conjunctivitis and to investigate the clinical and microbiologic cure of severe purulent conjunctivitis with or without dacryocystitis, using different antibiotic regimens. The effect of oral erythromycin ethylsuccinate at a dosage of 25 mg/kg every 12 hours (50 mg/kg/d) for 14 days was compared with the efficacy of 1% chloramphenicol ointment administered every four hours for 14 days. In Sweden, chloramphenicol is the most commonly used topical drug in the treatment of nonspecific purulent conjunctivitis.

PATIENTS AND METHODS

Patients

Infants born at the Södersjukhuset and Nacka hospitals, Stockholm, who developed ocular discharge during their first month of life were referred to me for examination and treatment. In addition to routine data, such as sex and birth weight, the age at onset of symptoms was recorded.

The clinical scoring of the conjunctivitis is described in Table 1.⁴ Clinical signs of epiphora, consistent with a congenital impatency of the nasolacrimal duct, were registered. If purulent exudate could be expressed from the lacrimal sac, the condi-

Table 1.—Three Criteria for Scoring Clinical Severity of Conjunctivitis*

Purulent discharge
Edema and erythema of the lids
Edema and erythema of the palpebral conjunctivae

*Intensity of criteria: mild, 1+; moderate, 2+; and severe, 3+.

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tion was diagnosed as dacryocystitis.

All parents gave their verbal informed consent to the study. The study protocol was approved by the Human Subject Committee.

Treatment Groups

Group 1.—Infants with a total clinical score of 3 to 5 were considered to have mild to moderate conjunctivitis. If no sign of dacryocystitis could be observed, these infants were treated with lid hygiene consisting of washing with 0.9% sterile sodium chloride solution six times daily for 14 days. The parents received four bottles of sterile saline solution to be used during the study period.

Groups 2 and 3.—Infants with a total clinical score of 6 or greater were considered to have severe conjunctivitis. These infants, as well as those with dacryocystitis, were randomly assigned to treatment with either topical chloramphenicol or oral erythromycin. Infants with dacryocystitis were also treated with lacrimal sac massage three times daily.

Chloramphenicol.—Infants born on odd-numbered days were treated with 1% chloramphenicol ointment six times daily for 14 days after lid hygiene with 0.9% saline solution.

Erythromycin.—Infants born on even-numbered days received 25 mg/kg of oral erythromycin ethylsuccinate every 12 hours for 14 days, combined with lid hygiene as described above. The parents were instructed to administer the drug with a small amount of milk between meals to prevent vomiting. The erythromycin syrup was administered with a 2-mL syringe that was lightly pressed toward the back of the tongue. The parents kept a treatment schedule record that was returned together with the remaining medicine at the end of treatment.

Collection of Specimens and Laboratory Methods

A conjunctival smear for Gram's staining was taken from the lower conjunctiva of the most inflamed eye. Additional specimens were taken from the same location in both eyes, as well as from one side of the nasopharynx; these were cultured for aerobic bacteria and *C trachomatis* according to procedures described elsewhere.⁴

Study Design

Clinical Follow-up.—The infants were examined at the initial visit, day 0, and days 3, 4, 10, 18, and 32. The clinical severity of the conjunctivitis was scored at each visit and the infant was examined for epiphora and dacryocystitis. At days 32 to 60 after the start of treatment, the lacrimal ducts were irrigated to diagnose a persistent obstruction of the nasolacrimal duct.

Definition of Clinical Cure.—A total clinical score of less than 3 at days 10, 18, and 32.

Definition of Clinical Failure.—A progression of the conjunctival inflammation with an increase of the score by 1 at day 3 or 4, or persistent conjunctivitis with a

Organism	Treatment Group, No. of Patients		
	Saline Solution	Chloramphenicol	Erythromycin Ethylsuccinate
<i>Chlamydia trachomatis</i>	0	5	9
<i>C trachomatis</i> and <i>Staphylococcus viridans</i>	0	1	0
<i>C trachomatis</i> and <i>Staphylococcus aureus</i>	0	2	2
<i>S aureus</i>	34	3	10
<i>S aureus</i> and <i>Staphylococcus pneumoniae</i>	1	0	1
<i>S aureus</i> and <i>Haemophilus influenzae</i>	2	0	0
<i>S aureus</i> and <i>S viridans</i>	2	0	0
<i>H influenzae</i>	4	0	2
<i>Branhamella</i>	1	1	0
<i>S pneumoniae</i>	8	0	0
<i>S viridans</i>	5	1	2
<i>S viridans</i> and <i>H influenzae</i>	1	0	1
<i>Escherichia coli</i>	0	0	1
<i>S aureus</i> and enterococci	1	0	0
<i>Staphylococcus epidermidis</i>	11	1	0
No organism	14	1	1
Total	84	15	29

Infants With Conjunctivitis	No. (%)	Microbiologic Cure, No.	Microbiologic Failure, No.
Clinical cure	47 (56)	39	8*
Clinical failure	37 (44)	20	17†
Total	84 (100)	59	25

* *Staphylococcus aureus* (n = 3), *Haemophilus influenzae* (n = 2), *Staphylococcus pneumoniae* (n = 1), and *Staphylococcus viridans* (n = 1).

† *Staphylococcus aureus* (n = 14), *H influenzae* (n = 1), *S pneumoniae* (n = 2), and *Branhamella* (n = 3).

total clinical score of 6 or greater at day 3 or 4 or 3 or greater at day 10.

Microbiologic Follow-up.—Cultures for *C trachomatis* and aerobic bacteria were obtained from both eyes and from the nasopharynx at day 0. At days 18 and 32, specimens were taken for the particular organism isolated at day 0. In infants who had a clinical failure at days 3 or 4 and at day 10, cultures were redone from both the eye and the nasopharynx on the same day on which the clinical failure was established.

Definition of Microbiologic Cure.—The organism isolated from the eyes or nasopharynx at day 0 could not be reisolated at days 18 and 32 or on the day on which clinical failure was determined.

Definition of Microbiologic Failure.—The organism isolated from the eyes and from the nasopharynx at day 0 could be reisolated at days 18 or 32 or on the day on which clinical failure was confirmed.

Statistics

The results were analyzed by the χ^2 test and Fisher's exact test. A *P* value less than .01 was considered significant.

RESULTS

One hundred twenty-eight infants with purulent conjunctivitis diagnosed according to our criteria were enrolled in the study. The culture results in the three different treatment groups are shown in Table 2.

The Natural Course of Mild to Moderate Conjunctivitis

Forty-seven (56%) of 84 infants with mild to moderate conjunctivitis treated with lid hygiene only were clinically cured at day 10 (Table 3). No relapse occurred in this group during the study period. However, eight clinically cured infants were microbiologic failures. *Staphylococcus aureus* was reisolated from the conjunctiva in three infants, *Haemophilus influenzae* was reisolated from two infants, and *H influenzae* together with *S aureus* was isolated from another infant. *Streptococcus pneumoniae* was recov-

ered from one infant and *S viridans* was recovered from another.

Thirty-seven infants with mild to moderate conjunctivitis who were treated with lid hygiene were clinical failures (Table 3). The initially isolated organisms could be reisolated from the eyes of 17 of these infants. Clinical failure was not associated with any particular organism.

Congenital nasolacrimal obstruction was diagnosed in 19 (51%) of 37 infants with clinical failure, compared with three (6%) of 47 infants with a clinical cure ($P < .01$). There was no significant difference in birth weight, sex, age at onset, or duration of conjunctivitis between infants who were clinically cured and infants who failed clinically.

The Effect of Oral Erythromycin Ethylsuccinate and Chloramphenicol Ointment on Chlamydial Conjunctivitis

All 11 infants with chlamydial conjunctivitis who were treated with oral erythromycin were clinically cured by day 10 (Table 4). *Chlamydia trachomatis* was initially also isolated from the nasopharynx of five of these infants. The organism was eradicated from the eye as well as from the nasopharynx in all infants. None of these patients had a relapse of *C trachomatis* infection during the study period. In contrast, persistent conjunctivitis was observed in all eight infants treated with topical chloramphenicol (Table 4). *Chlamydia trachomatis* was reisolated from the eyes as well as the nasopharynx of these infants.

The Effect of Oral Erythromycin Ethylsuccinate on Severe Conjunctivitis due to Other Organisms

Escherichia coli, *H influenzae*, and *S aureus*, respectively, were initially isolated from the most inflamed eye in three infants with severe conjunctivitis but no signs of dacryocystitis. All three were treated with erythromycin ethylsuccinate. The infant with *E coli* infection failed clinically and microbiologically, and an *E coli* strain resistant to erythromycin was reisolated. The two remaining infants were clinically and microbiologically cured.

The Effect of Oral Erythromycin Ethylsuccinate or Topical Chloramphenicol on Conjunctivitis With Dacryocystitis due to Organisms Other Than *Chlamydia*

Fourteen infants with conjunctivitis associated with dacryocystitis were treated with oral erythromycin ethylsuccinate. Four of them (29%)

Treatment Group	No. of Patients	Clinical, No. of Patients		Microbiologic, No. of Patients	
		Cure	Failure	Cure	Failure
Erythromycin	11	11	0	11	0
Chloramphenicol	8	0	8	0	8*

* Six of eight infants underwent culture for *Chlamydia trachomatis*.

Treatment Group	No. of Patients	Clinical, No. of Patients		Microbiologic, No. of Patients	
		Cure	Failure	Cure	Failure
Erythromycin	14	10	4	8	6*
Chloramphenicol	7	6	1	6	1†

* *Staphylococcus aureus*, *Streptococcus viridans*, and *Haemophilus influenzae*.
† *Branhamella*.

failed clinically (Table 5). Of the seven infants with conjunctivitis associated with dacryocystitis who received topical chloramphenicol, one exhibited clinical failure (Table 5). All five infants who were clinical failures turned out to have stenosis of the lacrimal duct. *Staphylococcus aureus*, *S viridans*, or *H influenzae* were reisolated from the eyes of four infants with clinical failure. *Branhamella* was reisolated from the eyes of three infants with clinical cure. All reisolates were sensitive to erythromycin and chloramphenicol in vitro.

Management of Treatment Failures

The 18 infants exhibiting persistent conjunctivitis without associated stenosis of the nasolacrimal duct, who were treated with lid hygiene only, received topical chloramphenicol and were clinically cured within ten days.

One infant who failed clinically and microbiologically while receiving oral erythromycin ethylsuccinate because of resistant *E coli* was treated with topical chloramphenicol and was cured within ten days.

The eight infants with *C trachomatis* conjunctivitis, who failed clinically and microbiologically while taking topical chloramphenicol, received oral erythromycin ethylsuccinate and were all cured with no scarring of the tarsal conjunctivae.

All 24 infants with persistent conjunctivitis due to stenosis of the nasolacrimal duct were treated with lacrimal sac massage three times daily, as well as topical chloramphenicol four times daily, for one week. Recurrent

conjunctivitis was noted in every infant until the nasolacrimal duct had opened. The duct opened spontaneously in all but five infants before the age of 6 months. In those five infants, the duct was probed at that age.

COMMENT

In the present study, mild to moderate conjunctivitis, without dacryostenosis, resolved within ten days in 44 (71%) of 62 infants treated with lid hygiene only. The microorganism isolated initially was reisolated from eight of 47 clinically cured eyes during a follow-up period of 32 days. These findings suggest that local defense mechanisms are operative in the infant eye and are capable of protecting ocular tissues from microbial invasion of the magnitude involved in mild to moderate conjunctivitis. An inhibiting effect by tear components on both pathogenic and nonpathogenic staphylococci has been demonstrated in vitro.²⁰ Furthermore, immunoglobulins can be detected in the tear fluid from the age of 4 weeks.³

In the present study, persistent conjunctivitis in mild to moderate cases was highly associated with an obstruction of the nasolacrimal duct, an observation that has previously been reported.¹⁷ No particular organism was linked with persistent mild to moderate conjunctivitis.

In the present study, dacryocystitis was a common complication in neonatal conjunctivitis, a finding that supports previous observations.¹⁷ Clinical failure in cases of dacryocystitis was always associated with persistent obstruction of the nasolacrimal duct.

However, infants with dacryocystitis who were treated with oral erythromycin failed microbiologically more often than did infants treated with topical chloramphenicol. This could partly be due to the well-established fact that the bacteriostatic effect of erythromycin is decreased in an environment with an increased pH, which is the case in a purulent process such as dacryocystitis. It is important to treat these infections and to prevent reinfection until the nasolacrimal duct has become patent.

It is recommended that the nasolacrimal ducts of infants beyond 4 months of age who have duct obstruction and recurrent conjunctivitis, with or without dacryocystitis, be probed to establish drainage and prevent further infection.¹⁷ However, it is important to bring the infection under control before the duct is probed.

In the present study, all patients with *C trachomatis* conjunctivitis were clinically and microbiologically cured when treated with 25 mg/kg of oral erythromycin ethylsuccinate every 12 hours for 14 days. No relapse occurred during an observation period of 32 days. These findings support previous results obtained by Heggie et al.⁸ In their study, 93% of infants with *C trachomatis* conjunctivitis were clinically and microbiologically cured with 50 mg/kg/d of oral erythromycin estolate divided into four daily doses

for 14 days. Cultures for *C trachomatis* were obtained two to four weeks after the completion of therapy. Less favorable results were reported by Patamasuon et al.,⁷ who used a lower dosage of oral erythromycin. They reported persistent *C trachomatis* conjunctivitis in 14% of infants treated with 20 to 40 mg/kg/d of oral erythromycin estolate or erythromycin ethylsuccinate for 21 days. These infants were followed up with *C trachomatis* cultures only one week after the end of therapy.

All infants with chlamydial conjunctivitis who were treated with topical chloramphenicol failed clinically and microbiologically. Failure to eradicate neonatal chlamydial conjunctivitis with topical antibiotics has been reported by others.⁸ In the present study, *C trachomatis* infection in the nasopharynx was eradicated with oral erythromycin.

The erythromycin ethylsuccinate was well tolerated by the patients. One of 26 infants developed watery stools after four days of therapy; the problem resolved the day after administration of the medicine was discontinued. Another five infants developed somewhat loose stools, but these returned to normal after the completion of 14 days of therapy. The erythromycin suspension was easy to administer with a 2-mL syringe.

Based on these observations, it can

be recommended that, in the acute stage of neonatal conjunctivitis, before the microbial cause is known, mild to moderate conjunctivitis without dacryostenosis may be treated with lid hygiene only. Severe conjunctivitis without stenosis of the nasolacrimal duct should be treated with lid hygiene combined with topical antibiotic (ie, chloramphenicol) ointment six times daily. If dacryostenosis is diagnosed, lacrimal sac massage should be added. Clinically suspected or culture-verified chlamydial conjunctivitis should be treated with 25 mg/kg of oral erythromycin ethylsuccinate every 12 hours for 14 days.

Other studies stress an early diagnosis by Gram's stain and culturing of *Neisseria gonorrhoeae* infection and prompt treatment.²¹ Severe conjunctivitis due to organisms other than *C trachomatis* or *N gonorrhoeae* can be treated with topical antibiotic ointment six times daily for at least one week. Infants with conjunctivitis associated with dacryocystitis should be managed with lacrimal sac massage several times a day, combined with topical antibiotics. In cases with persistent obstruction of the nasolacrimal duct and recurrent dacryocystitis, probing of the duct should be performed early, before 4 months of age.

Abbott Scandinavia AB, Stockholm, supplied the erythromycin mixture.

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