



DOI: 10.14744/eer.2022.40085  
Eur Eye Res 2022;2(2):80–83

EUROPEAN  
**EYE**  
RESEARCH

REVIEW

# Ocular prophylaxis in the newborn

 **Mahmut Celik**,  **Ozge Altun Koroglu**

Department of Pediatrics, Division of Neonatology, Ege University Faculty of Medicine, Izmir, Turkey

## Abstract

In the first 4 weeks of life, an ocular infection is seen in 1–12% of newborns and this clinical situation is called “ophthalmia neonatorum.” The etiology includes bacterial, viral, and chemical causes. Unfortunately, severe conjunctivitis progressing to corneal ulceration and blindness may develop in the newborns due to inadequate ocular prophylaxis. The development of these cases can be prevented by screening the mothers during pregnancy and giving treatment if necessary and/or providing the newborns with appropriate ocular prophylaxis.

**Keywords:** Newborn; ophthalmia neonatorum; prophylaxis.

Ophthalmia neonatorum is an ocular infection that occurs in 1–12% of newborns in the first 4 weeks of life.<sup>[1]</sup> While the term was previously defined as conjunctivitis caused by *Neisseria gonorrhoeae*, it is now used to describe any form of neonatal ocular infection.

Ophthalmia neonatorum is usually a mild illness, but conjunctivitis due to *N. gonorrhoeae* is a severe infection. Without treatment, the gonococcal eye infection can rapidly progress to corneal ulceration, globe perforation, and permanent visual impairment.<sup>[2]</sup> *Chlamydia trachomatis* is another microorganism that deserves attention for newborns. Infants born to women with untreated *C. trachomatis* infection at birth have a 50% chance of developing conjunctivitis and a 10–20% chance of developing pneumonia.<sup>[3]</sup>

Neonatal conjunctivitis may have different etiologies. The time elapsed after birth is essential in determining the etiology of neonatal conjunctivitis. Conjunctivitis that develops

in the first few hours is usually due to the chemical effect of the drugs given for prophylaxis. Gonococcal infections usually develop within 2–4 days, and chlamydial infections develop within 5–14 days. Herpes-induced conjunctivitis occurs within 5–7 days.<sup>[4]</sup> The causes and characteristics of ophthalmia neonatorum are summarized in Table 1.

To protect newborn infants, ocular prophylaxis is applied in the delivery room with other routine interventions such as vitamin K. In this review, evidence-based practice recommendations are presented in the light of scientific data regarding this protective practice, which varies from country to country.

## History fo Prophylaxis Practices

The beginning of ocular prophylaxis practices at birth dates to the 1800s. Keratitis due to gonococcal conjunctivitis was the leading cause of blindness in newborns in



**Cite this article as:** Celik M, Altun Koroglu O. Ocular prophylaxis in the newborn. Eur Eye Res 2022;2:80-83.

**Correspondence:** Ozge Altun Koroglu, M.D. Department of Pediatrics, Division of Neonatology, Ege University Faculty of Medicine, Izmir, Turkey

**Phone:** +90 232 390 12 82 **E-mail:** oaltunkoroglu@gmail.com

**Submitted Date:** 26.04.2022 **Accepted Date:** 05.05.2022



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**Table 1.** Causes and features of ophthalmia neonatorum

Cause	Clinical features
Chemical conjunctivitis	It may develop due to drugs used for prophylaxis. Conjunctival hyperemia and tearing begin within a few hours of drug administration. It usually heals spontaneously within 24–36 h without the need for treatment
Chlamydial conjunctivitis	It begins 5–14 days after birth, unilaterally or bilaterally. Lid edema, papillary conjunctival reaction and pseudo membrane formation may be seen. The secretion, which is serous in the early period, turns into a mucopurulent or bloody state in the later stages. In severe cases, conjunctival scarring may progress with pannus in the peripheral cornea and scarring in the cornea
Gonococcal conjunctivitis	It gives symptoms after the first 24–48 h. Chemosis, conjunctival membrane, pseudomembrane, and acute purulent secretion are among the findings. The eyelids are hard and edematous. Since it can pass through the intact corneal epithelium, it can cause corneal ulceration and endophthalmitis
Other bacterial conjunctivitis	They typically appear after 2–5 days, but they can appear at any time. Lid edema, conjunctival hyperemia, and purulent secretion are among the findings
Viral conjunctivitis	It can develop with herpes virus Types 1 and 2. It gives symptoms within 2 weeks. Edema of the eyelids, vesicles on the eyelid margins and body may be seen. Eye complications such as epithelial and stromal keratitis, keratouveitis, vitreous, retinal detachment, cataract, chorioretinitis, and optic neuritis; Systemic complications such as pneumonia, septicemia, and meningitis may accompany.

the 19<sup>th</sup> century. The development of ophthalmia neonatorum and blindness was significantly reduced when German gynecologist Crede started to use topical 2% silver nitrate prophylactically in newborns in 1881.<sup>[5]</sup> Although silver nitrate prophylaxis has a vast antimicrobial spectrum, other agents were introduced since silver nitrate has limited effect against *C. trachomatis* and causes chemical conjunctivitis. Silver nitrate concentration was reduced to 1% to reduce chemical conjunctivitis.<sup>[6]</sup> However, concerns about *C. trachomatis* necessitated the use of new methods.

Isenberg et al.<sup>[7]</sup> showed that topical administration of povidone-iodine is a very cheap and effective method. 2.5% povidone-iodine is more effective against conjunctival bacteria and less toxic than silver nitrate. In many countries, silver nitrate has been replaced by 0.5% erythromycin or 1% tetracycline ointment to offer protection against *C. trachomatis*. Povidone-iodine 2.5% or 1% and fusidic acid have also been suggested as alternative drugs.<sup>[4]</sup>

In our country, practices for ocular prophylaxis in the newborns differ from center to center. A questionnaire about ocular prophylaxis practices was performed in 24 university hospitals and 24 state hospitals, including obstetrics and pediatrics clinics, throughout Turkey in 2009. According to this survey, the prophylaxis rate for ophthalmia neonatorum was 66.7% in university hospitals; 50% in state hospitals; it was 58.3% in total. In the same study, gentamicin (64.3%) and tobramycin (8.3%) were the two most commonly used drugs for prophylaxis; Tetracycline, silver nitrate, povidone-iodine, bacitracin + neomycin, and penicillin G were found to be less used drugs.<sup>[8]</sup>

Today, many different approaches exist for ocular prophylaxis practices in newborns. Two main approaches in this regard differ based on the screening of mothers. Countries that carry out screening programs for possible neonatal conjunctivitis agents in pregnant women have avoided routine ocular prophylaxis for newborns. On the other hand, in countries that do not have a screening program for pregnant women and apply prophylaxis to newborns, the preferred agents, practice time, and methods vary. The most recent recommendations on this subject are summarized below and presented in Table 2.

### Current International Recommendations On Ocular Prophylaxis Practices For Newborns

The American Academy of Pediatrics recommends applying 0.5% erythromycin ointment to the eyes of all newborn infants (including those born by cesarean section) to prevent vision-threatening gonococcal ophthalmia if gonorrhoea is widespread in the area and prenatal care is not available or required by law.<sup>[1]</sup>

Application of the prophylaxis may be delayed for 1 h to facilitate parent-infant bonding. Prolongation of this delay is not investigated yet. Each eyelid should be gently wiped with sterile cotton before applying prophylaxis. After that, a 1 cm strip of 0.5% erythromycin ointment should be placed in each lower conjunctival sac. The ointment should ideally be applied using disposable tubes or ampoules rather than reusable tubes. The eyelids should then be gently massaged to spread the ointment. If erythromycin ointment is unavailable, 1% azithromycin ophthalmic solution

**Table 2.** Recommendations of health institutions for ocular prophylaxis in newborns

Institution	Suggestions
American Academy of Pediatrics	0.5% erythromycin prophylaxis is recommended for all newborns. If erythromycin ointment is not available, 1% azithromycin ophthalmic solution is recommended. If it is not available, 0.3% ciprofloxacin ophthalmic ointment may be considered
Centers for Disease Control and Prevention	Ocular prophylaxis with erythromycin ointment as a single agent is recommended for all neonates
Canadian Pediatric Association	The recommendations stand for screening all pregnant women, treating the mother, and prophylaxis with erythromycin if necessary. Routine prophylaxis is not recommended
World Health Organization	Ocular prophylaxis to all newborns with one of five different agents is recommended: Tetracycline hydrochloride 1% eye ointment, Erythromycin 0.5% eye ointment, povidone-iodine 2.5% solution (water-based), silver nitrate 1% solution, and chloramphenicol 1% eye ointment
T.R. Ministry of Health	Prophylaxis with the appropriate preparation chosen by the health care provider is recommended for all newborns
Turkish Ophthalmology Society	Prophylaxis with erythromycin 0.5% or 2.5% povidone-iodine or azithromycin eye drops is recommended for all newborns
Turkish Neonatology Society	Since 0.5% erythromycin and 1% tetracycline eye drops are not available in the country, it is recommended to use 0.3% gentamicin or 0.3% tobramycin instead

is recommended. If 1% azithromycin ophthalmic solution is unavailable, 0.3% ciprofloxacin ophthalmic ointment may be considered a less suitable alternative. Prophylaxis with topical antimicrobial agents is mandated by law in many regions, as it is highly effective in preventing blindness from gonococcal neonatal ophthalmia. Although these obligations have been abandoned in many countries over the past few decades, they have remained effective in the United States. The American Academy of Pediatrics advocates for legislation that allows the adoption of alternative strategies to prevent neonatal ophthalmia while supporting the reassessment of the continuing necessity of legal mandates in the United States for universal neonatal ocular prophylaxis.

The Centers for Disease Control and Prevention recommends ocular prophylaxis with erythromycin ointment as a single agent for all newborns in the first 24 h after birth.<sup>[9]</sup> In addition to ongoing routine ocular prophylaxis, recommendations for focusing on prenatal screening for *N. gonorrhoeae* also exist.

In Canada, current practices are different. Neonatal ocular prophylaxis with erythromycin, the only agent currently available in Canada, is not routinely recommended.<sup>[10]</sup> Pediatricians and other physicians caring for newborns are advised to advocate repealing regulations for ocular prophylaxis in areas currently required by law. Instead of neonatal ocular prophylaxis screening of mothers is recommended. All pregnant women should be screened for *N. gonorrhoeae* and *C. trachomatis* infections at the first

prenatal visit. Those who are infected should be treated during pregnancy, tested after treatment to ensure therapeutic success, and retested in the third trimester or, if that does not happen, during delivery. Their partners should also be treated. Women who are negative but at risk of contracting the disease should be screened once again later in pregnancy. For women not in a stable monogamous relationship, rescreening should be considered in the third trimester for *N. gonorrhoeae*, *C. trachomatis*, and other sexually transmitted diseases. Pregnant women who are not screened during pregnancy should be screened during delivery for *N. gonorrhoeae* and *C. trachomatis*.

On the other hand, the World Health Organization (WHO) guidelines recommend topical ocular prophylaxis for all neonates, for the prevention of gonococcal and chlamydial ophthalmia neonatorum.<sup>[11]</sup> For ocular prophylaxis, the WHO recommends one of the following options for topical application to both eyes immediately after birth:

- Tetracycline hydrochloride 1% eye ointment
- Erythromycin 0.5% eye ointment
- Povidone-iodine 2.5% solution (water-based)
- Silver nitrate 1% solution
- Chloramphenicol 1% eye ointment.

Cost and local resistance may determine drug choice for erythromycin, tetracycline, and chloramphenicol in gonococcal infection. When applying the topical treatment, care should be taken not to touch the eye tissue and to provide a water-based povidone-iodine solution.

## Current National Recommendations On Prophylaxis Practices in Turkey

In the guide published by the Ministry of Health in our country in 2017, it is stated that a suitable preparation can be selected by the relevant health institution for prophylaxis in newborn babies.<sup>[12]</sup> In the same guideline, it is stated that the Turkish Ophthalmology Society recommends erythromycin 0.5% or 2.5% povidone-iodine or azithromycin eye drops.

In the Turkish Neonatology Society Delivery Room Management Guideline 2021 Update, since 0.5% erythromycin and 1% tetracycline eye drops are not available in our country for *N. gonorrhoeae*, so it is recommended to use 0.3% gentamicin or 0.3% tobramycin instead (despite topical side effects).<sup>[13]</sup> In addition, to prevent topical side effects (eyelid swelling, dermatitis around the eyes), eye drops should be instilled into the lower eyelid as 1 drop in each eye and the excess amount should be wiped. There is no recommended agent that is readily available for *C. trachomatis* prophylaxis currently. Screening of mothers is preferred. Although it has been shown in studies that the effect of povidone-iodine is better and has less side effects, it is not recommended by the Turkish Neonatology Society due to the inadequacy of evidence and the lack of recently dated studies. To establish a new practice that will cover the important agents and protect newborns from blindness while preventing unnecessary treatments and possible side effects, new studies are needed for our country.

### Conclusion

Although screening of all pregnant women and prophylaxis seem appropriate, as is the practice in Canada, considering the difficulty of screening all women, prophylaxis for all newborn babies continues to be applied in most of the world, as recommended by the local and universal guidelines. The common single agent recommended as a safe prophylactic drug is erythromycin. However, since it is difficult to find, it is seen that different preparations are used according to availability. The effectiveness, cost, and safety of the different approaches for neonatal ocular prophylaxis warrant investigation in large populations.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions:** Concept: M.C., O.A.K.; Design: M.C., O.A.K.; Supervision: M.C., O.A.K.; Resource: M.C., O.A.K.; Materials: M.C., O.A.K.; Data Collection and/or Processing: M.C., O.A.K.; Analysis and/or Interpretation: M.C., O.A.K.; Literature Search: M.C., O.A.K.; Writing: M.C., O.A.K.; Critical Reviews: M.C., O.A.K.

**Conflict of Interest:** None declared.

**Financial Disclosure:** The authors declared that this study received no financial support.

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