NEONATAL CONJUNCTIVITIS - A REVIEW

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Conflict of interest: None

ABSTRACT

Ophthalmia neonatorum remains a significant cause of ocular morbidity, blindness and even death in underdeveloped countries. The organisms causing ophthalmia neonatorum are acquired mainly from the mother's birth canal during delivery and a small percentage of cases are acquired by other ways. *Chlamydia* and *Neisseria* are the most common pathogens responsible for the perinatal infection. Fortunately in most cases, laboratory studies can identify the causative organism and unlike other form of conjunctivitis, this perinatal ocular infection has to be treated with systemic antibiotics to prevent systemic colonization of the organism. Routine prophylaxis with 1% silver nitrate solution (crédés method) has been discontinued in many developed nations for the fear of development of chemical conjunctivitis. **Key words:** Crédés Prophylaxis; Neonatal Conjunctivitis; Ophthalmia Neonatorum; Sexually Transmitted Diseases. *Mallika PS, Asok T, Aziz S, Faisal HA, Tan AK, Intan G. Neonatal conjunctivitis – a review. Malaysian Family Physician. 2008;3(2):77-81*

INTRODUCTION

Neonatal conjunctivitis is often known as *ophthalmia neonatorum* (Latin name). It is defined as conjunctivitis occurring in a newborn during the first month of life with clinical signs of erythema and oedema of the eyelids and the palpebral conjunctivae, purulent eye discharge with one or more polymorph nuclear per oil immersion field on a Gram stained conjunctival smear.¹ Originally described in 1750, it is one of the most common infections occurring in the first month of life.²

Ophthalmia neonatorum leads to blindness in approximately 10,000 babies annually worldwide.³ The major causes of Ophthalmia neonatorum are, in decreasing order, chemical inflammation, bacterial infection and viral infection. The majority of infectious neonatal conjunctivitis are due to bacteria.⁴ The bacterial causes include sexually transmitted diseases agents (*Chlamydia trachomatis and Neisseria gonorrhoea*), microorganisms from the skin (*Staphylococcus aureus*) and the mother's gastrointestinal tract (*Pseudomonas sp*).⁵ The inflammation usually resolves spontaneously within a few days. Therefore, simple Gram stain and routine bacterial culture are often the only investigations that are required in most cases. ⁶ Although simple investigation suffices, treatment has to be adequate because systemic complication and severe visual loss can occur in infection particularly with *Chlamydia*

*trachomatis and Neisseria gonorrhoea.*⁷ Apart from bacteria, herpes viruses can also cause neonatal conjunctivitis.

The organisms causing neonatal conjunctivitis are usually acquired from the infected birth canal of the mother, though some may acquire the infection from their immediate surroundings.⁸ The predisposing factors, which can increase the chance of the newborn acquiring neonatal conjunctivitis, include increase shedding of these organisms in the vaginal tract of the mother during the last trimester, premature rupture of membranes and prolonged labor. Neonatal conjunctivitis following caesarean section could be due to intrauterine chlamydial infection as the result of early rupture of the membranes⁸ or trans-placental or transmembrane transfer of these organisms.⁹

The epidemiology of Ophthalmia Neonatorum has changed following the prophylactic use of 1% silver nitrate solution (Crédé method); there was a marked reduction in the incidence of ophthalmia in the United States, Europe, and the United Kingdom following the widespread application of the Crédé prophylaxis.¹⁰ However, the role of silver nitrate prophylaxis is only to prevent ophthalmia due to gonococcal infections; it is not effective against Chlamydia. Silver nitrate prophylaxis is not used currently due to the ineffectiveness in preventing chlamydial infection and the tendency to cause chemical conjunctivitis. This method of prophylaxis has been replaced by the use of erythromycin or tetracycline ointment.¹¹

Review Article

EPIDEMIOLOGY

Ophthalmia neonatorum is a worldwide problem. The pathogens responsible for causing the infection vary geographically due to the differences in the prevalence of maternal infection and the prophylactic use of antibiotics and silver nitrate solution.² In the developed world, Chlamydia has been reported as the most common infectious agent responsible for ophthalmia compared to gonococcus. However in developing nations, both chlamydial and gonococcal infections are prevalent. In Malaysia the incidence is significantly high due to lack of routine prophylactic measures and due to emergence of pencillinase-producing N. gonorrhoea (PPNG) strains. The actual incidence is unknown due to under-reporting. A study on gonococcal ophthalmia neonatorum in the state of Kelantan has shown an increase in the percentage of cases infected with penicillin resistant strains of N. gonorrhoea from 6.4% to 25.9%.¹² Lockie P et al ¹³ in their retrospective study involving 80 cases reported 7.5% due to PPNG. The Pencillinase-producing strains are believed to originate from South-East Asian region namely from Bangkok where 48.9% of strains of N. gonorrhoea isolated were due to PPNG.14

The prevalence of ophthalmia due to gonococcal infection is reported to be 0.04 per 1000 live births in Belgium and Netherlands, and 0.3 per 1000 live births in the United States.^{15,16} At the moment, *Chlamydia trachomatis* is the most frequent sexually transmitted pathogen in the developed nations with prevalence of 5 to 60 per 1000 live births in the United States, 4 per1000 live births in the United Kingdom and 40 per 100 live births in Belgium; whereas the prevalence of gonorrhoea among antenatal attenders in the African countries ranges from 4% to 15 %.¹⁷ Approximately 25% to 50% of infants exposed to *Chlamydia trachomatis* and *Neisseria gonorrhoea* develop neonatal conjunctivitis, without prophylaxis.¹⁸

ETIOLOGY

Ophthalmia neonatorum can be divided into aseptic and septic types.¹⁰ The aseptic type (chemical conjunctivitis) is generally secondary to the instillation of silver nitrate drops for ocular prophylaxis. Septic neonatal conjunctivitis is mainly caused by bacterial and viral infections. *Chlamydia trachomatis and Neisseria gonorrhoea* the two sexually transmitted agents are associated with systemic complications and severe visual loss if left untreated.^{19,20}

Chlamydia trachomatis is the most common cause of ophthalmia neonatorum in the developed countries because of higher prevalence of *Chlamydia* as sexually transmitted disease. This is due to the fact that 60% to 80% of genital

infections with *Chlamydia* in females are asymptomatic. Hence it is often labeled as "silent epidemic".²¹ The Center for Disease Prevention and Control (CDC) estimates 3 million cases of chlamydial infections occur per year. It is more prevalent than gonococcal infection and approximately four to six times as common as herpes virus infection.²²

Although gonococcus is the second commonest organism responsible for ophthalmia neonatorum, it is the most virulent infectious agent for neonatal conjunctivitis. It was previously the commonest cause of blindness within the first year of life, necessitating the use of prophylaxis at birth. Gonococcal ophthalmia neonatorum had been eradicated in the United States in the 1950's. However, it has now resurfaced following the increasing incidence of adult gonococcal infections and the development of antimicrobial resistance.²³

The other microbial causes of ophthalmia include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Escherichia coli*, *Klebsiella sp* and *Pseudomonas aeruginosa*.^{24,25}

CLINICAL FEATURES

The genital serovars type D-K of *Chlamydia trachomatis* causes neonatal conjunctivitis. It has a later onset than gonococcal conjunctivitis. The incubation period is 5-14 days and the colonization of the eye after birth does not always result in infection. Almost 40% of the infected neonates develop watery conjunctivitis which becomes more copious and purulent later. Most of the cases are mild and self-limited, but occasionally may be severe with eyelid swelling, chemosis, papillary reaction, pseudo-membrane, peripheral pannus and corneal involvement. If left untreated, 10-20% of the cases will develop infantile pneumonia. Other extra ocular involvement of *Chlamydia* includes nasopharyngeal, rectal and vaginal colonization and other form of diseases such as infant pneumonia syndrome.²⁶

Gonococcal conjunctivitis is more severe than chlamydial conjunctivitis. The incubation period is 2-5 days. However, it can occur earlier in cases of premature rupture of membranes. It is usually bilateral. The conjunctivitis is characterized by severe hyper-acute purulent discharge, eyelid edema and chemosis. Gonococci have the capacity to penetrate intact corneal epithelium, leading to corneal epithelial edema and corneal ulceration, which can progress to corneal perforation and endophthalmitis if unrecognized. Hence in all cases of neonatal conjunctivitis, the infant has to be screened for gonococci to prevent these serious consequences. Gonococcal infection of the newborn can also give rise to systemic complications like stomatitis, arthritis, rhinitis, septicemia and meningitis.²⁷

Malaysian Family Physician 2008; Volume 3, Number 2 ISSN: 1985-207X (print), 1985-2274 (electronic) ©Academy of Family Physicians of Malaysia Online version: http://www.ejournal.afpm.org.my/

Herpes simplex keratoconjunctivitis in an infant usually presents with generalized herpes infection. Vesicles around the eye and corneal involvement are also common.²⁸ Chemical conjunctivitis usually occurs within 24 hours of instillation of silver nitrate solution and resolves spontaneously within a few days. It can present with lid swelling associated with redness of the eyes, rarely with lacrimal stenosis. Ophthalmia Neonatorum due to other microbial causes usually run a milder course without corneal and systemic involvement.

LABORATORY DIAGNOSIS

Ophthalmia neonatorum is essentially a clinical diagnosis made by observation of signs and symptoms. The clinical differentiation between various types of neonatal conjunctivitis can be difficult.^{29,30} Hence lab diagnosis is of paramount importance in establishing the correct diagnosis and initiating the best treatment. Conjunctival scrapings for Gram stain and Giemsa stain should be obtained from the palpebral conjunctiva of all the infants with neonatal conjunctivitis. The presence of intracellular gram negative diplococci (IGND) has a high sensitivity and specificity and predictive value.³¹ Blood agar, chocolate agar and/or Thayer-Martin media can be used to isolate *Neisseria gonorrhoea* and other bacteria.

Chlamydia trachomatis can be isolated by the presence of intracytoplasmic inclusion bodies in the Giemsa stain in 60-80% of all infants. Conjunctival swab, smeared on to a microscopic slide and stained with Chlamydia trachomatis specific fluorescent monoclonal antibody (direct immunofluorescence test) often shows the presence of an impressively large number of punctate, fluorescing chlamydial elementary bodies, resembling "star-spangled sky at night".32 This antigen detection test is still considered the "gold standard" for the diagnosis of chlamydial infections.³³ Polymerase chain reaction (PCR) analysis for diagnosing chlamydial conjunctivitis has an advantage of early diagnosis and higher specificity compared to McCoy cell culture.³⁴ The other laboratory studies for diagnosing chlamydial infections include Micro immunofluorescence assay (MIF) for detection of Chlamydia trachomatis IgG and IgM antibodies and Elisa tests.

PROPHYLAXIS

Crédé introduced 2% silver nitrate as a prophylaxis treatment method for conjunctivitis in the newborns in Leipzig in 1881.³⁵ The widespread use of silver nitrate prophylaxis was associated with a drastic decline in the incidence of gonococcal ophthalmia throughout Europe and the United States. However, silver nitrate is toxic and for many years has been recognised to be a common cause of chemical conjunctivitis.³⁶ Currently, topical erythromycin and tetracycline are also used as alternatives for ocular prophylaxis.¹¹ However, all these agents are considered effective only for gonococcal ophthalmia, and found to be ineffective as prophylactic treatment against chlamydial conjunctivitis.³⁷ Bell *et al*³⁸ found no significant difference in the efficacy of silver nitrate, topical erythromycin and no prophylaxis in preventing ophthalmia neonatorum. Instead of prophylaxis, the authors concluded that prenatal recognition and prompt treatment may prevent the development of the disease.

TREATMENT

Ophthalmia neonatorum is an ocular emergency so all infants with neonatal conjunctivitis should be admitted. Specific treatment modalities are available for different types of neonatal conjunctivitis and treatment should be based on clinical picture and laboratory diagnosis (Gram stain & Giemsa stain). It is important to treat the infants with systemic rather than topical drugs to prevent systemic dissemination of the organism. As the causative organism is sexually transmitted, it is vital to treat the mother and her sexual partner(s).

Current WHO guideline for the management of sexually transmitted infections recommends that all cases of ophthalmia neonatorum be treated for both *N. gonorrhoea* and *C. trachomatis*³⁹). The co-infection rates are estimated to be around 2%.³⁹

Ophthalmia neonatorum due to C. trachomatis

WHO and American Academy of Pediatrics recommendation include oral erythromycin syrup, 50 mg/kg/day, in 4 divided doses for 14 days.⁴⁰ Topical erythromycin or tetracycline can be used as an adjunct therapy. The advantages of oral erythromycin include eradication of the nasopharyngeal carriers, treatment of associated pneumonitis and also being more effective than topical in preventing relapse of conjunctivitis.² Infected partners should receive oral doxycycline 100 mg twice daily for 7 days or azithromycin 1 g orally as a single dose.³⁹

Ophthalmia neonatorum due to *N. gonorrhoea*

Treatment of gonococcal conjunctivitis consists of Intravenous Penicillin G 100,000 Units /kg/day for 1 week. *N. gonorrhoea* isolates are resistant to penicillin in many urban areas in USA. Across Africa, rates of pencillinase-producing *N. gonorrhoea* range from 18 to 57% and many other parts of world (50% to 60%).^{31,15} Hence a third-generation cephalosporin drug should be used for 7 days in areas where pencillinase producing strains are endemic. A single dose of ceftriaxone 50 mg/kg as s single dose (maximum 125 mg) is highly effective and recommended by WHO guidelines.^{41,42} Alternative medications include spectinomycin 25 mg/kg (maximum 75 mg).⁴³ Infected mother should also be treated with single dose of ceftriaxone (25-50 mg/kg). The infant's eye should be

frequently irrigated with normal saline to eliminate the discharge.

Ophthalmia neonatorum due to Herpes simplex virus

Neonates suspected of conjunctivitis due to herpes simplex should be treated with low dose systemic acyclovir (30mg/kg/ day IV divided tid) or vidarabine (30 mg /kg/day in divided doses IV) for at least 2 weeks⁴⁴ to prevent dissemination of infection. Topical treatment may be with vidarabine ointment or trifluridine eye drops.

RECOMMENDATIONS AND CONCLUSION

Awareness of the perinatal implications and routine screening for *Chlamydia* in pregnant women will provide safer health care for the mother and her baby. Treatment of any maternal infection prior to delivery can help reduce the burden of this disease, and also help to decrease the incidence of childhood blindness not only in developing nations but also in developed countries.

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Can star fruits kill?

Apparently yes, if you have prior kidney problem. Recently newspaper reported a 66-year-old Malaysian Chinese who slipped into coma after taking star fruit in China. This problem is noted only among patients with kidney failure. Star fruit (*Averrhoa carambola*) has been noted to cause convulsions, hiccups, or death in uremic patients in many case reports. The exact constituent causing these effect remains uncertain but oxalate is a prime suspect. Renal patients should be advised to avoid star fruits.

Here are *The Star* news reports:

- 1. Sunday May 18, 2008. Of star fruits and kidneys. http://thestar.com.my/health/ story.asp?file=/2008/5/18/health/21254246&sec=health
- 2. Monday May 12, 2008. Star fruit victim still in coma. http://thestar.com.my/news/ story.asp?file=/2008/5/12/nation/21221945&sec=nation

Read more about this in PubMed (www.pubmed.gov) by typing "star fruit neurotoxin" (without quotes) in the search box.