

Received: 2018.04.19

Accepted: 2018.07.11

Published: 2018.11.10

A Survey of Current Prophylactic Treatment for Ophthalmia Neonatorum in Croatia and a Review of International Preventive Practices

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Source of support: Departmental sources

Background: Ophthalmia neonatorum, or neonatal conjunctivitis, is an acute infection that occurs within the first 28 days of life. This aim of this survey was to evaluate the current methods of preventive treatment for ophthalmia neonatorum in maternity hospitals in Croatia.

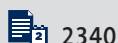
Material/Methods: The annual hospital birth rate in Croatia is approximately 40,000. A clinical survey was undertaken with data collected using questionnaires sent to all 32 maternity hospitals in Croatia. There was a 100% response rate to the questionnaires.

Results: Preventive treatment for ophthalmia neonatorum was administrated to all newborns in 75% (24/32) of Croatian maternity hospitals. In 45.8% of maternity hospitals, (11/32) these procedures were performed within the first hour after birth. In 54.2% of maternity hospitals (13/32), preventive treatment for ophthalmia neonatorum was administrated to all newborns from one to three hours after birth. The main treatment agent was tobramycin (83.3%). Other topical prophylactic treatments included povidone-iodine (8.3%), erythromycin (4.2%), and silver nitrate (4.2%). In 25% of obstetric units, prophylaxis for ophthalmia neonatorum was not used routinely, but in cases of diagnosed neonatal conjunctivitis, antibiotic treatment with tobramycin was mainly used.

Conclusions: A survey of all 32 maternity hospitals in Croatia showed variation in the prevalence of preventive treatment for ophthalmia neonatorum and the methods used. These findings support the need to implement standardized preventive measures that both conform to international clinical guidelines and recognize treatment availability in Croatia, where topical povidone-iodine is currently preferred for the prevention of ophthalmia neonatorum.

MeSH Keywords: **Conjunctivitis • Ophthalmia Neonatorum • Post-Exposure Prophylaxis • Postnatal Care**

Full-text PDF: <https://www.medscimonit.com/abstract/index/idArt/910705>



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Background

Ophthalmia neonatorum, or neonatal conjunctivitis, is an acute mucopurulent conjunctivitis that occurs within the first 28 days of life [1,2]. Ophthalmia neonatorum is a relatively common condition that can be caused by chemicals, bacteria, or viruses and affects between 1.6–12% of all newborn infants, and up to 23% of newborn infants in developing countries [1–6]. The prevalence of ophthalmia neonatorum varies in different parts of the world and is closely associated with socioeconomic conditions, the level of general health education, the standard of maternal healthcare, as well as the implementation of prevention programmes [3–10].

Conjunctivitis in newborn infants may be prevented with the use of topical prophylactic treatment of the infant or by prenatal screening and treatment of infected mothers [1–4]. Although there is published clinical evidence that supports the use of topical ophthalmic preventive treatment, some of these have side effects, may be costly, or may have adverse effects on the health of newborns [1,2,8–11].

The causes of ophthalmia neonatorum can be categorized into non-infectious and infectious causes. The most common non-infectious form is chemical conjunctivitis that can result from the application of some prophylactic agents. Infections causing ophthalmia neonatorum include bacteria and viruses, with chlamydia being the most common infectious cause [2,6,7]. Most cases of infectious conjunctivitis occur from transfer from the birth canal during delivery and can include infections associated with sexually transmitted diseases (STDs) in the mother, resulting in gonococcal or chlamydial ophthalmia neonatorum [2,8]. Infection may also be spread from the people handling the baby soon after birth and, more rarely, during pregnancy due to transplacental passage [2,8].

Regardless of the use of prophylaxis, ophthalmia neonatorum is still one of the major causes of blindness, particularly in developing countries [1,12–14]. Currently, *Chlamydia* is the most common single cause of infective neonatal conjunctivitis, accounting for between 2–40% of cases, with *Neisseria gonorrhoeae* infection reported in less than 1% of cases. The incidence of infection from these two pathogens has notably declined in the past two decades due to decreased prevalence of STDs in the population, and due to the improvement of prenatal screening and care. The complications of ophthalmia neonatorum are mainly related to gonococcal conjunctivitis [1,15] (Table 1).

Due to the potential complications related to ophthalmia neonatorum, many countries have now implemented routine prophylaxis or preventive treatment for ophthalmia neonatorum in newborns [6,10,11]. The agents currently used in the prevention of ophthalmia neonatorum include topical 1% silver

nitrate; targesin (a silver and protein compound); 1% tetracycline; topical macrolide antibiotics, including 0.5% erythromycin or azithromycin; topical aminoglycosides, including gentamicin and tobramycin; chloramphenicol; fluoroquinolones, including ciprofloxacin; 1.25% or 2.5% povidone-iodine; and fusidic acid [12,4,6,8,9,16–28] (Table 2). The use of topical antibiotic prophylaxis can be associated with the development of antimicrobial resistance [1,2]. Therefore, in the past few decades, the use of antibiotics and other topical agents that may cause local irritant or hypersensitivity reactions have resulted in controversy regarding the best type of treatment for the prevention of ophthalmia neonatorum [5,7,11,18].

Therefore, the aim of this survey was to evaluate the current methods of preventive treatment for ophthalmia neonatorum in the 32 maternity hospitals in Croatia and to review the findings in the context of current international clinical guidelines to encourage the development and implementation of national guidelines for the prevention of ophthalmia neonatorum.

Material and Methods

Survey questionnaire

The annual hospital birth rate in Croatia is approximately 40,000. A clinical survey was undertaken with data collected using questionnaires sent to all 32 maternity hospitals in Croatia. There was a 100% response rate to the questionnaires.

The participants were ensured anonymity and involvement in the survey was voluntary. The questionnaire included direct questions of the use of prophylactic treatments to prevent ophthalmia neonatorum, the agents used, and details about the methods of administration of the treatments and treatment frequency. Where no preventive treatments were used, this was also recorded.

Statistical analysis

Descriptive statistical analysis of demographic information was used.

Results

Analysis of the data obtained from the questionnaires used in the survey showed that topical preventive treatment or prophylaxis for ophthalmia neonatorum was being routinely administered by 75.0% (24/32) of all maternity hospitals in Croatia. Regarding the timing of treatment, 45.8% (11/24) of the maternity hospital that routinely used preventive treatment reported that topical treatment was applied in the delivery room

Table 1. Aetiology and clinical characteristic of neonatal conjunctivitis.

Aetiology	Time of onset	Clinical presentation	Ocular complications	Systemic complications
Chemical	First 24 hours of life	Mild lid oedema, mild serous discharge, self-limited, lasts 2–4 days	None	None
<i>Chlamydia trachomatis</i>	5–14 days	Different degree of lid swelling, mild to moderate serous or purulent discharge, conjunctival injection (more pronounced on palpebral conjunctiva)	Chronic infection may cause corneal scarring, pannus and symblepharon	Pharyngeal colonization, pneumonitis and otitis media
<i>Neisseria gonorrhoeae</i>	2–5 days	Hyperacute onset, severe lid swelling, chemosis, copious, purulent discharge	Corneal ulceration, corneal perforation, endophthalmitis which may occur within 24 hours	Bacteriemia, sepsis, meningitis, arthritis, death
Bacterial	4–28 days	Subacute course, variable presentation depending on type of bacteria, lid swelling with purulent discharge	<i>Pseudomonas</i> sp. may cause corneal ulcer, corneal perforation and endophthalmitis	None
Herpes simplex virus	1–14 days	Mild conjunctival injection, serosanguineous discharge, corneal epithelial defects, possible vesicular eyelid rash	Recurrences may cause corneal scarring and profound amblyopia, chorioretinitis, optic neuritis and cataracts	Meningitis and disseminated CNS disease with mortality rate up to 85%

CNS – central nervous system. Modified from: Kaštelan S, Kasun E, Štajcer Ž, Kasun B [2].

Table 2. Characteristics of potential prophylactic agents for neonatal conjunctivitis.

Prophylactic agents	CT	NG	B	Possible antimicrobial resistance	Chemical conjunctivitis (incidence)	Side effects
Silver nitrate 1%	S	S	S	No	Yes (50–90%)	Corneal epithelial lesions
Tetracycline 1%	S	S	S	Yes	Yes (<10%)	No
Erythromycin 0.5%	S	S	S	Yes	Yes <10%	Early emission of meconium
Azithromycin 1.5%	S	S	S	Yes	Yes	Corneal erosion, punctate keratitis, xerophthalmia
Povidone-iodine 2.5%	S	S	S	No	Yes (5–10%)	No
Tobramycin	R	S	S	Yes	/	/
Gentamicin	R	S	S	Yes	/	Periocular ulcerative dermatitis
Chloramphenicol 1.5%	R	S	S	Yes	/	Aplastic anemia
Ciprofloxacin	S	S	S	Yes	Yes	Corneal infiltrates, keratitis
Fusidic acid	S	S	S	Yes	/	/

/ – no data was found in the literature; S – sensitive to prophylactic agents; R – resistant to prophylactic agents; B – bacteria (*S. aureus*, *S. epidermidis*, *S. pneumoniae*, *Haemophilus* sp.); CT – *Chlamydia trachomatis*; NG – *Neisseria gonorrhoeae*.

during the first hour after birth; 54.2% (13/24) reported that topical treatment was applied between one and three hours post-partum. In 25% (8/32) of maternity hospitals, preventive treatment or prophylaxis for ophthalmia neonatorum was not routinely used. However, in cases where newborns showed

symptoms of conjunctivitis, the antibiotic, tobramycin, was the treatment of choice (Table 3).

The findings of the survey showed that in the 24 maternity units that routinely used topical preventive treatments for

Table 3. The use of prophylaxis and the treatment of ophthalmia neonatorum including the time and place of prophylaxis application as well as the method of treatment.

	Prophylaxis		Time of prophylaxis	
		N (%)		N (%)
Maternity hospitals N=32	All newborns	24 (75.0)	In the first hour after births delivery room	11 (45.8)
			From one to three hours after birth	13 (54.2)
	Treatment	N (%)	Method of treatment	N (%)
	Newborns with eye infection	8 (25.0)	Drops + Ointment	5 (62.5)
			Drops	3 (37.5)

ophthalmia neonatorum, the treatments varied and included two types of topical antiseptic, povidone-iodine and silver nitrate, and two antibiotics, tobramycin and erythromycin.

Currently, in the 24 maternity units in Croatia that routinely used topical prophylactic treatment for ophthalmia neonatorum, the most commonly used included topical tobramycin solution in 83.3% (20/24) of maternity units, a 2.5% solution of povidone-iodine in 8.3% (2/24) of maternity units, 0.5% erythromycin ointment in 4.2% (1/24) of maternity units, and 1% silver nitrate solution in 4.2% (1/24) of maternity units.

Discussion

In Croatia, there is no medico-legal requirement to implement preventive treatment of ophthalmia neonatorum, or neonatal conjunctivitis, at birth and there are no standardized clinical recommendations or guidelines issued by the Croatian health authorities. According to data obtained from this survey, topical treatment to prevent ophthalmia neonatorum was routinely used at birth by 75.0% (24/32) of all maternity hospitals, with the main treatment being topical tobramycin in 83.3% (20/24) of maternity units. Only 16.7% (4/24) maternity hospitals used topical preventive treatments that are currently recommended by international guidelines, including erythromycin, silver nitrate, and povidone-iodine. Povidone-iodine was used by only 8.3% (2/24) of maternity units in Croatia, but in our opinion could be recommended as a topical agent due to its availability in Croatia, and because it has the broadest antibacterial spectrum as well as viricidal capabilities and, unlike topical antibiotics, bacterial resistance has not been reported. A significant problem facing Croatia is the lack of availability of the majority of topical antibiotics, which are routinely used in other countries, including erythromycin and tetracycline [10,11].

Currently, in developed countries, due to the reduced prevalence of sexually transmitted diseases (STDs) in pregnant women, improved perinatal screening, and the use of prophylactic treatment at birth, blindness caused by ophthalmia neonatorum has become rare [8,11]. In some developed countries,

where the incidence of ophthalmia neonatorum is very low, a strategy of early treatment of infected neonates, rather than routine prophylaxis, has been adopted. For this strategy to be effective regular and standardized follow-up of infants must be ensured.

Growing and diverse populations, trends in immigration, increasing urbanization, and increasing sexual promiscuity are predisposing factors for an increase in the incidence of ophthalmia neonatorum [1,9]. Some countries, including Australia, Sweden, Denmark, Norway, Ireland and Great Britain have abandoned the use of routine prophylaxis after birth in favor of antenatal maternal screening for STDs and general improvements in postnatal evaluation and care. In Great Britain, where routine prophylaxis for ophthalmia neonatorum has been discontinued for approximately 60 years, there have been no reported cases of blindness caused by gonococcal infection [2,18]. Although gonococcal ophthalmia neonatorum in Great Britain is rare, there is some evidence suggesting that ophthalmia neonatorum is generally under-reported with cyclical fluctuations in incidence [18]. Furthermore, clinical studies from Sweden, Florida in the USA, and Denmark have also shown that the incidence of ophthalmia neonatorum increased to some degree following the discontinuation of preventive or prophylactic treatment [5,18,29,30].

However, in countries where topical prophylactic treatment of newborn infants to prevent ophthalmia neonatorum is currently implemented, there remains no consensus regarding the preferred treatment agent, and a variety of topical treatments are used. In the USA, the current clinical recommendations are to apply the topical prophylactic agent to the eyes in all newborns within 24 hours of birth, and 0.5% erythromycin ophthalmic ointment is the recommended treatment [16]. Among the other potential prophylactic agents, tetracycline ophthalmic ointment and silver nitrate are no longer available in the United States, and a 2.5% povidone-iodine topical solution has not yet been approved for this purpose [16]. In Israel, preventive treatment of ophthalmia neonatorum is routinely used with topical erythromycin [27]. A shortage of single-dose erythromycin ointment necessitated the use of shared erythromycin

drops during a one-year period without increasing the rate of neonatal bacterial conjunctivitis during this time, indicating that shared eye drop bottles can be used without increasing the incidence of infection, if properly administered [27].

According to current health policy in Mexico, preventive treatment for ophthalmia neonatorum in neonates is a medico-legal requirement and consists of the application of a single drop of ophthalmic chloramphenicol in both eyes shortly after birth [17]. In Slovenia, neonatal prophylaxis is a mandatory intervention for all newborns and is performed in the first three hours after birth with the topical application of 1% silver protein acetyl tannate eye drops, which contain organically bound silver and have a similar effect to topical silver nitrate [4]. In Austria, where seven different topical treatments are used, there is a similar approach to the prevention of ophthalmia neonatorum as in Croatia, as than 90% of obstetric units in Austria routinely apply topical erythromycin, or silver nitrate, or tetracycline for newborns in maternity hospitals [5]. Only 24.6% of hospitals and midwives in Austria have been reported to use gentamicin, neomycin, or chloramphenicol [5].

In Croatia, mothers and their newborn infants are usually discharged from the maternity hospital between three days and five days after delivery. However, the onset of symptoms of ophthalmia neonatorum usually develops several days after hospital discharge. This important clinical finding provides additional support for the implementation of routine prophylactic treatment for the prevention of ophthalmia neonatorum that is given immediately following delivery and would be of particular importance in countries such as Croatia where cervical swabs are not routinely taken in pregnant women, or where ante-natal and postnatal care is inadequate or unavailable.

The efficacy of maternal screening depends mainly on the incidence of carriers of STDs, the availability of diagnostic facilities, and the availability of therapy. These screening measures for maternal STDs would require modifications to the infrastructure and resources of health services, including a well-organized medical system with appropriate antenatal care to screen, diagnose, and treat STDs in pregnant women [1,2]. Until the time when these clinical practices can be fully implemented in Croatia, our recommendation would be the mandatory use of preventive treatment or prophylaxis for ophthalmia neonatorum in newborns immediately after birth.

Worldwide, in terms of the topical prophylactic treatment used to prevent ophthalmia neonatorum due to STDs, including chlamydia and gonorrhea, the gold standard remains the method introduced by Credé in 1881, with 1% silver nitrate solution [6,7,9]. However, since *Chlamydia trachomatis* has become more prevalent than *Neisseria gonorrhoeae*, 'Credé's prophylaxis' is controversial and used less commonly, due to its

ineffectiveness against *Chlamydia* and the fact that silver nitrate can cause chemical conjunctivitis [9]. For these reasons, prophylaxis with silver nitrate has been replaced in many countries with 0.5% erythromycin or 1% tetracycline ointment, even though increasing multidrug-resistant bacterial strains continue to require studies for new topical antibiotics [1,9].

The characteristics of an ideal preventive treatment for ophthalmia neonatorum would include the following: a high degree of efficacy in protecting the newborn infant from all bacterial and viral pathogens; it should be inexpensive; it should not be resistant to bacterial strains; the treatment should not cause chemical conjunctivitis; and the treatment should preferably be available in single-dose packaging [2,5]. Currently, none of the available topical agents possess the characteristics required for the ideal prophylactic treatment for ophthalmia neonatorum.

Recently, povidone-iodine has been shown to be effective in preventing ophthalmia neonatorum, with treatment results that have been shown to be comparable with those of silver nitrate and erythromycin for gonococcal ophthalmia neonatorum, and povidone-iodine has been shown to be superior in the prevention of chlamydial ophthalmia neonatorum [1,5,6,17,23,31,32]. Povidone-iodine offers additional antiviral activity against both human immunodeficiency virus (HIV) and herpes simplex virus (HSV), is relatively inexpensive, is associated with a low rate of chemical conjunctivitis, and is not associated with the development of antibiotic resistance, although temporary discoloration of the sclera is associated with its topical use [8,10,11]. However, the transient brown staining of the sclera can be useful as an indicator of the effective application of povidone-iodine, providing visual evidence that the medication was administered correctly. All these characteristics indicate that povidone-iodine may represent a more suitable, if not yet ideal, topical agent for the prevention of ophthalmia neonatorum, particularly in developing countries. Considering its availability in Croatia, and the inaccessibility of some other recommended treatments, povidone-iodine represents a reasonable choice for use in maternity hospitals in Croatia.

Conclusions

There is still no optimal agent for effective and safe preventive treatment or prophylaxis of ophthalmia neonatorum. The ideal treatment should be highly effective in preventing all infectious causes of conjunctivitis, including chlamydial and gonococcal infection while being non-toxic, not associated with the development of microbial resistance, and it should also be inexpensive and widely available. This study has included a survey involving all 32 maternity units in Croatia, with findings that support the need for standardized national guidelines for the prevention

of ophthalmia neonatorum. However, because some women in Croatia still do not receive adequate antenatal care, and as cervical swabs are not taken routinely, it would be beneficial to continue and extend the practice of the majority (75%) of maternity hospitals in Croatia in routinely using prophylactic treatment for ophthalmia neonatorum within one to three hours following birth. However, the type of topical agent used should be chosen by consensus, taking into consideration all

the positive and negative characteristics of a potential medication as well as its availability in Croatia, with povidone-iodine potentially being the optimal choice.

Conflict of interest

None.

References:

1. Zar HJ: Neonatal chlamydial infections: Prevention and treatment. *Paediatr Drugs*, 2005; 7(2): 103–10
2. Kaštelan S, Kasun E, Štajcer Ž, Kasun B: Ophthalmia neonatorum. *Gynaecol Perinatol*, 2014; 23(4): 121–26
3. Gilbert C, Foster A: Childhood blindness in the context of vision 2020 – The right to sight. *Bull World Health Organ*, 2001; 79(3): 227–32
4. Došler AJ, Petročnik P, Mivšek AP et al: Neonatal prophylaxis: Prevention of vitamin K deficiency haemorrhage and neonatal ophthalmia. *Zdr Varst*, 2015; 54(3): 184–93
5. Assadian O, Assadian A, Aspöck C et al: Prophylaxis of ophthalmia neonatorum – a nationwide survey of the current practice in Austria. *Wien Klin Wochenschr*, 2002; 114(5–6): 194–99
6. Matejcek A, Goldman RD: Treatment and prevention of ophthalmia neonatorum. *Can Fam Physician*, 2013; 59(11): 1187–90
7. Canadian Paediatric Society Infectious Diseases and Immunization Committee Recommendations for prevention of neonatal ophthalmia. *Paediatr Child Health*, 2002; 7(7): 480–88
8. Zuppa AA, D'Andrea V, Catenazzi P et al: Ophthalmia neonatorum: what kind of prophylaxis? *J Matern Fetal Neonatal Med*, 2011; 42(6): 769–73
9. Schaller UC, Klaus V: Is Credé's prophylaxis for ophthalmia neonatorum still valid? *Bull World Health Organ*, 2001; 79(3): 262–63
10. Zlot O, Gharaibeh A, Mezer E et al: Ophthalmia neonatorum treatment and prophylaxis: IPOS global study. *Graefes Arch Exp Ophthalmol*, 2016; 254: 577–82
11. Darling EK, McDonald H: A meta-analysis of the efficacy of ocular prophylactic agents used for the prevention of gonococcal and chlamydial ophthalmia neonatorum. *J Midwifery Womens Health*, 2010; 55(4): 319–27
12. Gul SS, Jamal M, Nusrat Khan N: Ophthalmia neonatorum. *J Coll Physicians Surg Pak*, 2010; 20(9): 595–98
13. Amini E, Ghasemi M, Daneshjou K: A five-year study in Iran of ophthalmia neonatorum: Prevalence and etiology. *Med Sci Monit*, 2008; 14: CR90–96
14. Ghahramani M, Ghahramani AA: Epidemiological study of ophthalmia neonatorum and impact of prophylaxis on its incidence. *Acta Med Iranica*, 2007; 45: 361–64
15. Kesson AM: Management of neonatal herpes simplex virus infection. *Pediatr Drugs*, 2001; 3(2): 81–90
16. US Preventive Services Task Force (USPSTF): Ocular prophylaxis for gonococcal ophthalmia neonatorum: reaffirmation recommendation statement. *Am Fam Physician*, 2012; 85(2): 195–96
17. Ramirez-Ortiz MA, Rodríguez-Almaraz M, Ochoa-Díaz López H et al: Randomised equivalency trial comparing 2.5% povidone-iodine eye drops and ophthalmic chloramphenicol for preventing neonatal conjunctivitis in a trachoma-endemic area in Southern Mexico. *Br J Ophthalmol*, 2007; 91(11): 1430–34
18. Moore DL, MacDonald NE, Canadian Paediatric Society, Infectious Diseases and Immunization Committee: Preventing ophthalmia neonatorum. *Paediatr Child Health*, 2015; 20(2): 93–96
19. Bell TA, Grayston JT, Krohn MA, Kronmal RA: Randomized trial of silver nitrate, erythromycin, and no eye prophylaxis for the prevention of conjunctivitis among newborns not at risk for gonococcal ophthalmia. *Eye Prophylaxis Study Group. Pediatrics*, 1993; 92(6): 755–60
20. Isenberg SJ, Apt L, Wood M: A controlled trial of povidone-iodine as prophylaxis against ophthalmia neonatorum. *N Engl J Med*, 1995; 332(9): 562–66
21. Benevento WJ, Murray P, Reed CA, Pepose JS: The sensitivity of *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and herpes simplex type II to disinfection with povidone-iodine. *Am J Ophthalmol*, 1990; 109(3): 329–33
22. Normann EK, Bakken O, Peltola J et al: Treatment of acute neonatal bacterial conjunctivitis: A comparison of fucidic acid to chloramphenicol eye drops. *Acta Ophthalmol Scand*, 2002; 80(2): 183–87
23. David M, Rumelt S, Weintraub Z: Efficacy comparison between povidone iodine 2.5% and tetracycline 1% in the prevention of ophthalmia neonatorum. *Ophthalmology*. 2011; 118(7): 1454-1458.
24. Khan FA, Hussain MA, Khan Niazi SP et al: Efficacy of 2.5% and 1.25% povidone-iodine solution for prophylaxis of ophthalmia neonatorum. *J Coll Physicians Sur Pak*, 2016; 26(2): 121–24
25. Moussa F, Alaswad B, Garcia J: Erythromycin eye ointment: Effect on gastrointestinal motility. *Am J Gastroenterol*, 2000; 95: 826–30
26. Binenbaum G, Bruno CJ, Forbes BJ et al: Periocular ulcerative dermatitis associated with gentamicin ointment prophylaxis in newborns. *J Paediatr*, 2010; 156(2): 320–21
27. Ulanovsky I, Shnaider M, Geffen Y et al: Erythromycin prophylaxis for neonatal conjunctivitis: ointment versus drops. *Isr Med Assoc J*, 2016; 18(7): 404–6
28. Taketomo CK, Hoddig JH, Kraus DM: Pediatric and neonatal dosage handbook with international trade names index 2016/2017. 23rd ed. United States: Lexicomp, Wolters Kluwer; 2016
29. Dharmasena A, Hall N, Goldacre R, Goldacre MJ: Time trends in ophthalmia neonatorum and dacryocystitis of the newborn in England, 2000–2011: database study. *Sex Transm Infect*, 2015; 91(5): 342–45
30. Gadeberg OV, Bollerup AC, Kolmos HJ et al: Neonatal conjunctivitis after the abolition of compulsory Crede prophylaxis. *Ugeskr Laeger*, 1991; 153: 284–88
31. Bramantyo T, Roeslani RD, Andriansjah A, Sitorus RS: The efficacy of 1% chloramphenicol eye ointment versus 2.5% povidone-iodine ophthalmic solution in reducing bacterial colony in newborn conjunctivae. *Asia Pac J Ophthalmol (Phila)*, 2015; 4(3): 180–83
32. Ali Z, Khadije D, Elahe A, Mohammad M et al: Prophylaxis of ophthalmia neonatorum comparison of betadine, erythromycin and no prophylaxis. *J Trop Pediatr*, 2007; 53(6): 388–92