

COMPARISON OF POVIDONE IODINE AND ERYTHROMYCIN WITH CONTROL CASES IN PREVENTION OF OPHTHALMIA NEONATARUM

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Abstract- Neonatal conjunctivitis (ophthalmia neonatarum) continues to involve many neonates in areas with no eye prophylaxis. Povidone iodine solution is an effective antimicrobial agent with broad antibacterial and antiviral activity and it is less expensive and less toxic than the other agents. It seems to be a good alternative for routine eye prophylaxis, especially in developing countries. In a prospective trial, 360 infants born over a period of ten month in years 2000-2001 were divided in three groups randomly. Each infant received a 2.5% povidone iodine solution, or 0.5% erythromycin ointment or no prophylaxis as a control group. There were 17.5%, 10%, and 5.8% of infectious conjunctivitis in control, erythromycin and povidone iodine groups respectively. In spite of reduction of clinical and infectious conjunctivitis in erythromycin compared to control group and in povidone iodine compared to erythromycin group, the only and most significant difference was between povidone iodine and control groups ($P=0.0036$ for clinical conjunctivitis and $P=0.0089$ for infectious ones). The most common organisms were gram-negative bacilli and *Staphylococcus aureus* in all groups and *Chlamydia trachomatis* was responsible for 9.5% of infectious conjunctivitis (4th common agent) with an incidence of 1.7% in control group. As well, birth in unhygienic environment (mother defecation) and meconium staining of amniotic fluid were significantly associated with higher conjunctivitis rate but vaginal infection of mother had no such effect. We found that there is a high incidence of conjunctivitis with no eye prophylaxis. Povidone iodine is more effective, easier to use and costs less in comparison with erythromycin and has no toxic reaction. So it seems that 2.5% povidone iodine solution is a good alternative for routine eye prophylaxis.

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Key Words: Ophthalmia neonatarum, povidone iodine, erythromycin, prophylaxis

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INTRODUCTION

Ophthalmia neonatarum, defined as conjunctivitis in the first four weeks of life, has an incidence of less than 2 percent in developed countries to over 23 percent in some areas with no eye prophylaxis and a low socioeconomic status (1-3). However it remains a common health problem and is the most common ophthalmic complication of neonates, overall with the potentiality of producing long term sequelae and blindness (1,2). The major risk factor and the most common organisms responsible for it have been attributed to sexually transmitted diseases and its etiologies (1,2,4). Since, there is no eye prophylaxis in our country and also no study about ophthalmia neonatarum, comparison of different prophylactic agents, major risk factors and organisms responsible for it (especially STD and its etiologies like *Chlamydia trachomatis* is the most common agent in many reports (1,2,4,5), this study was designed to determine the effect of 2.5% povidone iodine solution in comparison with 0.5% erythromycin ointment and no eye prophylaxis in preventing of conjunctivitis and also to find out the major risk factors, the most common agents and the best strategies for preventing its occurrence and sequelae.

MATERIALS AND METHODS

As a randomized control trial in Imam Khomeini Hospital, neonatal conjunctivitis, its clinical and laboratory findings and risk factors were studied on 360 term neonates born by vaginal delivery in years 2000-2001. They were divided randomly into three groups of 120 newborn, receiving a drop of 2.5% povidone iodine solution, a 1 cm strip of erythromycin ointment or no eye prophylaxis as a control group. Medications were applied soon after birth when they were cleaned. Exclusion criteria were prematurity, prolonged rupture of membrane (>18 hours), mother receiving antibiotic in her last month of pregnancy, ocular malformation,

complicated delivery, diseased neonate and uncooperative parents. A pediatrician visited all of these 360 cases in 24 hours and at 7 days of life. They were followed up to 28 days with training mothers about disease and having phone contact with them. If there were any signs of conjunctival discharge, redness or edema, smears for gram and Giemsa staining, bacterial culture and direct fluorescent antibody (DFA) test for Chlamydia (on specimens preparing by scraping of palpebral conjunctiva) was performed. We considered and assessed different variables such as mother's age, parity, education, vaginal infection and prenatal care, meconium staining of amniotic fluid, birth in unhygienic environment (mother defecation), sex and birth weight of neonates, the age when signs were seen, results of gram and giemsa staining, bacterial culture and DFA test. The clinical conjunctivitis were considered infectious if there were positive bacterial culture or DFA test and noninfectious otherwise. To evaluate independent variables, infants with clinical conjunctivitis were compared with those not afflicted. The data were analyzed by fisher exact test.

RESULTS

There was no significant statistical difference for variables such as mothers' age, parity, education, vaginal infection and also for sex and birth weight of neonates, between those with or without conjunctivitis in all groups. Clinical conjunctivitis was detected in 9 (7.5%) neonates of povidone iodine group, 14 (11.71%) of erythromycin group and 26 (21.7%) of control group and 7, 12 and 21 cases of them were infectious, respectively (Table 1). Among these, the significant difference was between clinical conjunctivitis in povidone iodine and control groups (P=0.0036) and nearly so in erythromycin and control

groups (P=0.056) The most common microorganisms in order of frequency were gram-negative bacilli, Staphylo-coccus aureus and coagulase negative Staphylococci (staph-CON) (Table 2) with no significant difference between three groups. In control group, we detected two cases of Chlamydia (9.5% of infectious conjunctivitis) with an incidence of 1.7%. We could not find any cytological finding to suggest viral infections and Giemsa, and staining was also negative for two Chlamydia cases. and also between infectious conjunctivitis in povidone iodine and control groups (P= 0.0089) (Table 1). The most common microorganisms in order of frequency were gram-negative bacilli, Staphylococcus aureus and coagulase negative Staphylococci (staph-CON) (Table 2) with no significant difference between three groups. In control group, we detected two cases of Chlamydia (9.5% of infectious conjunctivitis) with an incidence of 1.7%. We could not find any cytological finding to suggest viral infections and Giemsa, and staining was also negative for two Chlamydia cases. We found significant relationship between thick meconium staining and clinical conjunctivitis (P< 0.0001) (Table 3). It is notable that 5 of 9 cases of noninfectious conjunctivitis were associated with thick meconium (45.5%) in comparison with 11 of 40 cases of infectious ones (27.5%) in whom 8 of them were also associated with unhygienic labor. Birth in unhygienic environment was a risk factor with significant relationship in conjunctivitis occurrences (Table 4) usually between 2nd and 4th days of life and the most common microorganisms were gram-negative bacilli (48.6% of conjunctivitis appeared between 2nd and 4th day of life, usually with gram-negative bacilli and 40% between 5th and 7th days of life, usually with gram-positive cocci). Only one of neonates in povidone iodine group had noninfectious conjunctivitis, in first 24 hours of life with redness of conjunctiva and 2 cases like this in control group and all of them were also meconium stained.

Table 1: Distribution of types of conjunctivitis among neonates according to microbial culture and DFA test

Group	Betadine	Erythromycin	Control	Total
Type of conjunctivitis	No (%)	No (%)	No (%)	No (%)
Infectious 1	7(5.8)	12(10)	21(17.5)	40(11.1)
gr (-) bacilli	3(2.5)	6(5)	7(5.8)	16(4.5)
Staph. aureus	3(2.5)	4(3.)	6(5)	1-(3.6)
Staph CON	1(0.8)	2(1.7)	4(3.3)	7(1.9)
Chlamydia t			2(1.7)	2(0.5)
Mixed growth			2(1.7)	2(0.5)
Non infectious 2	2(1.7)	2(11.7)-	5(4.2)	9(2.5)
Total (clinical) 3	9(7.5)	14(11.7)	26.(21.7)	49(13.6)

1- P = 0.0089 (povidone iodine vs. control), P =0.1337), P =0. 1153 (erythromycin vs control), P =1.0000 (povidone iodine vs erythromycin), 2- P = 0.0036 (povidon iodine vs con (erythromycin vs. control), P =0.389 (povidone iodine vs erythromycin, 3- P =0. 1153 (povidone iodine vs control, P = 0.057 (erythromycin vs control), P = 0.3804 (povidone iodine vs erythromycin)

Table 2. Distribution of different microorganisms in infectious conjunctivitis in all groups according to microbial culture and DFA test

Group Organism	Betadine	Erythromycin	Control	Total
	No (%)	No (%)	No (%)	No (%)
gr (-) bacilli 1	4(22.8)	6(50)	7(33.3)	16(40)
Staph. aureus 1	3 (42.8)	4 (3 31. 3)	6(28.6)	13(32.5)
Staph. CON 1	1(14.4)	2(16.7)	4(19.1)	7(17.
Chlamydia t			2(9.5)	2(5)
Mixed growth			2(9.5)	2(5)
Total	7(100) 1	12(100)	21(100)	40(100)

1 There was no significant difference between these groups ($p > 0.05$)

Table 3. Distribution of conjunctivitis in all groups according to meconium staining of amniotic fluid

Group Variable	Betadine		erythromycin		control		total	
	Conj -	Conj +	Conj -	Conj +	Conj -	Conj +	Conj -	Conj +
Thin meconium	6	1	7	4	5	2	18	7
Thick meconium	1	4	0	5	2	7	3	16
No meconium	104	4	99	5	87	17	290	26
Total	111	9	106	14	94	26	311	49
p-value	< 0.0001							

Table 4. Distribution of conjunctivitis in all groups according to unhygienic environment (mother defecation) during labor

Group	Betadine		Erythromycin		Control		Total	
	Conj -	Conj +	Conj -	Conj +	Conj -	Conj +	Conj -	Conj +
Unhygien								
yes	25	5	19	8	21	17	65	30
No	85	4	87	6	74	9	246	19
Total	110	9	106	14	95	26	311	49
Odds ratio	4.1 (1.02-16.40)		6.1 (1.9-19.7)		6.4 (2.5-16.2)			
P-value	0.047		0.0029		0.0001			

DISCUSSION

In this study, we found that there was a high incidence of conjunctivitis, with no eye prophylaxis (21.7%) and the major risk factors were birth in unhygienic environment, meconium staining of amniotic fluid and probably colonization of newborns after birth due to unsterile handling of neonates (as showed by 40% of conjunctivitis occurrence between 5th and 7th days of life, usually with gram-positive cocci). The fourth most common agent in control group with an incidence of 1.7% although not as common as many reports (4-6), seems not to be a rare vaginal infection of mothers had not significant effect in occurrence of conjunctivitis. There was also no gonococcal conjunctivitis and this may be due to low number of cases. However, sexually transmitted diseases and its etiologies were not major risk factors in producing ophthalmia neonatarum and this is why

we do not see complication of this common disease in our country (Chlamydia t. and N. gonorrhoea, are two most important agents in ophthalmia neonatarum complications) unlike most areas of the world with no eye prophylaxis (4-6). Povidone iodine solution had significant effect on prophylaxis of ophthalmia neonatarum and decreasing infectious conjunctivitis but erythromycin had not such significant effects. In one study, Chen et al (7) showed the same results but in Isenberg study that was done on 3117 neonates both povidone iodine and erythromycin had significant effect but there also was superiority of povidone Iodine (4). Povidone iodine had the same effect in decreasing of infectious conjunctivitis produced by different 10) microorganisms as there many reports indicating no microbial resistance to povidone iodine (7-10). There was no significant toxic reaction to povidone iodine and meconium seems to produce conjunctival inflammation so that 5 of 9 cases of noninfectious conjunctivitis were

associated with thick meconium. In conclusion, 2.5% povidone iodine solution with regard to its broad spectrum antimicrobial effect, lack of toxicity, less cost and much easier for application by nursing staff (due to its solution form and discoloration of conjunctiva) seems to be the best choice in prophylaxis of ophthalmia neonatarum, especially in developing countries.

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