SHORT REPORT

SINGLE LOW-DOSE CEFTRIAXONE FOR THE TREATMENT OF GONOCOCCAL OPHTHALMIA — IMPLICATIONS FOR THE NATIONAL PROGRAMME FOR THE SYNDROMIC MANAGEMENT OF SEXUALLY TRANSMITTED DISEASES

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We prospectively analysed a total of 21 baby-mother pairs with culture-proven *Neisseria gonorrhoeae* treated with a single low dose of ceftriaxone, namely 62.5 mg for babies and 125 mg for mothers respectively. *N. gonorrhoeae* was eradicated from all babies' eyes with no residual damage, as well as from the mothers' cervices.

A single low dose of 62.5 mg ceftriaxone has emerged as the treatment of choice for gonococcal ophthalmia neonatorum because of its excellent activity against *N. gonorrhoeae*, including penicillinase-producing strains.

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Conjunctivitis is a common ocular inflammation involving all age groups and occurring worldwide. The incidence of acute conjunctivitis of the newborn has been reported to be high, occurring in about 12% of all newborns.[1] Accurate figures for developing countries are not readily available but it is considered to be a common condition, with the majority of patients presenting to primary health care (PHC) facilities.

Gonococcal ophthalmia neonatorum is a serious condition, which if left untreated can lead to blindness. It manifests in the newborn about 2 - 5 days after birth and produces an acute purulent discharge.[2] Single-dose therapy for gonococcal ophthalmia neonatorum using ceftriaxone has been proposed previously at a single intramuscular (IM) dose of 125 mg.[3,4] The national programme for the syndromic management of sexually transmitted diseases (STDs) in South Africa[5] recommends the use of spectinomycin at 25 mg/kg IM for neonates and 2 g IM for mothers and their sexual partner/contact as first choice, while ceftriaxone is mentioned as an alternative at a single dose of 25 - 50 mg/kg IM for the neonate and 125 mg for the mother.

This clinical study was undertaken to evaluate the single low-dose therapy at 62.5 mg IM in neonates diagnosed as having gonococcal ophthalmia while administering 125 mg IM to their mothers in order to eliminate cervical carriage.

PATIENTS AND METHODS

Neonates presenting to the eye clinic at King Edward VIII Hospital, Durban, with acute conjunctivitis were recruited for the study. Informed consent was obtained from the accompanying mothers. Babies' eyes were examined macroscopically by an ophthalmologist using ordinary light. Swab specimens were collected from all baby-mother pairs from the following sites: eyes of the baby, and urethra, cervix and rectum of the mother. Specimens were inoculated onto modified New York City medium[6] for the isolation of *Neisseria gonorrhoeae* and slide smears were made for direct immunofluorescence testing for *Chlamydia trachomatis* antigen (MicroTrak, Syva, UK).[7]

N. gonorrhoeae isolates were confirmed on the basis of oxidase production and a positive glucose fermentation test. The strains were tested for penicillinase production (β-lactamase) and minimum inhibitory concentrations were determined for ceftriaxone using the agar dilution method. Auxo- and serotyping of all gonococcal isolates were performed according to previously described methods.[8,9]

Ceftriaxone was administered to neonates at a single dose of 62.5 mg IM and to the mothers at 125 mg IM. Mothers were provided with cotton wool balls and instructed by nursing staff to soak in tap water and wash off the purulent eye discharge of their babies as necessary. Follow-up swab specimens were collected from all the abovementioned sites 24 hours after treatment, and were processed as described for the isolation and detection of *N. gonorrhoeae* and *C. trachomatis* respectively. All neonates were hospitalised and observed for 48 hours before being discharged. The mothers were also hospitalised as boarder mothers. In baby-mother pairs where *C. trachomatis* antigens were detected, the neonates were given an oral suspension of erythromycin at 62.5 mg four times a day for 7 days, while the mothers were treated with 500 mg erythromycin four times daily for 7 days. A follow-up clinic visit for both baby and mother was arranged for 7 days later.

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Table I. Characteristics of neonates (*N* = 21)

	N	%
Age		
Mean (days)	11	
Range (days)	2 - 30	
Clinical features		
Discharge with severe lid swelling	7	33
Discharge with mild to moderate lid swelling	14	67
Severe chemosis	3	14
Mild to moderate chemosis	18	86
Corneal ulceration	0	0
Mode of delivery		
Vaginal	21	100
Caesarean section	0	0
Place of delivery		
Home	5	23
Clinic/hospital	16	77

Table II. Typing results and susceptibility profile of *Neisseria gonorrhoeae* isolates (*N* = 21)

	N	%
Auxotype		
Proline-requiring	20	50
Prototrophic	18	45
Arginine- and proline-requiring	2	5
Serotype		
A6	17	43
A8	4	10
B1	2	5
B3	3	8
B4	7	16
B5	4	10
B22	3	8
Penicillinase-producing strains	10	25
Ceftriaxone MICs		
< 0.008 µg/ml	39	98
0.015 - 0.03 µg/ml	1	2

MICs = minimal inhibitory concentrations.

Results

A total of 21 baby-mother pairs were recruited. Patient data are presented in Table I. None of the neonates presented with ulceration of the cornea but in 3 there was severe chemosis. All babies were delivered vaginally and none of the mothers had had a caesarean section. Eye swabs from all neonates yielded *N. gonorrhoeae* and in 7 neonates (33%), *C. trachomatis* was also detected. *N. gonorrhoeae* was cultured from the genital sites of all mothers except one. *C. trachomatis* was detected in endocervical specimens of all mothers whose neonates had chlamydial infection. A total of 40 gonococcal isolates were available for further characterisation and the data are shown in Table II. Proline-requiring and prototrophic strains were similar in number. The predominant serotype was A6 and the same auxotype and serotype were obtained from all baby-mother pairs. Penicillinase-producing strains accounted for 25% of all isolates and all isolates demonstrated very low minimal inhibitory concentrations (MICs) for ceftriaxone.

The 24-hour follow-up specimens were all negative for *N. gonorrhoeae*.

Discussion

The use of single-dose ceftriaxone for the treatment of gonococcal urethritis has been established in both local studies[10] and those carried out elsewhere.[11] However, what has been of significance has been the reduction in the dose administered — the 1989 Centers for Disease Control (CDC) guidelines for treatment of STDs recommended the use of a single 250 mg IM dose,[12] while the 1993 and current 1998 guidelines advocate a single dose of 125 mg IMI.[13] This is not surprising in view of the fact that studies have shown efficacy in adults even at a dose of 62.5 mg.[14]

In this study 21 baby-mother pairs were treated with single 62.5 and 125 mg doses respectively. Efficacy was determined by doing a test of cure within 24 hours of therapy, with excellent results showing complete resolution of ocular inflammation and clearance of cervical carriage. This finding is not unexpected as uretheral clearance of *N. gonorrhoeae* in adult males has been achieved within 4 hours .

While much work has been done on adult male gonococcal urethritis, there appears to be a lack of information on gonococcal ophthalmia neonatorum. The CDC guidelines[13] state that this condition should be managed with the same dose administered for adults. The findings of our study indicate that half the dose, namely 62.5 mg, effected elimination of the offending organism and resolution of symptoms within 24 hours, with no residual damage at 1-week follow-up.

The national programme for the syndromic management of STDs[5] proposes spectinomycin as first-choice treatment for gonococcal ophthalmia neonatorum, but this agent is not being used as it is not available at the majority of PHC facilities. The guidelines propose ceftriaxone as a second-line agent and do not recommend a specific dose, but indicate the use of 25 - 50 mg/kg. Based on the clinical findings of this study together with the extremely low MIC values shown for gonococcal isolates, a 62.5 mg dose is appropriate and cost effective for the management of gonococcal ophthalmia neonatorum.

In 7 of the 21 neonates investigated, concurrent *C. trachomatis* infection was detected. With regard to neonatal conjunctivitis the national STD treatment protocols[5] advocate the additional prescription of erythromycin suspension for 7 days, and this is supported by the findings of this study. Five of the 21 neonates

were delivered at home and we could also not ascertain whether eye prophylaxis was administered to the remaining babies delivered at the clinics and hospitals. Hence, the impact of prophylaxis could not be measured.

Characterisation of gonococcal isolates on the basis of nutritional requirements (auxotyping) showed the isolates to belong to two large groups, the wild prototrophic strains and those requiring proline for growth. Serotyping showed a predominance of strain A6, with the other strains demonstrating great diversity. There was matching for the isolates from neonates and mothers; however, for better epidemiological work the newer techniques of Opa typing might be more relevant.[15]

This study demonstrated good clinical efficacy with single low-dose ceftriaxone for the management of gonococcal ophthalmia neonatorum and elimination of cervical gonococcal infection from the infected mothers. The national STD treatment protocols[5] should recommend the use of a single 62.5 mg dose for neonates and a dose of 125 mg IM for lactating and infected pregnant women.

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