Clinical and laboratory study

ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF NEISSERIA GONORRHOEAE IN WESTERN AUSTRIA

F. Allerberger,H.Kofler,C.Brezinka,F.M.Fink,and M.P.Dierich

ABSTRACT

From January 1991 to April 1992 24 Neisseria gonorrhoeae-isolates from clinical specimens were collected at the Federal Public Health Laboratory in Innsbruck (Austria) and screened for resistance to penicilin G, erythromycin, tetracycline, spectinomycin, ceftriaxone, cefuroxime, ciprofloxacine, and silver nitrate. Patients originated from the Austrian provinces Salzburg, Tirol, and Vorarlberg, and presented with manifest gonorrhoea. Two of 24 isolates were penicillinase-producing N.gonorrhoeae; both strains were isolated from men who had just returned from Thailand or Kenya; the isolate from Africa was also resistant to tetracycline. Five of 24 infections were acquired abroad, sextourism being involved in four cases. The antimicrobial resistance pattern found in gonococci in western Austria revealed that topical silver nitrate and erythromycin are equally acceptable for use in prophylaxis of neonatal ophthalmia. Penicilin is still the drug of choice in the treatment of endemic infections. If gonorrhoea has been acquired abroad, especially in Asia or Africa, ceftriaxone, spectinomycin or ciprofloxazine are recommended for therapy.

KEY WORDS:
Neisseria gonorrhoeae, gonococcal ophthalmia, susceptibility pattern.

INTRODUCTION

Gonorrhoea is one of the most prevalent bacterial infections in the world. The organism is uniquely adapted to humans and is transmitted almost exclusively by sexual contact. Gonococcal infections are not always symptomatic, and a reservoir of infected, asymptomatic individuals maintains this organism in the general population (1). Infected mothers may transmit Neisseria gonorrhoeae to their infants. In 1881, when Credé reported that the conjunctival instillation of an aqueous solution of silver nitrate reduced the incidence of gonococcal ophthalmia from 10% to 0,3%, neonatal gonococcal ophthalmia was a leading cause of blindness (2). Today, the most common specific organism causing neonatal ophthalmia is Chlamydia trachomatis. Changing epidemiologic circumstances and chemical conjunctivitis due to Credé prophylaxis fueled reservations about the use of silver nitrate. At the obstetric department of the university hospital in Innsbruck an 0,5% erythromycin ointment is now used instead of silver nitrate. Using antibiotics in the prophylaxis of ophthalmia neonatorum we must be careful not to overlook changes in the resistance patterns of gonococci.

It was the aim of this study to monitor the antimicrobial susceptibility of Neisseria gonorrhoeae isolates from western Austria and to assess current regimens used in propylaxis and treatment of gonococcal infections.

MATERIAL AND METHODS

From January to April 1992 susceptibility-testing was perfomed for all Neisseria gonorrhoeae strains isolated from clinical routine specimens at the Federal Public Health Laboratory in Innsbruck. For the detection of carbohydrate utilization and penicillinase activity the quad-ferm system (api,Montalieur-Vercieu,France) was used. The nitrocefin disk test "Cefinase" (BBL Microbiology Systems, Cockeysville, MD) was employed as an additional ß- lactamase test. A DNA probe test (PACE 2, Gen-Probe Incorporated,San Diego,CA) was used for final culture confirmation.

Antimicrobial resistance testing was perfomed using a modified Bauer-Kirby test (3,4,5,6). In brief, a suspension of the organism in Mueller-Hinton broth was prepared to a density equivalent to a # 0,5 McFarland turbidity standard. The surface of two chocolate agar plates supplemented with 1% Iso Vitalex was swabed and, after the plate surfaces had dried, 0 paper-disk were applied to the agar surface. The 10 unit penicilin disk, 30 µg tetracycline disks, 15 µg erythromycin disks, 30 µg cefuroxime disks, 30 µg cefuroxime disks, and 5 µg ciprofloxacin disks were provided by commercial vendors (Oxoid, Hampshire, England; Becton Dickinson, Heidelberg, Germany). The 100 µg spectinomycin disks were prepared using a spectinomycin standard kindly provided by the Upjohn Company (Puurs,Belgium). The 10 µg and 25 µg spectinomycin disks commercially available in Austria are inappropriate since they cannot discriminate between susceptible strains and strains with different levels of resistance (4,6). Plates were incubated at 35°C in a candle jar for 24 hors. Zones were measured and interpreted as follows: penicilin: <= 19 mm resistant, >=47 mm susceptible; erythromycin: < 21 mm resistant, > 32 mm susceptible; tetracycline: < 30 mm resistant, > = 37 mm susceptible; cefuroxime: < 29 mm resistant, > = 31 mm susceptible; ceftriaxone: < 29 mm resistant, > = 35 mm susceptible; ciprofloxacin: < 27 mm resistant, > 39 mm susceptible; spectinomycin: < 19 mm resistant, > 24 mm susceptible. The oligodynamic effect of silver was tested by filling wells cut from the seeded agar with 50 µl silver nitrate (1%) and interpreting the occurrence of a zone of inhibition as "susceptible".

RESULTS

During the study period Neisseria gonorrhoeae was isolated from 24 patients from the three western provinces of Austria (Vorarlberg,Tirol,Slazburg). Patients ranged in age from 15 to 50 years. All patients had clinically manifest gonorrhea. Female patients accounted for 7 isolates, males for 17. Five infections were acquired abroad; sextourism was involved four times (Thailand 3 x, Kenya 1 x). One truck-driver acquired gonorrhoea in Italy.

Two of 24 isolates were penicillinase-producing N.gonorrhoeae (PPNG); both strains were isolated from men who had just returned from Thailand or Kenya. One of these isolates was also resistant to tetracycline; the 50-year old patient who had acquired gonorrhoea in Africa had already been treated with penicilin before a urethral swab was taken; thereafter he underwent tetracycline-therapy, again without clinical response. The invitro susceptibility pattern reported by the laboratory provided the explanation for the failure; ceftriaxone finally proved to be effective.

The remaining isolates were fully susceptible to the antimicrobial agents tested. Table 1 summarizes data on patients and shows the resistance pattern of the isolates.

DISCUSSION

In 1884 BUMM achieved the first successful culture of the gonococci on coagulated human blood serum, and by transferring the pure culture to the human urethra he established the specificity and etiological role of "Gonococcus Neisser" (7,8). In 1879 NEISSER had described the regular and exclusive occurrence of gonococci in 46 cases of gonorrhoea in adults and 7 cases of ophthalmia neonatorum (9).

Although the prophylaxis of gonococcal ophthalmia of the newborn with a drop of 1% silver nitrate in each eye (Crede's prophyaxis) became a milestone of 19 th century preventive medicine, reservations about the use of silver nitrate have been voiced for over 50 years. Since silver nitrate may cause chemical conjunctivitis and early reports suggested that neonatal ocular prophylaxis with erythromycin or tetracycline ointment might prevent chlamydial conjunctivitis, the Centers for Disease Control recommended tetracyclin-and erythromycin-ointment (10,11). Many states amended their health codes to conform with recommendations of the Centers for Disease Control and many hospital, including the university hospital in Innsbruck, subsequently changed from silver nitrate to erythromycin or tetracycline.

Using antibiotics in the prophylaxis of ophthalmia neonatorum we must be careful not to overlook changes in the resistance patterns of gonococci. The use of rapid diagnostic procedures in routine diagnosis of sexually transmitted diseases are increasingly replacing the conventional demonstration of Neisseria gonorrhoea by culture methods. To gurantee the efficacy of antibiotics in prophylaxis and therapy of ophthalmia neonatorum special studies are necessary to elucidate the situation with regard to

Table 1. Summarized data on 24 cases of gonorrhoea and resistance pattern of the isolates from western Austria, 1991/1992.

Patient	Sex	Age	acquired in:	Penicillin G	Erythromycin	Tetracycline	Spectinomycine	Ceftriaxone	Cefuroxime	Ciprofloxazine	Silvernitrate
1	f	26a	Tirol	s	s	s	s	s	s	s	s
2	f	26a	Vorarlberg	s	s	s	s	s	s	s	s
3	m	33a	Tirol	s	s	s	s	s	s	s	s
4	m	21a	Tirol	s	s	s	s	s	s	s	s
5	f	27a	Tirol	s	s	s	s	s	s	s	s
6	m	23a	THAILAND	R	s	s	s	s	s	s	s
7	m	37a	Tirol	s	s	s	s	s	s	s	s
8	m	22a	THAILAND	s	s	s	s	s	s	s	s
9	f	35a	Salzburg	s	s	s	s	s	s	s	s
10	m	30a	Vorarlberg	s	s	s	s	s	s	s	s
11*	m	50a	KENIA	R	s	R	s	s	s	s	s
12	m	33a	Vienna	s	s	s	s	s	s	s	s
13	m	20a	Tirol	s	s	s	s	s	s	s	s
14	m	34a	Tirol	s	s	s	s	s	s	s	s
15	m	43a	THAILAND	s	s	s	s	s	s	s	s
16**	f	19a	Tirol	s	s	s	s	s	s	s	s
17***	m	27a	Tirol	s	s	s	s	s	s	s	s
18	f	15a	Tirol	s	s	s	s	s	s	s	s
19	m	30a	Tirol	s	s	s	s	s	s	s	s
20	m	36a	ITALY	s	s	s	s	s	s	s	s
21	m	46a	Tirol	s	s	s	s	s	s	s	s
22	m	18a	Tirol	s	s	s	s	s	s	s	s
23	m	33a	Tirol	s	s	s	s	s	s	s	s
24	f	23a	Tirol	s	s	s	s	s	s	s	s

f = female, m = male, s = susceptible, R = resistant

*** patient had been treated with penicillin and tetracycline without success before antibiogram was reported out**
**** native of Croatia**
*****native of U.S.A.**

resistance.

While penicillinase-producing gonococci are widely disseminated in Asia and Africa, such strains are rarely seen in Austria (12). In the present study no resistant strain was found in any of the 19 cases of gonorrhoea contracted in Austria. In this country penicillin is therefore rightly still the antibiotic of choice for the treatment of gonorrhoea. Recommended dose: 4,5 mio. IU penicillin (e.g. Na-benzylpenicillin 3,5 mio. IU + clemizol benzyl penicillin 1,0 mio. IU) once i.m. (13). If cultures reveal penicillin-resistant gonococci: ceftriaxone 1 g i.m., spectinomycin 2 g i.m., or ciprofloxacin 500 mg p.o.

If the infection has been acquired abroad, especially in Asia or Africa, the organisms can be assumed to be possibly penicillinase-producing and tetracycline-resistant. In this situation penicillins and tetracyclines can no longer be considered reliable treatment for gonorrhea. A careful and complete sexual history must be obtained from each patient. In the U.S. nowadays ceftriaxone is generally recommended for therapy, due to frequent resistance of endemic

N.gonorrhoeae to previously useful antimicrobial agents (14,15). Of the 24 culture-proven cases summarized in this study, 4 (17%) were due to sextourism to Asian or African countries with high HTV-infections rates. The AIDS-pandemic does not seem to have dramatically altered sexual behaviour in western Austria so far.

Cost containment should be a concern to everyone in medicine. The use of appropriate antibiotics can reduce the financial burden: penicillin therapy is 4 to 9 times cheaper than ceftriaxone, spectinomycin, or a pack of ciprofloxacin tablets.

According to our present knowledge, it does not appear that prophylaxis with either silver nitrate or topical antibiotics is effective in preventing chlamydial ophthalmia (16,17). Therefore topical silver nitrate and erythromycin are each considered equally acceptable for use, although silver nitrate may cause more chemical conjunctivitis. On the other hand, the antibacterial properties of silver, the so called oligodynamic effect, can so far be relied upon without continuous control of gonococcal resistance patterns. The in vitro sensitivity to erythromycin shown by all of our gonococcal isolates supports the use of this macrolide antibiotic for the prophylaxis of ophthalmia neonatorum. Despite rare reports of failure of erythromycin in the world literature, there have been no data demonstrating an increase in gonococcal ophthalmia with the use of this antibiotic (18,19).

Antimicrobial resistance in gonococci is changing, emphasizing the need to maintain surveillance and use the most effective therapies to control infection and reduce sequelae.

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AUTHORS' ADDRESSES

Doz. Dr. Franz Allerberger, Institut of Hygiene and Federal Public Health Laboratory, Fritz Pregl Str 3, A-6020 Innsbruck
Dr. Heinz Kofler, Department of Dermatology and Venerology, University of Innsbruck, Anichstrasse 35, A-6020 Innsbruck
Dr. Christoph Brezinka, Department of Gynecology and Obstetrics, same address
Dr. Franz-Martin Fink, Departement of Pediatrics, same address
Prof. Dr. Manfred P. Dietrich, Institut of Hygiene and Federal Public Health Laboratory, Fritz Pregl Str 3, A-6020 Innsbruck