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Antibiotic prescribing during an outbreak of meningococcal disease

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SUMMARY

During a prolonged outbreak of meningococcal disease caused by serogroup B serotype 15 sulphonamide-resistant strains in one British health district, there was considerable variation in attack rates by town. General practitioner (GP) antibiotic prescribing rates were compared in high and low incidence towns. The only significant difference found was that erythromycin prescribing was more frequent in the high incidence towns (rate ratio 4·0, 95% CI 3·2–4·8, in March 1987 and 3·0, 95% CI 2·4–3·7, in November 1987). This was probably due to increased GP consultation rates for upper respiratory tract infection (URTI), but higher erythromycin usage may have increased meningococcal acquisition rates or susceptibility to meningococcal disease. Antibiotic prescribing rates should be further investigated in defined areas of high and low incidence of meningococcal disease.

INTRODUCTION

Persistent differences in meningococcal disease attack rates between Gloucestershire towns were noted during a prolonged outbreak due to serogroup B serotype 15 sulphonamide-resistant strains [1]. We investigated the possibility that higher GP prescribing rates for sulphonamides were associated with increased attack rates caused by sulphonamide-resistant organisms.

METHODS

Cases of meningococcal disease were ascertained as described previously [1]. The four Gloucestershire towns with the highest incidence in the first 5 years of the outbreak between 1 January 1982 and 31 December 1986 (total 52 cases, population 125700, mean annual incidence 8·3/100000, range 4·8–13·5) were matched by size to four towns with low incidence (6 cases, population 124000, mean incidence 1·0/100000). The outbreak continued during the following 5 years with relatively unchanging attack rates in the high and low incidence towns (mean annual incidence 10·5 and 2·2/100000 respectively). The percentage of employees and self-employed persons in manual occupations (Social Class III N, IV, V) was 43·7% in the high incidence towns compared to 37·0% in the low incidence towns ($P < 0{\cdot}0001$) (1991 Census, Office of Population Censuses and Surveys).

All GPs were selected from the two pairs of smaller towns with five or fewer GPs; in the two pairs of larger towns, five GPs were randomly selected from Family Practitioner Committee lists. Consent to obtain antibiotic prescribing information was given by 33 of the 38 selected GPs; pairing of GPs between high and low incidence towns left 28 (14 pairs) for analysis. Numbers of antibiotic prescriptions by GP were obtained from the Prescription Pricing Authority (PPA) for two arbitrarily selected months in 1987 (March and November). Seven antibiotic groups were analysed including 98% of all antibiotics prescribed.

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Table 1. *Number and rate/1000 practice population of antibiotic prescriptions in Gloucestershire towns with high and low incidence of meningococcal disease*

	March 1987				November 1987			
	High attack rate towns		Low attack rate towns		High attack rate towns		Low attack rate towns	
GP list size...	24674		24651		23843		21910	
Antibiotic	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Penicillin V	191	0·8	104	0·4	100	0·4	108	0·5
Flucloxacillin	23	0·1	27	0·1	103	0·4	30	0·1
Amoxycillin	552	2·2	575	2·3	492	2·1	406	1·9
Cephalosporins	64	0·3	72	0·3	67	0·3	62	0·3
Tetracyclines	188	0·8	198	0·8	167	0·7	197	0·9
Erythromycin	515	2·1*	129	0·5	327	1·4*	101	0·5
Sulphonamides (including Cotrimoxazole)	199	0·8	185	0·8	167	0·7	178	0·8
Total	1732	7·0	1290	5·2	1420	6·0	1082	4·9

* $P < 0·001$ Wilcoxon signed rank test.

Differences between each GP pair in prescribing rates per 1000 practice population were analysed by the Wilcoxon signed rank test.

RESULTS

Antibiotic prescribing was higher in the high incidence towns in both months surveyed (Table 1); the differences were almost entirely due to an excess of erythromycin prescriptions (rate ratios from pooled data 4·0, 95% CI 3·3–4·8 in March, and 3·0, 95% CI 2·4–3·7 in November). In both months, 12 out of 14 GPs in high incidence towns wrote more prescriptions for erythromycin (range 1–175, median 18) than their counterparts (range 0–43, median 6) ($P < 0·001$).

DISCUSSION

No difference was found in rates of sulphonamide prescribing between towns with high and low incidence of meningococcal disease. The markedly higher rate of erythromycin prescribing in the high incidence towns was unexpected and was found in both months examined.

In a follow-up survey of the study GPs, a higher proportion of GPs in the high incidence towns than in the low incidence towns used erythromycin as an agent of first or second choice for the treatment of respiratory infections (10/12 *vs.* 4/10 for adults, 11/12 *vs.* 6/10 for children, $P =$ ns). Equal proportions of GPs in high and low incidence towns used it for treatment of skin infections or in patients with penicillin allergy. An increased frequency of upper respiratory tract infections (URTI) in the high incidence towns could have resulted both in higher meningococcal disease attack rates [2, 3] and independently in higher erythromycin prescribing rates. The high incidence towns had a higher proportion of people in manual social classes who might be expected to have a higher incidence of respiratory tract infections [4]. Public anxiety in the high incidence towns could also have led to higher GP consultation and higher antibiotic prescribing rates for URTI. We were not able to obtain data on GP prescribing rates before the outbreak.

However, a higher incidence of URTI in towns with increased incidence of meningococcal disease would not explain why GPs in these areas were more likely to use erythromycin than other antibiotics for the treatment of URTI. Could increased use of erythromycin itself have led to an increased incidence of meningococcal disease?

Increased erythromycin prescribing had not led to a selective increase in erythromycin-resistant meningococci; the Meningococcal Reference Unit in Manchester tested a sample of 35 meningococcal isolates from Gloucestershire which were all erythromycin sensitive. Increased erythromycin usage might have promoted colonization with erythromycin-resistant organisms. Since *Mycoplasma hominis* is known to be resistant to erythromycin and as it had been implicated as a possible cofactor for meningococcal disease during a serogroup A epidemic in Chad [3], a case control study was undertaken in the UK, but *M. hominis* was not isolated from any of 25 cases of meningococcal disease or their controls (K. Cartwright, unpublished data).

Alternatively, erythromycin could have predisposed to meningococcal colonization and invasion by eradicating oropharyngeal bacteria which inhibit meningococci [5]. In a study in southwest England, erythromycin prescriptions were not increased in the 2 weeks preceding onset of disease in meningococcal cases when compared with controls (J. M. Stuart, unpublished data), but exposure to antibiotics in the preceding months or in family members was not assessed. A high secondary attack rate among household contacts of cases was recently recorded in France during a time when another macrolide antibiotic, spiramycin, was routinely recommended for prophylaxis in household contacts [6].

An association between high antibiotic prescribing rates and a high incidence of meningococcal disease might be due to confounding factors such as URTI. However, it is more difficult to explain the selective increase in erythromycin prescribing which was observed during this outbreak. Antibiotic prescribing rates should be checked in other areas with high and low incidence of meningococcal disease.

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