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Abstract

Variations in chemoprophylaxis for meningococcal disease: a retrospective case note review, analysis of routine prescribing data and questionnaire of general practitioners

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Competing interests

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Abstract

Background

Invasive meningococcal disease is a significant cause of mortality and morbidity in the UK. Administration of chemoprophylaxis to close contacts reduces the risk of a secondary case. However, unnecessary chemoprophylaxis may be associated with adverse reactions, increased antibiotic resistance and removal of organisms, such as *Neisseria lactamica*, which help to protect against meningococcal disease. Limited evidence exists to suggest that overuse of chemoprophylaxis may occur. This study aimed to evaluate prescribing of chemoprophylaxis for contacts of meningococcal disease by general practitioners and hospital staff.

Methods

Retrospective case note review of cases of meningococcal disease was conducted in a district from 1st September 1997 to 31st August 1999. Routine hospital ambulatory prescribing data was searched for chemoprophylactic prescriptions of rifampicin. A questionnaire of general practitioners was undertaken to obtain more de

Results

Prescribing by hospital doctors was in line with recommendations by the Communicable Disease Control. General practitioners prescribed 118% more than was recommended. Size of practice and training status did not affect prescribing, but there were significant differences by geographical area. Prescribing occurred in areas with high disease rates and associated public close contacts did not appear to receive prophylaxis.

Conclusions

Receipt of chemoprophylaxis is affected by a series of patient, doctor and High publicity appears to increase demand for prophylaxis. Some true contacts appropriate chemoprophylaxis and are left at an unnecessarily increased

Background

Invasive meningococcal disease is a significant cause of morbidity and mortality in the United Kingdom and the commonest infectious cause of death under the age of 30. In 1997, 3000 cases were notified with an overall case fatality rate of around 8%. The risk of a secondary case of meningococcal disease amongst household contacts is 450 and 1650 times that of the general population [3-6]. This is in part due to household and kissing contacts frequently carry the same pathogenic strain.

Chemoprophylaxis is given to close contacts of cases to eliminate nasopharyngeal meningococci. Prophylaxis reduces, but does not eliminate, the risk of secondary infection. If prophylaxis is not given to appropriate contacts then preventable secondary cases occur. Unnecessary use of prophylaxis is associated with increased antibiotic resistance effects, and removal of non-virulent meningococci and *N. lactamica*; both of which provide immunity and provide a competitive flora against colonisation with virulent strains [9-11].

UK guidelines identify who should receive prophylaxis [12], and in this study we examined prescribing of prophylaxis by hospital staff and general practitioners against

Methods

All confirmed and clinical cases [13] of invasive meningococcal disease at Southern Derbyshire Health Authority between 1st September 1997 and 31st August 1999 were identified from the Notifications of Infectious Diseases database and data from the surveillance of meningococcal infections undertaken by the Communicable Disease Centre, Trent. Data on contacts identified at the time were obtained from Communicable Disease Control's (CCDC) records and were assessed against the guidelines [12]. Data were recorded regarding the method of contact (telephone, and by whom if face to face contact had taken place), whether confirmed by laboratory investigations, the serogroup of identified organisms and time of identification.

General practitioner prescribing data from Prescribing Analysis and Cost (PACT) (1997 to 31st August 1999) were examined to identify possible chemoprophylaxis (rifampicin, ciprofloxacin and ceftriaxone. Hospital dispensing data for rifampicin (for chemoprophylaxis in the hospital protocol during this period) were examined from March 1999 to 31st August 1999. Computerised data were not available for

All 2-day courses of rifampicin were assumed to be for eradication of meningococci. Ciprofloxacin is widely used in general practice, but the only indications for its use in the British National Formulary are gonorrhoea and chemoprophylaxis for meningococcal disease [15]. All prescriptions for single dose ciprofloxacin were assumed to be for meningococcal disease. The assumption was made for single 250 mg doses of ceftriaxone.

As PACT data do not identify individual patients a questionnaire was sent to

Southern Derbyshire. This covered the use of rifampicin, ciprofloxacin and prophylaxis during the study period. The questionnaire also requested the initials of the index case for the contact, the drug prescribed and the Practices were free to obtain the information by whatever method they found in the context of their own practice. This information was linked with the data on contacts to identify which contacts had been prescribed prophylaxis. Practices had the option to indicate if they were unable to retrieve the relevant data.

For those who had received a prescription, an assessment was made and they were placed into one of the following groups:

- known to the CCDC and prophylaxis recommended
- known to the CCDC, related to a known case of meningococcal disease and prophylaxis recommended
- not known to the CCDC but related in time and place to a known case, and prophylaxis recommended
- known to the CCDC and not related to a known case of meningococcal disease

Statistics

Student's t tests on log transformed data were used to compare the mean number of additional prescriptions per GP by serogroup, whether confirmed or clinical case and method of contact tracing. Mann Whitney U test was used to compare the level of additional prescribing per response status to questionnaire and training status of the practice. The size of the practice and the number of additional prescriptions per GP were compared using Spearman rank correlation. Mann Whitney U test was used to determine levels of additional prescribing at local authority level. Linear regression was used to explore possible relationships between the level of additional prescribing at Local Authority level and Townsend deprivation score and rate of invasive meningococcal disease.

Results

During the study period 134 cases (66 male, 68 female) of meningococcal disease were identified. Of these 88 (66%) were confirmed by laboratory diagnosis and 46 (34%) were not. Of the 88 that were groupable, 50 (67%) were serogroup B, 24 (32%) were serogroup Y.

The population estimate for 1998 for Southern Derbyshire was 567,457. The rate of invasive meningococcal disease was 7.8 per 100,000 per annum. The rate of clinical cases in Derbyshire [13] was 11.8 per 100,000 per annum compared to the England and Wales rate of 6.1/100,000 (rate ratio 1.9, 95% CI 1.5–2.5, $p < 0.0001$)

Contact tracing

In 34 (25%) cases the patient or other key informants were interviewed. In 24 (18%) cases the patient was interviewed by another public health physician and in 51 (38%) cases contact tracing was done by telephone. In 25 (18%) of cases it was impossible to determine the number of contacts.

952 close contacts were identified for whom prophylaxis had been recommended. The mean number of contacts per case was 7.2 and the mean number of contacts for each case visited by a public health physician was 8.3 where contact tracing was done by telephone was 8.3 (Student's t test $p = 0.03$). There were no significant differences in the mean number of contacts by serogroup, by whether face to face contact tracing was performed by the public health physician in training, nor by whether the case was confirmed by laboratory diagnosis.

The degree of contact with the index case was determined for 697 (73.2%) of cases and is shown in Table 1.

[Table 1.](#) Nature of contact.

Prescribing

For 568 (60%) contacts chemoprophylaxis was prescribed by hospital staff and a general practitioner (GP) was asked to prescribe. For 88 (9%) contacts the prescriber was unspecified.

During the six month period for which hospital prescribing data were available, 11 were identified from the dispensing records. Of these 11 were for the eligible cases. A further five were contacts where chemoprophylaxis was not recommended, in instance the prescription might have related to one of three recent cases that had been identified by the CCDC. For six identified contacts no record could be found, although a prescription had been dispensed, although for two of these the GP had prescribed.

Of the 296 contacts for whom GPs were asked to prescribe, 277 were practices in Derbyshire. 604 prescriptions for chemoprophylaxis were identified from the PACT data (118%) more than recommended by the CCDC. The rates of disease and additional prescriptions per GP for each local authority area are shown in Table 2. It was demonstrated by linear regression between the mean number of additional prescriptions for each local authority area and the rate of invasive disease ($p = 0.30$) and the score ($p = 0.72$). The two areas with high rates of disease (including clonal spread and publicity both had significantly higher prescribing. The other large authority area with high disease, but little publicity, had a significantly lower level of additional prescriptions.

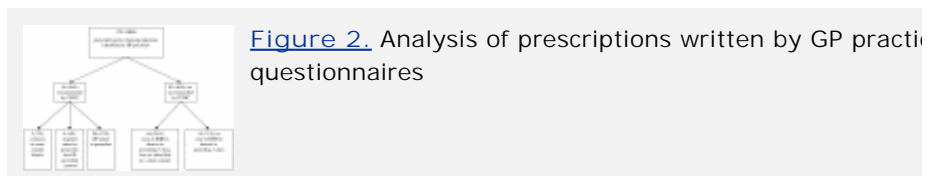
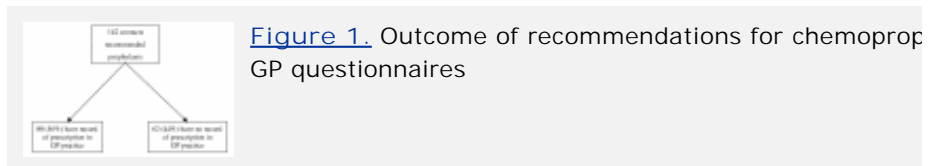
[Table 2.](#) Rates of meningococcal disease and additional prescriptions per GP (from PACT data) by local authority area

At a practice level, there were no significant differences in estimated additional prescriptions, response status to questionnaire, training status or size of practice.

GP Questionnaires

Fifty-seven out of 80 practices (71%) replied to the questionnaire. Of the 23 practices that did not reply, 10 were unable to supply data. Data was therefore obtained from 47 practices. Chemoprophylaxis was recommended for 142 identified contacts who were prescribed by 47 practices whilst the practices identified 179 chemoprophylaxis prescriptions.

Figure 1 shows whether or not a record of prescribing existed for the contacts recommended to have prophylaxis. Figure 2 shows how many of the recommended contacts had been prescribed chemoprophylaxis.



In these practices, PACT identified a total of 305 courses of chemoprophylaxis. Of these, 179 were identified by GP practices. The number of prescriptions for rifampicin, ciprofloxacin and

in Table 3. There is no difference between the ratio of prescriptions recorded for rifampicin and ciprofloxacin.

[Table 3.](#) Comparison of PACT and GP questionnaire data

Discussion

This study demonstrated that after a case of invasive meningococcal disease, more courses of chemoprophylaxis are dispensed than would be expected from a strict adherence to the United Kingdom guidelines [12]. However, some people who are at increased risk do not receive prophylaxis. No practice characteristics examined accounted for the variation in prescribing between practices, nor did the rate of invasive meningococcal disease vary with social deprivation in the local authority areas. However, it is plausible that the publicity in the two areas with highest levels of additional prescribing made requests to GPs to prescribe prophylaxis.

There are a number of possible limitations of this study. Firstly, contact data were incomplete. Not all recommendations for prophylaxis may be recorded and it is not possible to ascertain the degree of contact from the records. Secondly, data from some practices were incomplete. These practices may not be representative. Finally, the numbers of additional prescriptions per GP were similar for responders and non-responders, which suggests that this has not affected the results.

The mean number of contacts per case of meningococcal disease in our study was similar to that found in other studies in the UK [14,16]. Significantly less close contacts were identified by a public health physician conducted a face to face interview with the key informant than those identified by contact tracing is more appropriate with less unnecessary prophylaxis if all contacts are interviewed personally. It is, however, possible that there may be a difference between the use of telephone interviews and experience at contact tracing. Where face to face interviews took place there was no significant difference between those identified by the CCDC and public health doctors in training.

There were significant discrepancies between the numbers of prescriptions recorded by the practices and those identified by the CCDC. PACT is an accurate record of prescriptions recorded in community pharmacies. Short courses of rifampicin have no other indications and these are for chemoprophylaxis [14]. By contrast, single dose courses of ciprofloxacin are used for the treatment of gonorrhoea. However, less than 10 isolates of *Neisseria meningitidis* were identified from general practice in the district each year. [D Bullock, personal communication]. Patients with meningococcal disease will be referred to the genito-urinary medicine service. Even if they were prescribed ciprofloxacin in practice the difference this would make to the overall results presented here is small. If significant amounts of single dose ciprofloxacin were being used for indications other than chemoprophylaxis, then the ratio of PACT prescriptions to those recorded by the CCDC would be for ciprofloxacin than for rifampicin. As this was not the case, it is likely that the majority of courses were for chemoprophylaxis of meningococcal disease.

The data provided by general practices may have underestimated the prevalence of chemoprophylaxis. Prescriptions may not be recorded in the records, may not be recorded in a computer system or may not be retrieved during a search. This may be the case if a patient is attended by an out of hours service. Although these prescriptions are recorded in the practice the patient is registered with on PACT, the correspondence between the practice and the out of hours service may not find its way into the main patient record or may not be recorded. It is therefore likely that the data from the GP questionnaires underestimated the prevalence of prescribing.

Hospital prescribing was in line with the recommendations of the CCDC. GPs had prescribed twice as many courses of prophylaxis (from PACT data) as the CCDC. Additional prescribing must be for one of the following reasons:

- for true close contacts who have been missed by the CCDC, which, although
- for contacts of cases in other districts. In this study only 5% of recommendations were from other districts. It is likely that the reverse is also true, so this could account for a proportion of additional prescriptions.
- for people whose degree of contact does not warrant prophylaxis
- for contacts of patients who do not have meningococcal disease (e.g. contacts perceived by the public to have meningococcal disease, but in fact have not). In this situation the GP would be required to prescribe prophylaxis solely on the basis of patient request. GPs would consult the Public Health Department in this situation, which would provide recognition of cases of meningitis or reassurance that it was not meningitis.

It is impossible from the data available to further assess the nature of the reasons for over-prescribing but it is probable that it results from a combination of the suggested possibilities.

A UK study in 1995 [14] showed over-prescribing by a factor of three, although the PACT data and did not include hospital data or obtain further information on patients. This study may overestimate prescribing and almost certainly include some appropriate prescriptions. An audit from Denmark [17] also found that unnecessary prophylaxis was prescribed. In the Danish study was 0.9 person/case (in our study 2.4 person/case). In our study we interviewed an adult associated with each case and also identified the case. Our methodology did not allow this comparison to be performed. Contacts were likely to underestimate the level of additional prescribing because they do not know about prescriptions supplied outside the immediate household.

Over-prescribing varied by local authority area and was significantly higher in local authority areas 1 and 4 which wrote significantly more additional prescriptions. Both these areas had high levels of disease with local publicity surrounding the cases. In the other area (2) with a similarly high rate of disease levels of demand were lower. No evidence of an association between over prescribing and rates of meningococcal disease or social deprivation could be found. We speculate that high disease levels resulted in higher levels of demand for chemoprophylaxis from people with the cases, but not true close contacts. This is supported by a lower level of demand in other high disease rate area. This area (2) has no discrete communities in which disease have been identified and the public did not react in the same way as in more rural, areas. This over-prescribing is likely to be patient driven, as contacts are not always inappropriate contacts to treat.

On almost 50% of occasions that GPs were asked to prescribe, there is no record in practice that the prescription was written. There are a number of possible reasons for this. Firstly, prescriptions may not have been written, leaving some people at increased risk of disease. This is supported by the fact that 10 out of 80 prescriptions according to PACT data than the number of courses recommended. Secondly, prescriptions have been issued but no record kept which has implications for clinical governance. If attended by the out of hours service, the prescription may have been written but not transferred to the main general practice record or not entered on the system. Even if the GP has written a prescription the contact may still not receive prophylaxis. It is possible that some contacts did not come forward to request it or did not present it to a pharmacy. The prescription charge may have acted as a barrier. Contacts may have found that rifampicin was not immediately available and consequently did not return to collect their antibiotics. Further work is needed to determine the extent to which these barriers may operate.

Conclusions

Receipt of chemoprophylaxis is affected by a series of patient, doctor and

Additional prescribing occurs at all stages in the process. High publicity a demand, although a significant number of contacts appear never to receive treatment. Our study also raises issues about the quality of documentation and subsequent supply of antibiotics to contacts. Further research is required to explore reasons why some contacts seem not to receive prophylaxis.

A number of steps could be taken to ensure that use of chemoprophylaxis is possible. Face to face interviews with key informants by public health practitioners could help prevent overprescribing. Further research is necessary to clarify this issue. It could also be avoided by ensuring that general practitioners are aware of the evidence and advice to help make decisions about prophylaxis. When publicity occurs in the media to ensure that reliable information on the level of the risk of serious infection is available to the public.