Changing patterns of malaria in south-east Scotland: implications for practitioner awareness and prophylactic advice

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Summary: The medical records of all 229 patients with malaria admitted to the Edinburgh City Hospital between 1969 and 1988 were studied retrospectively. A total of 137 were from Africa, 44 from the Indian subcontinent, 19 from the Far East, 18 from New Guinea, 5 from the Middle East and 3 from South America. The number of yearly admissions rose markedly after 1983, mainly due to an increase in *Plasmodium falciparum* cases. Ninety-four cases (15 with severe parasitaemia) mainly from Kenya and Nigeria were due to *P. falciparum* infection and 99 to *P. vivax*. There were no deaths. A seasonal distribution of onset of fever in patients with *P. vivax* infections originating from the Indian subcontinent showed that most patients presented during the summer.

Prophylaxis had generally been irregular or non-existent but many compliant patients may have been receiving an inadequate dose of chloroquine on a mg/kg body weight basis. General practitioners are likely to see at least one case of malaria every 4 years. They are encouraged to seek advice from a specialist unit whenever necessary whether before or after their patient travels abroad. Travellers, in particular to Kenya and Nigeria, and Asian immigrants to the UK returning on holiday to their country of origin should be strongly advised to take regular prophylaxis including on return to the UK.

Introduction

The last 20 years have witnessed a dramatic change in the incidence, species proportions, drug resistance and geographical distribution of malaria worldwide.^{1,2} In 1970 only 49 cases of *Plasmodium falciparum* infection were notified in the UK rising to 1,028 in 1988 with the percentage of UK cases seen at the Hospital for Tropical Diseases, London (LHTD) falling from 65% in 1970 to 30% in 1988 (Chiodini, personal communication). Therefore while the number of cases at LHTD has risen ten-fold, the number of cases of *P. falciparum* seen elsewhere in the UK has risen twenty-fold. Over the ten years 1977–86 the annual incidence of malaria in the UK increased by 51% from 1,529 to 2,309 cases and the proportion of cases due to *P. falciparum* increased from one fifth to one third.³ Chloroquine resistance in *P. falciparum* malaria has become widespread^{4,5} and it may be increasing in virulence.^{6,7}

The only previous study of malaria in Edinburgh was confined to children.⁸ We conducted a retrospective survey of malaria presenting in Edinburgh

City Hospital from 1969 to 1988 to determine the extent to which national trends are being reflected in a Scottish Regional Centre. We also examined the monthly incidence of *P. vivax* malaria to determine whether a seasonal pattern of *P. vivax* malaria reported elsewhere in the UK^{9,10} is observed in Edinburgh and the possibility that breakthrough malaria in some patients may be associated with inadequate doses of chloroquine prophylaxis on a mg/kg body weight basis.¹¹

Methods

Admissions in Edinburgh with malaria for the years 1969–1988 inclusive were identified from Scottish hospital inpatient statistics and City Hospital case notes. The City Hospital Tropical Medicine Unit (1961–1972) and Infectious Diseases Unit (1972 onwards) was the site of referral for patients with malaria from south-east Scotland throughout the period under study.

Results

Of 229 admissions the male to female ratio of 164:65 (i.e. 3:1) remained constant throughout.

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The mean age was 29 years (range 2–80). The number of cases per year rose over the period studied from a mean of 10.6 patients per year in the first 5 years (53 admissions) to 15.2 patients per year in the last 5 years (76 admissions). The most marked increase has been since 1983 and was largely due to *P. falciparum* malaria.

Species

There were 99 cases due to *Plasmodium vivax*, 94 to *P. falciparum*, 6 to *P. ovale*, 5 to *P. malariae* and 3 to mixed infections. Parasite speciation was not performed in 22 patients. From 1985 onwards parasites were identified in all cases and comprised only *falciparum* or *vivax* species.

Prophylaxis

Most prophylaxis was inadequate, the most common failure being irregular prophylaxis after return to the UK. In only 5 patients with *falciparum* infection were both body weights and chloroquine dose recorded and all of these received a dose of less than 5 mg/kg base weekly.¹² Two were children receiving 2.2 and 2.3 mg/kg and 3 adults were using 3.0, 3.6 and 4.3 mg/kg base weekly.

Morbidity, mortality and clinical findings

There were no deaths. Fifteen cases had severe parasitaemia (>10%) and 5 of these had renal failure, 2 cerebral malaria and 1 required a blood transfusion. One patient had haemoptysis due to thrombocytopenia and required platelet transfusions. Thrombocytopenia was very common, both in *P. falciparum* and *P. vivax* infections. Thirty-four patients (15%) had a concurrent tropically acquired illness.

Continent and country of origin

A total of 137 infections (60%) were acquired in Africa. Forty-four cases were from the Indian subcontinent, 19 from the Far East, 18 from New Guinea, 5 from the Middle East and 3 from South America. The country of origin was not recorded in 3 case notes.

Patients returning from Africa

Of the 137 infections originating from Africa, two-thirds (66%) were due to *P. falciparum* (91 cases), 17% to *P. vivax* (24 cases), 3% each to *P. ovale* and *P. malariae* and in 10% (13 cases) no parasites were identified. Of these, 63% were Britons returning from travel or work in Africa and most of the remainder were African postgraduate students.

Four countries (Nigeria, Kenya, Ghana and Tanzania) accounted for 65% of cases. One third (6/15) of all cases presenting to our Unit with severe parasitaemia or complicated malaria originated from Kenya and Nigeria. Most complications related to thrombocytopenia with subsequent bleeding. Two patients (one of whom required exchange transfusion for 30% parasitaemia) from Nigeria had cerebral malaria and renal failure requiring dialysis and 1 from Kenya was dialysed for blackwater fever.

Patients returning from the Indian subcontinent

Forty-four patients presented from the Indian subcontinent, the annual incidence increasing markedly over the first 15 years and falling over the last 5. Most (31) patients were settled immigrants returning from holidays in their country of origin. Twenty-two had taken no prophylaxis and 8 were poor compliers. Nine were visitors from the Indian subcontinent (either holidaymakers or new immigrants) none of whom had received prophylaxis. Four were Britons, 3 of whom were poor compliers. Of the 44 cases, 93% were due to *P. vivax*, 28% presenting within 1 month of return and 40% within 3 months, but 60% presented from 4 until 12 months or longer after return.

Seasonal distribution in P. vivax patients

Most patients presented between the months of May and September. In our patients, month of return and month of illness rose to a peak and fell during the year in concert for the whole group. However, patients who had travelled to the Indian subcontinent and returned to the UK during the winter months tended to develop malaria during the following summer.

Discussion

The populations of Lothian region and particularly of Edinburgh city have been gradually declining over the past 20 years and are currently 741,199 and 433,480, respectively, whilst the Borders region has stayed relatively static at 102,700.¹³ Concomitantly, however, the number of foreign residents has been rising and in addition many temporary foreign residents include students and visitors to the Edinburgh Festival. The annual incidence of malaria, however, is only 1.7 per 10,000 for Borders and Lothian regions compared with 3.3 for the whole of the UK. This discrepancy is probably due in part to the magnetic role of LHTD which attracts a disproportionately large number of cases due to its location near the 3 London airports. Our study indicates that the average general practi-

tioner in our area will see 1 case of malaria every 3–4 years with a 50% likelihood that this case will be due to potentially life-threatening *P. falciparum*.

The increased incidence of infection which we found in men, young adults and children has been previously documented³ and may be due to more adventurous travel in young adult males who may comply less well with prophylaxis (as also may children).

The proportion of *falciparum* cases increased from less than one third in 1969–73 to greater than half in 1984–88 in contrast to a survey in Leicester where, from 1983–88 only one third had *falciparum* infections.¹⁴ The Edinburgh results, however, concur with those for the UK as a whole in which the incidence of *P. falciparum* malaria is now greater than *P. vivax*.¹⁵

The absence of mortality in our cases compares with an overall UK average of 1%¹⁵ and our complication and severe parasitaemia rate of 14% compares to about 75% in Leicester.¹⁴ This indicates that where general practitioners refer patients early to a Regional Infectious Diseases Unit mortality is low even when the overall annual caseload of malaria for that Unit is relatively low.

A seasonal distribution of *P. vivax* malaria has been demonstrated in 3 different UK centres.^{9,10,14} Walker's large study from Glasgow demonstrated a marked discrepancy between month of return to the UK and month of illness which, when compared to the seasonal distribution of travel to Bombay and the rest of India, strongly suggested that factors other than increased transmission during the summer months are involved.¹⁰ Is a higher ambient temperature or humidity mediated via humoral factors to the dormant hepatic hypnozoite needed to stimulate reactivation?⁹ Our own results suggest that this may only be the case for patients returning from the Indian subcontinent. Subspecies differences in the behaviour of *P. vivax* parasites are known to occur.¹⁶ A larger study is needed to confirm our observations that seasonal reactivation of *vivax* malaria only occurs in patients from the Indian subcontinent.

Prophylaxis

Prophylaxis is still taken irregularly or not at all, the most common failure being failure to continue prophylaxis on return to the UK. Failure to seek any prophylaxis is particularly common among Asians resident in the UK who are returning to the Indian subcontinent on holiday. Many of these people believe themselves still to be immune. In a study of malaria in the UK in 1982, one third (312) of UK patients presenting with *P. vivax* malaria

were non-white British residents and their children visiting abroad.¹⁷

Clear guidelines for malarial prophylaxis have been issued which recommend chloroquine, where appropriate, to be used in a dose of 300 mg base weekly for adults and children over 12 years and weighing 40 kg.¹⁸ However, while the World Health Organisation advises 300 mg weekly for adults weighing 50–70 kg¹⁹ and 5 mg/kg for children under 40 kg,²⁰ wide interindividual variation in blood concentrations are known to occur in adults on the same dose, and there is only a weak correlation between whole blood concentration and weight in those on regular long-term chloroquine prophylaxis.²¹ Corachan and Gascon reported a retrospective study of 106 patients in 1988 presenting with malaria in Barcelona.¹¹ Of these, 11 had *P. falciparum* malaria and had taken prophylaxis regularly before, during and after their overseas trip. Nine of those who weighed more than 75 kg had used 300 mg chloroquine weekly. Our own survey of this aspect was hampered by inadequate recording of body weight and dosage of chloroquine prophylaxis but the limited data available support the contention that many adults using chloroquine may have taken an inadequate dose. In an era in which chloroquine resistance is a major problem, clear data on the influence of body weight on chloroquine pharmacokinetics are needed in order to clarify a truly rational approach to maximize the effectiveness of available chemoprophylactic regimes.

Conclusions

The incidence of malaria and of antimalarial drug resistance is increasing worldwide; with greater ease of intercontinental travel, these problems are reflected in a Scottish regional centre. The risks of acquiring a potentially fatal plasmodium infection should be more widely publicized. Prophylaxis is still often taken irregularly or not at all and the importance of this should be emphasized to travellers, in particular to travellers to popular holiday areas such as Kenya and to Asians resident in the UK who are returning on holiday to their country of origin. Particular reference should be paid to the importance of continuing prophylaxis on return to the UK. However, many compliant patients may have been receiving an inadequate dose of chloroquine on a mg/kg basis. General practitioners should not hesitate to contact the regional specialist unit whenever the diagnosis is considered or whenever they have any doubts concerning antimalarial prophylaxis.

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