MIXED BAG

Return of chloroquine antimalarial efficacy in Malawi

Malaria continues to be a leading killer of the world's poorest children. Six decades after chloroquine was widely used in a global programme to eradicate malaria, *Plasmodium falciparum* continues to plague sub-Saharan Africa.

In 1993 Malawi was the first country in Africa to replace chloroquine with the combination of sulfadoxine and pyrimethamine for the treatment of malaria. At the time, the clinical efficacy of chloroquine was less than 50%. Since then, sulfadoxine-pyrimethamine has been the only available treatment for uncomplicated malaria in government health facilities.

Chloroquine resistance first emerged in South-east Asia and South America in the late 1950s and by the late 1970s it had made its way across to Africa, where it contributed to increased transmission of malaria and deaths.

According to the authors of this paper in the *New England Journal of Medicine* it has been suggested that reducing the use of chloroquine could result in the re-emergence of chloroquine-sensitive *P. falciparum*, allowing this safe and affordable drug to be reintroduced. Although studies in Asia and West Africa have shown that the growth of the parasite *in vitro* was inhibited after chloroquine use was reduced, a return to clinical efficacy has not yet been demonstrated.

Resistance in chloroquine-resistant falciparum malaria is associated with a point mutation in the *P. falciparum* chloroquine-resistance transporter gene. The authors of this paper previously measured the prevalence of this molecular marker in Blantyre, Malawi, before, during and after the withdrawal of chloroquine from use. From 1992 to 2000, the prevalence of the marker gradually decreased, disappearing completely by 2001. However, in neighbouring countries, where chloroquine continued to be used, more than 90% of *P. falciparum* infections were caused by chloroquine-resistant parasites.

A randomised clinical trial involving 210 children with uncomplicated *P. falciparum* malaria in Blantyre was carried out. The children were treated with either chloroquine or sulfadoxine-pyrimethamine and followed up for 28 days to assess how clinically effective the drug was. They found that treatment failure occurred in 1 of 80 participants assigned to chloroquine, compared with 71 of 87 participants assigned to sulfadoxine-pyrimethamine.

It would appear that chloroquine, a safe and inexpensive treatment for malaria, is once again highly effective in Malawi, 12 years after it was withdrawn from use because of high rates of treatment failure. What is more, infection and fever cleared more quickly in the chloroquine group than in the sulfadoxine-pyrimethamine group. Chloroquine was not entirely absent in Malawi. The drug was available over the counter and used mainly by travellers as prophylaxis and by adult Malawians to self-treat symptoms of malaria. So complete elimination of chloroquine use appears not to be necessary to allow the survival advantage enjoyed by chloroquine-resistant parasites to be lost when the drug is largely absent.

The authors suggest that the introduction of combination antimalarial therapies elsewhere in Africa and the reduction in chloroquine use may result in a resurgence of chloroquine-susceptible falciparum malaria throughout the region. They recommend that chloroquine should be completely withdrawn from use where its clinical efficacy is already impaired. To prevent the re-emergence of resistance, chloroquine should be reintroduced in combination with other drugs.

Laufer M, *et al*. *NEJM* 2006; 355: 1959-1966.

Screening for chronic kidney disease

Current guidelines in most parts of the world advocate screening for chronic kidney disease only in those with hypertension or diabetes. However, more widespread screening of the general population has been proposed; in the developed world everyone who goes to the GP. However, these recommendations are based on consensus procedures and the different screening strategies have not been compared for their ability to detect chronic kidney disease. Another assumption is that anyone with advanced renal disease (stages 3 - 5) will require kidney replacement, but the natural course of the disease in those with newly detected renal insufficiency is not well described.

The authors of this paper in the *British Medical Journal* set out to find an effective screening strategy for detecting patients with chronic kidney disease and to describe the natural course of the disease. The study took place in Norway, using participants in a large-scale general health survey between 1995 and 1997. Participants were 65 604 people aged over 20, who comprised slightly more than 70% of the adults aged over 20 in that particular county of Norway. They looked at end-stage renal disease (ESRD) and cardiovascular mortality.

They found that 3 069 people out of the 65 604 had chronic kidney disease (estimated glomerular filtration rate less than 60 ml/min/1.73 m^2). This meant that to find one case of chronic kidney disease they would need to screen 20.6 people. Restricting screening to those aged over 55 or with hypertension or diabetes would identify 93% of patients with

chronic kidney disease and need only 8.7 people screened to identify one case. Screening only people with known hypertension or diabetes detected 44.2% of all cases and needed 6 people screened to identify one case. During the 8 years of follow-up in this study only 38 of the 3 069 people with chronic kidney disease progressed to ESRD. The risk of progression was particularly low in those without hypertension or diabetes, women and those aged at least 70 with a glomerular filtration rate of 45 - 49 ml/min/1.73 m^2. However, in contrast, there was high cardiovascular mortality: 3.5, 7.4 and 10.1 deaths per 100 person-years among people with a glomerular filtration rate of 45 - 49, 30 - 44 and less than 30 ml/min/1.73 m^2 respectively.

The authors concluded that screening people with hypertension, diabetes and age over 55 was the most effective strategy to detect patients with chronic kidney disease. However, the risk of end-stage renal failure among those detected was low.

Hallan SI, *et al. BMJ* 2006; 333: 1047-1050.

The human face of epilepsy

There are 40 million people worldwide who suffer from epilepsy. Around 80% of them live in the developing world where resources for care are extremely limited. There are qualitative and anecdotal reports that people in Africa who suffer from epilepsy are disadvantaged socially and economically, but there are few quantitative data available.

The authors of this recent study in the *Lancet Neurology* did a cross-sectional study of people with epilepsy who were matched with people with a non-stigmatised chronic medical condition and living in Zambia. Participants were verbally questioned to determine their demographic characteristics, education, employment status, housing and environmental quality, food security, health care use, personal safety and perceived stigma.

They found that people with epilepsy were stigmatised, less likely to be employed and, if employed, in poor employment and had less education. Their housing was likely to be of poor quality; they had little access to water and were unlikely to have electricity in their home. They also had greater food insecurity than the control group. During pregnancy, women with epilepsy were more likely to deliver at home than in a hospital or clinic. The personal safety of people with epilepsy was also a problem. Rape rates among women with epilepsy were 20% compared with 3% in the control group.

The conclusion is that epilepsy places yet another burden on lives already far from ideal.

Birbeck G, *et al. Lancet Neurology* 2006; DOI:10.1016/S1474-4422(06)70629-9a.

Bridget Farham