Under-utilized approaches to control anaemia in developing countries
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SUMMARY

Anaemia remains a major public health problem despite the knowledge that various interventions could reduce its impact on morbidity and mortality. It is of the utmost importance for the future that interventions are delivered and used to the maximum of their potential, and that new and innovative interventions are developed and their place assessed for the control of anaemia.

Chapter 1: Introduction

Background information is provided which describes the extent of the problem of anaemia, its causes, existing interventions and potential new interventions. Information is also provided on the study site and population in Malawi where the research presented in this thesis was conducted.

Chapter 2: Reducing childhood mortality in poor countries. Anaemia prevention for reducing of mortality in mothers and children

The relationship of anaemia as a risk factor for child and maternal mortality is described. Maternal case fatality rates, mainly from hospital studies vary from <1% to >50%. These large differences in risk were related primarily to differences in available obstetric care for women living in areas with inadequate antenatal and delivery care facilities. The relative risk of mortality associated with moderate anaemia (haemoglobin 40-80 g/l) was 1.35 (95% CI : 0.92-2.00), and for severe anaemia (<47 g/l) was 3.51 (95% CI : 2.05-6.00). Nutrition related anaemia mortality is likely to be greater than malarial related anaemia mortality. With good antenatal and obstetric care most anaemia related deaths are preventable, and policies to reduce anaemia prevalence should not be divorced from efforts to provide adequate antenatal and delivery facilities for women in developing countries. In children although mortality was increased with anaemia (<50 g/l), the evidence for increased risk with less severe anaemia was inconclusive. A survival analysis of Malawian infants indicated that if haemoglobin decreased by 10 g/l after 6 months of age, the risk of dying subsequently before 12 months of age increased 1.72 times. Evidence from a number of studies suggests that mortality due to severe malarial anaemia in children is greater than that due to iron deficiency anaemia. Primary prevention of nutritional and malarial anaemia in young children could lead to reductions in child mortality.

Chapter 3: Haematological profiles of the people of rural southern Malawi: an overview

An overview from four studies of anaemia in children, adolescents, pregnant women and adults is presented for people living in southern Malawi. Anaemia is universally present in all age groups with the highest prevalence in infants (100%) and adolescent primigravidae (93.8%). Nutritional deficits of iron, folate and vitamin A and B_{12} are major contributory factors. Chronic malarial haemolysis significantly contributes to anaemia. Anaemia was significantly
more common in male children with glucose-6-phosphate dehydrogenase (G6PD) deficiency ($p < 0.002$). This enzymopathy occurred in 23.5% of male and 30% of female infants. Neonatal jaundice was associated with G6PD deficiency.

The prevalence of $-\alpha^{3.7/\alpha}$ thalassaemia genotype was estimated at 41.0% and $-\alpha^{3.7/-\alpha^{3.7}}$ at 8.7%. Haemoglobin AS was present in 18.1% of infants and haemoglobin SS in 2.5%. *P. falciparum* prevalence was significantly higher in infants with HbAS compared to HbAA (21.4% versus 6.7%, $p < 0.001$) which suggests that an increased risk of early onset moderate parasitaemias in young infants stimulates the development of active immunity protecting older heterozygotes from severe malaria infection. Innovative community approaches are required to break the cycle of ill health which anaemia holds on this community. Intervention in adolescent girls are of particular importance as they can break the cycle in both pregnant women and their infants.

**Chapter 4: The effect on haemoglobin of the use of iron cooking pots in rural Malawian households in an area with high malaria prevalence: a randomised trial**

Innovative low cost sustainable strategies are required to reduce the high prevalence of iron deficiency anaemia in developing countries.

The aim of this study was to assess the effects of cooking in iron or aluminium cooking pots in Malawian households in an area with a high malaria prevalence. To achieve this we undertook a community-based randomised controlled intervention trial. Analysis was by intention to treat and consistency of use. The primary outcomes were change in haemoglobin and iron status.

The study population comprised 164 participants eating from aluminium cooking pots and 158 from iron cooking pots. The mean haemoglobin change was significantly increased after 6 weeks in adults who consistently ate from an iron cooking pot (plus 3.6 g/l compared to minus 3.2 g/l, mean difference between groups 6.8 g/l, 95% CI +0.86, +12.74). In children no significant haemoglobin change was observed in consistent pot users, although they showed a significant reduction in iron deficiency (iron 8.6 µg ZP/g Hb and aluminium 10.8 µg ZP/g Hb, mean difference 2.2 µg ZP/g Hb, 95% CI +1.08, +3.32).

We concluded that rural Malawian adults in a high malaria transmission area who consistently consume food prepared in iron cooking pots show a significant rise in haemoglobin after 6 weeks use. Children showed a reduction in iron deficiency, but no significant improvement in haemoglobin, possibly because of their high malaria parasite prevalence. Household provision of iron cooking pots in developing countries could provide an innovative way to prevent iron deficiency and anaemia in malarious areas where regular iron supplementation is problematic.
Chapter 5: Acceptability of the use of iron cooking pots to reduce anaemia in developing countries

The aim of this study was to evaluate acceptability, compliance and attitude towards the use of iron pots compared to aluminium pots, for cooking in a community which traditionally did not use iron pots. To achieve this an randomised controlled trial was conducted in two rural Malawian villages. The study population comprised 52 households who received an iron cooking pot and 61 who received an aluminium cooking pot.

Pot characteristics were assessed by a questionnaire after 3, 6, 11 and 20 weeks of use. Within households using iron pots there was a significant decrease in acceptability score with usage, from an initial value of 13.7 to 11.4 (range 1-20), (p = 0.01). Answers to questions concerning cooking characteristics showed that after 3 weeks use the aluminium pot scored better, whereas after 20 weeks fewer answers differed between the iron and aluminium pot groups. Almost a third of the households planned to continue using iron pots daily after 20 weeks, although they had ready access to their former aluminium pot. The presence of a group of consistent pot users suggests that if households were convinced about daily use, then they were likely to maintain consistent use. Some householders considered that iron pots required less firewood for cooking than aluminium pots. The main problems related to lower acceptability were rusting and pot weight. About 25% of problems with iron pots were unrelated to their cast iron characteristics. Overall 23.4% of the households indicated they would buy an iron pot.

We concluded that the low acceptability of iron pots for cooking could limit their value as an intervention to control iron deficiency anaemia. Design modifications and better instructions on pot use should improve acceptability. The study highlights the need to assess acceptability of interventions in order to facilitate their adoption in traditional communities.

Chapter 6: Food prepared in iron cooking pots as an intervention for reducing iron deficiency anaemia in developing countries: a systematic review

The aim of this analysis was to complete a systematic review of the effect of preparing food cooked in iron pots on haemoglobin concentrations and to assess compliance with pot use. For this the following sources were searched: the Cochrane Database of Systemic Reviews, the Database of Abstracts of Reviews of Effectiveness, the Cochrane Controlled trials Register, the Cochrane Methodology Register, the Health Technology Assessment Database, the NHS Economic Evaluation Database (Cochrane Library, Issue 3, 2002), Medline (1966 to May 2002) and EMBASE (1988 to May 2002). Reference lists of published trials were examined for other potentially relevant trials and authors of selected trials were contacted to obtain information about ongoing or unpublished trials. Selection criteria included randomized trials which compared the effect of food cooked in cast iron pots with food cooked in non-cast iron pots consumed by participants of a minimum age of four months.
One reviewer applied inclusion criteria to potentially relevant trials. Two reviewers assessed trial quality and extracted data.

Three trials were eligible for inclusion in the review. There is some evidence from these studies that eating food prepared in iron pots increases the haemoglobin concentration of anaemic/iron deficient individuals. This effect seems to be modified by compliance, users age, and the presence of malaria and hookworm. Compliance with pot use varies considerably between countries depending on several factors, including: size of the cooking pot, targeted user groups, whether the pot is used as an extra or replacement pot, and familiarity with cast iron pots.

It is concluded that the introduction of iron pots or improving their use in communities in developing countries for the preparation of food maybe a promising innovative intervention for reducing iron deficiency and iron deficiency anaemia. Further research is required to monitor the use and effectiveness of this intervention.

Chapter 7: Iron contents of Malawian foods when prepared in iron cooking pots

The aim of this study was to determine the iron content of Malawian foods prepared in iron pots and to examine the effects of continuous cooking time and added oil on the iron content of the food prepared. Foods prepared, which included a staple (Nsima), relish vegetables and beans, had an increased iron content when prepared in an iron compared to a glass pot. For these three foods iron content per gram increased by 3.15 μg, 35.8 μg and 147.32 μg respectively. Continuous use of the iron pot for cooking could have a positive effect on the amount of iron added to the food as, for the three foods iron content increased respectively by a further 2.9 μg iron/gram, 7.6 μg iron/gm and 20.1 μg iron/gm. This effect needs further study. Food pH was significantly negatively correlated with food iron content. The use of oil reduced iron added to stir-fried vegetables by 52.37 μg/gm and increased iron added to Nsima by 1.2 μg/gm. Malawian foods increased their iron content when cooked in iron pots. This method of food preparation potentially provides a low-cost sustainable means of improving the iron intakes of families and communities where this traditional method of food preparation is acceptable.

Chapter 8: Analysis of the effects of malaria chemoprophylaxis in children on haematological responses, morbidity and mortality

This paper reviews the evidence for beneficial effects of malaria chemoprophylaxis on haematological responses, morbidity, mortality, health service utilization and rebound immunity in children. As anaemia may play an important role in childhood mortality, it is important to assess evidence from controlled trials of the potential of malaria chemoprophylaxis to reduce childhood anaemia. An analysis of trials found good evidence that malaria chemoprophylaxis improves mean haemoglobin levels and reduces severe anaemia, clinical malaria attacks, parasite and spleen rates. Significant reductions in outpatient attendance
and hospital admissions have been achieved, and substantial evidence from Gambian studies shows reductions in mortality. Chemoprophylaxis in children does not seem to produce any sustained impairment of immunity to malaria, although rebound effects may be greater in children who receive prophylaxis during infancy. Short periods of targeted prophylaxis are likely to be preferable to continuous drug administration. Evidence of the protective efficacy of malaria chemoprophylaxis in children shows that this strategy could be considered within integrated health programmes for specific time periods. Intermittent routine combination therapy early in childhood may be appropriate for those living under holoendemic conditions. Large-scale studies over a number of years are needed to address this issue and the impact of this approach on health service utilization, mortality, and the emergence of drug-resistant parasites.

Chapter 9: Discussion

This chapter presents an overview of the analysis and research undertaken and identifies priority areas for future work.