Under-utilized approaches to control anaemia in developing countries

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Citation for published version (APA):
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**

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Source of support: Bush Hospital Foundation

Running head: Use of iron pots in malarious areas
ABSTRACT

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

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

Findings
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).

Interpretation
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.
INTRODUCTION

An estimated 3.6 billion people are iron deficient and of these 2 billion are anaemic (WHO 1997). The most vulnerable are women of reproductive age and children under 5 years in developing countries (WHO 1997). The two main interventions, aimed at reducing iron deficiency, supplementation and iron fortification have had limited success in solving this problem and innovative approaches are required to improve strategies for the control of iron deficiency anaemia. There is a growing interest in the use of iron pots as some early studies showed their value and demonstrated good bioavailability (Brittin & Nossaman 1986; Martinez & Vannucchi 1986). Despite their potential, only two studies have been conducted on humans to investigate the effect of cooking with iron pots on haemoglobin (Borigato & Martinez 1998; Adish et al. 1999). Both were conducted on children and in areas with low malaria prevalence. We report the results of a randomised controlled trial that assessed the effect on haemoglobin and iron status of the introduction of iron cooking pots into rural Malawian households living in a highly malarious area (Verhoeff et al. 1999; Slutsker et al. 1994).

METHODS

The study was undertaken from May to November 2000 in the Shire Valley in southern Malawi. Malaria transmission occurs year round with the highest intensity from January to June. Small-scale agriculture of maize, sorghum, cotton and sugar-cane is the primary source of food and income.

Two villages (Meja and Tsamba) were selected because of their accessibility by road, the willingness of the population to participate and their size. A census showed the population of the two villages was 753 (277 in Meja and 476 in Tsamba). The mean age was 21.1 years, the male/female ratio 0.97 and 63% were illiterate. The objectives of the study were explained to the villagers and all residents were invited to participate. Inclusion criteria were (parental) consent, age one year or older, a finger prick haemoglobin ≥ 70 g/l and residence in Meja or Tsamba. Exclusion criteria were individuals with haemoglobin levels <70 g/l or pregnant women with haemoglobin <80 g/l on enrolment or at any time during follow-up, or individuals who used iron supplements and/or received blood transfusions during the follow-up period. Excluded individuals who were anaemic were treated with a therapeutic course of iron or if necessary referred to hospital.

Village households were randomly assigned to receive either one iron or one aluminium cooking pot per household and were followed for a period of 20 weeks. Pots were allocated using a random number selected by drawing lots. The sample size was calculated assuming that iron pot users would have an increase in their haemoglobin level of 10 g/l at the 6 week follow-up. This assumption was based on a previous study by Adish et al (1999). A sample size of 41 households per study arm with an average of 4 individuals per household would
be able to detect this difference with 95% confidence and 80% power. From each household that volunteered to participate up to 6 individuals were selected. These included the father and mother in the nuclear family, adolescent girls and 1-11 year old children. Children less than a year of age were not selected as most were breast fed and they were likely to receive little food prepared from the cooking pots. The youngest children in the household were selected in preference to older children and adolescent girls in preference to children.

The aluminium pots were 6-litre in volume (Near East Ltd, Blantyre, Malawi), with a flat base, two insulated handles and a lid with an insulated handle. The cast iron pots had a 10-litre volume (Falkirk size 4, Zimcast, Zimbabwe) and weighed 12 kg. They had a round base with three legs for standing, two side handles and a lid with a handle which were not insulated. Participants were asked to use these pots for the preparation of their daily food. No comparative information on pots was disclosed. All families were briefed on the importance of compliance.

Baseline socio-demographic variables between the groups were compared. Haemoglobin levels were measured with a Haemocue® haemoglobin photometer (HemoCue Inc, CA 92691, United States) on enrolment and after 6 and 20 weeks follow-up. Blood zinc protoporphyrin (ZP) was measured in a random sample of participants on enrolment and at 20 weeks follow-up as a screening tool for iron deficiency (Labbé et al 1999). ZP was measured in unwashed blood samples using a zinc protoporphyrin hematofluorometer model 206 (AVIV Biomedical Inc, New Jersey 08701, United States) using normal cover slip slides (Chimsuku 1994). The accurate functioning of the machines was daily ascertained by the use of standards and if needed they were recalibrated. Allocation was not concealed to the laboratory analyst.

Thick blood films stained with Field's stain were obtained after the 20-week follow-up for malaria parasites. These were read until at least 100 white blood cells had been counted with no parasites seen before a slide was considered as negative. Parasite density was expressed in geometric mean values per μl blood assuming 8000 white cells per μl. Individuals with malaria parasites were treated with pyrimethamine-sulfadoxine.

Participants were interviewed at 3, 6, 11 and 20 weeks after enrolment to ascertain the frequency, consistency and acceptability of pot use. Children who became ill were referred to the district hospital for a physical examination by a doctor. The main outcome was mean haemoglobin change at the 6 and 20 week follow-up by group. A secondary outcome was the prevalence of iron deficiency, defined as a zinc protoporphyrin >3.1 μg ZP/g Hb (Labbé et al 1999).

Statistical analysis was based on intention to treat (whether participants had received an iron or aluminium pot) and on consistency in pot use. The frequency of pot use was monitored by weekly household visits. Participants were classified as consistent pot users if they stated that they had eaten food prepared in the pot at least seven times in the week preceding the 6 and 20 week assessments. We compared the two study groups by use of the Wilcoxon two sample test, Fisher exact and χ² tests. Changes in haemoglobin between baseline and 6 and 20 weeks were compared by paired t-tests after verification of normality. All tests were two-tailed.
Ethical approval was obtained from the Ethics Committee of the Liverpool School of Tropical Medicine, Liverpool, UK and the Health and Science Research Committee of the College of Medicine in Blantyre, Malawi.

RESULTS

The village census registered 753 people of whom 502 (71.4%) were eligible for the study; 70 individuals were not present during the enrolment and 71 did not agree to participate. Of the 361 people that entered the study, 28 were excluded because of an enrolment haemoglobin $<70$ g/l; 3 developed a haemoglobin $<70$ g/l during the follow-up period of the study, and 8 used iron supplements during the study period. These eight individuals had all received aluminium pots. The final study groups comprised of 164 participants using aluminium and 158 iron cooking pots (figure 1).

At baseline there were no significant differences in the demographic characteristics among the groups except with regard to the prevalence of iron deficiency in the age group $\geq 12$ years amongst all users. The participants using the iron cooking pot had a significantly higher prevalence of iron deficiency $p<0.02$(Table 1).

A high proportion of children ($>75\%$) and adults ($>55\%$) were anaemic at baseline. Mean zinc protoporphyrin (ZP) at enrolment was significantly higher in the adult iron pot users (Table 2). There was a significantly higher loss to follow-up in the iron pot group ($p<0.01$). On the basis of intention to treat, no significant changes in mean haemoglobin were observed between the two groups during follow-up (Table 2).

For subjects older than 12 years mean haemoglobin change was significantly increased after 6 weeks in consistent iron pot users (iron $+3.6$ g/l vs aluminium $-3.2$ g/l, mean difference $+6.8$ g/l, 95% CI $+0.86$, $+12.74$, $p = 0.04$). This difference remained significant after 20 weeks (iron $+5.3$ g/l vs aluminium $-2.2$ g/l, mean difference $7.5$ g/l, 95% CI $+0.23$, $+14.77$, $p = 0.01$) (Table 2). The mean values for ZP were not significantly different between the two adult groups at enrolment, or after 20 weeks. However the ZP values within the groups increased significantly over time, ($p<0.01$).

For children younger than 12 years of age, there were no significant haemoglobin differences between groups at 6 and 20 weeks. Consistent iron pot users had lower ZP values at 20 weeks compared with consistent aluminium pot users ($8.6$ µg versus $10.8$ µg ZP/g Hb, mean difference $2.2$ µg ZP/g Hb, 95% CI $+1.08$, $+3.32$, $p = 0.03$). There was no significant increase in ZP values over time.

A high proportion of children and adults had malaria parasites in their blood films. There was no significant difference in parasite prevalence or parasite density between the two intervention groups. Children under 12 years had significantly higher parasite prevalence than older subjects ($45.3\%$ versus $17.5\%$, $p<0.001$) (Table 2).
Figure 1. Trial profile

502 people eligible

- 70 not present at enrolment
- 71 reconsidered and refused

361 entered the study

- 28 enrolment haemoglobin <70 g/litre
- 3 developed Hb <70 g/l during research study
- 8 met an exclusion factor

322 entered study

164 in households randomly assigned aluminium pots
- 123 followed up to 6 weeks
- 129 followed up to 20 weeks

158 in households randomly assigned iron pots
- 90 followed up to 6 weeks
- 102 followed up to 20 weeks
Table 1. Baseline study characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Age &lt;12 years</th>
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<th>Age ≥ 12 years</th>
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<tbody>
<tr>
<td></td>
<td>All users</td>
<td>Consistent users</td>
<td>All users</td>
<td>Consistent users</td>
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<tr>
<td></td>
<td>Aluminium</td>
<td>Iron</td>
<td>Aluminium</td>
<td>Iron</td>
</tr>
<tr>
<td>Participants, %</td>
<td>49.2 (63)</td>
<td>50.8 (65)</td>
<td>70.8 (46)</td>
<td>29.2 (19)</td>
</tr>
<tr>
<td>Mean age ± SD, years</td>
<td>6.8 ± 2.7</td>
<td>6.5 ± 2.9</td>
<td>7.1 ± 2.9</td>
<td>5.9 ± 3.1</td>
</tr>
<tr>
<td>Male/female ratio</td>
<td>1.1</td>
<td>0.9</td>
<td>1.3</td>
<td>1.7</td>
</tr>
<tr>
<td>Participants living in Meja, %</td>
<td>46 (29)</td>
<td>36.9 (24)</td>
<td>50 (23)</td>
<td>26.3 (5)</td>
</tr>
<tr>
<td>Participants literate, %</td>
<td></td>
<td></td>
<td></td>
<td>24.2 (22)</td>
</tr>
<tr>
<td>Iron deficiency prevalence, %</td>
<td>95.5 (22)</td>
<td>96.6 (29)</td>
<td>94.1 (17)</td>
<td>100 (9)</td>
</tr>
<tr>
<td>Anaemia prevalence, %†</td>
<td>86.7 (75)*</td>
<td>79.5 (78)</td>
<td>83.6 (55)</td>
<td>80.0 (20)</td>
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<td>58.2 (110)</td>
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</table>

Parenthesis: sample size
*
† n includes those treated with iron supplement for severe anaemia at baseline, but excluded from the trial
†† Anaemia age specific cut-off points from reference 12
‡ p<0.02
### Table 2. Haematological parameters

<table>
<thead>
<tr>
<th></th>
<th>Age &lt;12 years</th>
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<th>Age ≥12 years</th>
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<tbody>
<tr>
<td></td>
<td>All users</td>
<td>Consistent users</td>
<td>All users</td>
<td>Consistent users</td>
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<tr>
<td></td>
<td>Aluminium</td>
<td>Iron</td>
<td>Aluminium</td>
<td>Iron</td>
</tr>
<tr>
<td>Mean Hb at enrolment, g/litre</td>
<td>100.2 (63) 100.9 (65) 99.8 (46) 98.6 (19)</td>
<td>122.1 (101) 120.6 (93) 121.0 (67) 115.5 (14)</td>
<td>13.2 16.4 13.9 16.7</td>
<td>20.0 18.5 19.6 13.8</td>
</tr>
<tr>
<td>Mean Hb at 6 weeks, g/litre</td>
<td>100.0 (49) 99.1 (44) 99.8 (39) 100.3 (18)</td>
<td>118.3 (74) 117.8 (46) 118.1 (63) 120.9 (13)</td>
<td>13.5 13.4 14.3 15.0</td>
<td>19.4 14.0 19.7 12.1</td>
</tr>
<tr>
<td>Mean Hb change at 6 weeks, g/litre</td>
<td>0 (49) -2.1 (44) 0.6 (39) 0.4 (18)</td>
<td>-2.6 (74) -0.6 (46) -3.2 (63)* 3.6 (13)*</td>
<td>1.6 10.2 13.2 10.6</td>
<td>10.6 10.9 10.0 9.6</td>
</tr>
<tr>
<td>Mean Hb at 20 weeks, g/litre</td>
<td>105.7 (51) 104.6 (48) 105.2 (41) 105.4 (19)</td>
<td>120.3 (78) 118.5 (54) 118.3 (61) 120.8 (14)</td>
<td>15.0 14.6 15.5 15.9</td>
<td>16.4 18.1 15.7 16.1</td>
</tr>
<tr>
<td>Mean Hb change at 20 weeks, g/litre</td>
<td>4.1 (51) 3.7 (48) 4.0 (41) 6.8 (19)</td>
<td>-2.6 (78) -0.8 (54) -2.2 (61)* 5.3 (14)*</td>
<td>13.4 15.0 14.2 19.0</td>
<td>12.9 12.7 13.2 8.7</td>
</tr>
<tr>
<td>Mean ZEP at enrolment, µg/gHb</td>
<td>7.5 (22) 6.9 (29) 7.8 (17) 6.8 (9) 4.2 (63)* 5.2 (56)* 4.6 (40) 4.6 (9)</td>
<td></td>
<td>2.8 2.3 2.9 2.0</td>
<td>2.1 1.9 2.3 1.2</td>
</tr>
<tr>
<td>Mean ZEP at 20 weeks, µg/gHb</td>
<td>10.9 (71)* 9.9 (25) 10.8 (14)* 8.6 (9)*</td>
<td>8.3 (47) 7.9 (32) 8.3 (37) 8.6 (10)</td>
<td>2.7 4.3 2.9 2.1</td>
<td>2.4 2.4 2.5 2.9</td>
</tr>
<tr>
<td>Mean ZEP change, µg/gHb</td>
<td>3.8 (14) 2.3 (16) 3.8 (14)* 1.0 (6)*</td>
<td>4.3 (39) 3.2 (26) 4.2 (31) 4.2 (8)</td>
<td>2.0 2.8 2.0 1.9</td>
<td>2.3 2.2 2.4 2.5</td>
</tr>
<tr>
<td>Positive malaria film, %</td>
<td>50.8 (63) 40 (65) 56.5 (46) 57.9 (19)</td>
<td>18.8 (101) 16.1 (93) 22.4 (67) 21.4 (14)</td>
<td></td>
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</tr>
<tr>
<td>Geometric mean parasite density, per µl</td>
<td>104 (32) 109 (26) 104 (26) 98 (13)</td>
<td>108 (19) 110 (15) 110 (15) 159 (3)</td>
<td></td>
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</tr>
</tbody>
</table>

Hb: haemoglobin; ZEP: zinc erythrocyte protoporphyrin; (): sample size; [ ]: SD; *: significant difference (p < 0.05); †: mean of the difference between haemoglobin at baseline and 6 or 20 weeks for paired samples.
DISCUSSION

These results demonstrate that regular use of iron pots for cooking will improve haemoglobin concentration in adults and reduce iron deficiency in children living under malaria endemic conditions. The absence of a haemoglobin change in children could relate to their higher prevalence of malaria parasitaemia. Adults who have lower parasite prevalence would be less likely to experience malarial anaemia, whereas children will have experienced more frequent parasitaemias due to their younger age. The effects of increased iron consumption could also increase their risk of parasitaemia (Oppenheimer 2001). Significant reductions in childhood anaemia have been reported in two previous studies of consumption of food cooked in iron pots (Borigato & Martinez 1998; Adish et al. 1999). One of these was not in a malarious area and the other, in Ethiopia, was in an area of low malaria prevalence.

The absence of a significant change in haemoglobin with analysis on the basis of intention to treat suggests that consistency in eating out of iron pots is required to ensure adequate consumption of the additional available iron. With consistent use a haematological response occurred within six weeks in adults, indicating that the increased iron content from cooking is readily bioavailable.

The observation that in all (but one) of the subgroups the mean ZP value was significantly higher after 20 weeks, compared with the enrolment ZP, may relate to the time the second samples were taken which was at the beginning of the hunger season when diets were more nutritionally deficient. This could be an indication of seasonal variation in the occurrence of iron deficiency in this population.

The amount of iron intake using iron cooking pots is uncertain and estimates of 14.5 mg in adults and 7.4 mg in children have been reported (Liu et al. 1990). Appropriate preparation of food to reduce inhibitors of iron absorption would improve absorption. Food preparation and cooking methods in these households were not studied as part of this study, but this is an important area for further research.

Iron pots were not a traditional cooking utensil in this community and the significantly higher loss of follow-up in the adult iron pot group reflects their negative attitude towards use of pots. The substantial number of villagers who refused to participate probably relates to issues of acceptability. The iron pots, because of their size, were less suitable for smaller households with fewer members who may have used the pots less consistently. Villagers were also aware that many of their neighbours were using the more preferred control pots: much lighter flat based aluminium pots with insulated attached handles, and no legs. This aspect of acceptability is of great importance since it does not matter how good the efficacy of eating food cooked in iron pots is in preventing iron deficiency, if the people are not willing to use them. It is however encouraging to see that despite these selection preferences a large number of participants consistently used the iron pots over a 20 week period, although traditionally they were not used in this community.
The pots available for this study were imported from a manufacturer in Zimbabwe and the investigators had no influence on their design or weight. Their technical design could be improved and villagers made specific suggestions on preferences, which should improve acceptability. Their use and cost in communities which traditionally use iron pots should also be assessed, particularly in relation to iron overload. Concerns about long-term use should not delay assessment in appropriate at risk communities (Brabin 1999).

Enrolment in this study was targeted towards those most likely to be iron deficient which represented 71.4% of the villagers. The anaemia status of the remaining village population was unknown, but most individuals were likely to have some degree of iron deficiency. In view of this, the introduction of iron pots on a larger scale might be justifiable in communities where iron deficiency anaemia is common and where regular iron supplementation is impossible and food fortification problematic. The fact that iron pots serve the whole family for many years lowers their estimated cost. Local production would also greatly reduce cost, as importation expenses would not occur.

The current recommendations to provide iron supplementation to young children on a daily basis for long periods (Stoltzfus & Dreyfuss 1998) are unrealistic in many rural areas of poor developing countries. In view of these difficulties the use of iron cooking pots could provide an innovative strategy to control iron deficiency anaemia which has fewer logistical difficulties and lower cost than other approaches.

Acknowledgements
The Bush Hospital Foundation gave financial assistance and logistical field support was provided by SUCOMA. This study was completed in part fulfilment of a Masters in Tropical Medicine dissertation (PPG) at the University of Liverpool, School of Tropical Medicine.
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