

Reduced in-hospital mortality after improved management of children under 5 years admitted to hospital with malaria: randomised trial

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ABSTRACT

Objective To test whether strict implementation of a standardised protocol for the management of malaria and provision of a financial incentive for health workers reduced mortality.

Design Randomised controlled intervention trial.

Setting Paediatric ward at the national hospital in Guinea-Bissau. All children admitted to hospital with severe malaria received free drug kits.

Participants 951 children aged 3 months to 5 years admitted to hospital with a diagnosis of malaria randomised to normal or intervention wards.

Interventions Before the start of the study, all personnel were trained in the use of the standardised guidelines for the management of malaria, including strict follow-up procedures. Nurses and doctors were randomised to work on intervention or control wards. Personnel in the intervention ward received a small financial incentive (\$50; £25; €35/month) and their compliance with standard case management was closely monitored.

Main outcome measures In-hospital mortality and cumulative mortality within 4 weeks of hospital admission.

Results In-hospital mortality was 5% for the intervention group and 10% in the control group (risk ratio 0.48, 95% confidence interval 0.29 to 0.79). The effect may have been stronger in patients with positive malaria slides (0.36, 0.16 to 0.80). Cumulative mortality 4 weeks after discharge was also lower in the intervention group (0.61, 0.40 to 0.95).

Conclusions Supervising healthcare workers to adhere to a standardised treatment protocol was associated with greatly reduced in-hospital mortality. Financial incentives may be important for the dedication and compliance of staff members.

Trial registration Clinical Trials NCT00465777.

INTRODUCTION

Paediatric hospital wards in developing countries have failed to respond adequately to the challenge of saving severely sick children.¹ Problems have been identified in triage and emergency care, in monitoring procedures and follow-up of treatment guidelines, and in the unavailability of drugs.² These factors have

contributed to high mortality in hospitals in which health personnel are poorly paid and unmotivated. Staff training alone is not a solution, and organisational difficulties and follow-up of patients have been identified as important problems.²

Mortality on the paediatric ward of the national hospital in Guinea-Bissau is high.³ It varies between 12% and 18%, and malaria specific mortality was 12% in 2004. Drug kits for emergency management of children with severe and complicated malaria were introduced between 1 October 2000 and 16 October 2003. However, we found no clear reduction in mortality after the kits were introduced. We evaluated in a randomised trial whether a standardised protocol for the management of malaria—including the enforcement of strict procedures for monitoring of patients, availability of free drugs, and small financial incentives—could reduce mortality on the paediatric ward.

MATERIAL AND METHODS

This study was carried out on the paediatric ward of the national hospital. This is the national referral paediatric ward, but it serves also as a primary healthcare contact for children from Bissau city and suburbs.

STUDY DESIGN

We conducted a randomised controlled study of the effect of a composite intervention (improved management of malaria, free emergency drugs for malaria, and financial incentive) on the hospital mortality rate. One part of the ward was designated the intervention ward and the other was designated the reference or control ward.

Training and randomisation of staff: Medical staff and nursing staff from both the intervention ward and control ward were trained in the use of the standardised protocol for managing malaria. After training, three doctors and eight nurses were randomly selected for the intervention ward and the remaining personnel continued to work on the control ward, also staffed by three doctors and eight nurses.

Outpatient clinic: In the outpatient clinic, patients consulted with the doctor in charge as usual and the doctor decided whether or not to admit the child to

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hospital. All children who were admitted with a clinical diagnosis of malaria and who met the criteria for enrolment were invited to participate in the study. A laboratory technician collected thin and thick blood films. The films were read on the ward and the results were given to the doctor. The slides were then sent to the Bandim Health Project (BHP), where they were read again by a researcher. These readings were used in the study. Consenting children living in Bissau city and surroundings suburbs, were randomly referred to the standard ward or the intervention ward.

Inclusion criteria: We included children aged 3 months to 5 years who had clinically suspected malaria, defined as axillary temperature $>37.5^{\circ}\text{C}$ or a history of recent fever with no other obvious cause. We also required the presence of one or more of the following conditions: unable to eat, suck, or drink; more than three vomiting episodes in the previous 24 hours; unable to sit or stand; impaired consciousness; cerebral malaria (two or more convulsions over the preceding 24 hours); coma; or severe anaemia ($<50\text{ g/l}$).

Follow-up: Children were followed up at 28 days either in the hospital or by a project nurse in the community.

The intervention: People working in both wards were trained in the use of the standard protocol for management of malaria and all patients received the drug kits free of charge. See bmj.com for content of the kit.

Intervention ward: All staff working on the intervention ward rigorously followed the procedures recommended in the national standardised guidelines on the management of malaria and filled in the case record forms; the doctors evaluated the nurses' quality of work and the study supervisor systematically controlled the quality of implementation of the recommended procedures. Results of supervision were registered in the form. Nurses and doctors received a small amount of money (\$50 (£25; €35)/month for the nurses; \$160 for doctors) for the additional forms they

had to fill out. This is roughly what they would earn if they did extra part time work and is equivalent to monthly rent in Bissau for these categories of staff. Children assigned to the intervention ward were re-evaluated by the study doctor on duty until 10 pm. The nurse on duty called one of the study doctors if a seriously sick child was recruited after 10 pm.

Control ward: In the control ward, procedures were the same as usual. The national guidelines on the management of malaria were supposed to be followed. However, the lack of supervision meant that people could choose whether or not to follow the recommendations. The doctors were not obliged to evaluate the nurses' work, and the doctors themselves were not evaluated.

Main outcomes: The primary end point was in-hospital mortality. The secondary end points were cumulative mortality after discharge at day 28 and length of hospital stay.

Sample size calculation: We estimated that 474 children were needed in each arm to observe—with 80% power and a 5% significance level—a 50% reduction in mortality (from around 10% in the control group to 5% in the intervention group).

Statistical methods: We calculated risk ratios for in-hospital mortality and mortality after discharge. The length of hospital stay in days was compared for the two groups. Children who fled from the hospital were excluded in the analysis of in-hospital case fatality; however, if we obtained information from them at the 28 day follow-up they were included in the analysis of mortality after discharge. Although most of the children absconding from the ward were alive at the 28 day visit, we also conducted an analysis considering lost to follow-up at the hospital as a negative outcome. We compared the mean duration of stay on the ward and time to discharge between the two groups using Cox regression. To compare mortality for the same age group before the trial we compared mortality during the year of the trial with mortality between December 2003 and November 2004—the 12 months before the start of the trial.

Mortality in the two groups of children clinically diagnosed with malaria. Values are number/total number (%) unless stated otherwise

Variable	Group		Risk ratio (95% CI)	P value
	Intervention	Control		
Mortality at discharge	21/457 (5)	46/477 (10)	0.48 (0.29 to 0.79)	0.002
In-hospital mortality				
Patients from the BHP area	5/138 (4)	9/136 (7)	0.55 (0.19 to 1.59)	0.26
Patients living outside the BHP area	16/319 (5)	37/341 (11)	0.46 (0.26 to 0.81)	0.005
Patients positive for malaria on microscopy	8/316 (3)	23/329 (7)	0.36 (0.16 to 0.80)	0.008
Patients negative for malaria on microscopy	13/141 (9)	23/148 (16)	0.59 (0.31 to 1.12)	0.10
Mortality after 28 days				
Cumulative	29/443 (7)	50/469 (11)	0.61 (0.40 to 0.95)	0.02
Patients positive for malaria on microscopy	12/307 (4)	26/324 (8)	0.49 (0.25 to 0.95)	0.02
Patients negative for malaria on microscopy	17/136 (13)	24/145 (17)	0.76 (0.42 to 1.34)	0.33

BHP, Bandim health project.

RESULTS

The trial was conducted between 1 December 2004 and 16 January 2006. During this time, 3122 children between 3 months and 5 years were admitted to the hospital. Of these, we randomised 951 children: 460 (48%) to the intervention group and 491 (52%) to the control group. Background characteristics were similar in the two groups. See bmj.com.

In the 12 months before the trial, overall mortality at the hospital in children aged between 3 months and 5 years was 13% (413/3076). During the period of the study, 3122 children were admitted to the hospital; no information on outcome was available for 331 children who left without discharge. Of the remaining 2791 children, mortality was 13% (351/2791).

In-hospital mortality

We excluded the 17 children who fled from the analysis of in-hospital mortality. All patients included in the trial were clinically diagnosed with malaria. Of the 67 children who died in hospital, 36 had a diagnosis of malaria only, 20 had anaemia as a secondary diagnosis, six had pneumonia, four had diarrhoea, and one had convulsions. In the intervention group, 21/457 (5%) patients died and in the control group 46/477 (10%) patients died (risk ratio 0.48, 95% confidence interval 0.29 to 0.79, $P=0.002$). The effect was similar in boys (10/251 (4%) *v* 26/270 (10%); 0.41, 0.20 to 0.84) and girls (11/206 (5%) *v* 20/207 (10%); 0.55, 0.27 to 1.12). Children living in or outside the BHP study area had a similar reduction in mortality, although mortality was lower for children from the study area (table).

Mortality was significantly higher in children without confirmed malaria (12%) than in those clinically diagnosed with malaria (5%) ($P=0.04$; table). Because the inclusion criteria were based on a clinical diagnosis of malaria, we looked at the effect of intervention on the basis of whether malaria was confirmed by microscopy or not. Most of the effect of the intervention was seen in children who had malaria positive slides (0.36, 0.16 to 0.80).

Fewer patients absconded in the control group than in the intervention group (3/460 (0.7%) *v* 14/491 (2.9%); 0.23, 0.07 to 0.79). If lost to follow-up at the hospital was included as a negative outcome, the risk ratio for a negative outcome was 0.43 (0.27 to 0.67).

Length of hospital stay

The mean length of stay on the paediatric ward was shorter in the intervention group (7 days, standard deviation 3.2) than in the control group (8 days, 4.2), as the rate of discharge was 35% shorter in the intervention group (18% to 55%, $P<0.0001$).

Mortality at 28 days of follow-up

At the 28 day visit, we obtained information on 422 children in the intervention group—17 were lost to follow-up. In the control group, we obtained information on 423 children—22 were lost to follow-up. Children from the intervention group were twice as likely to come for the 28 days visit at the hospital than children from the control group (55% *v* 25%; 2.15, 1.79 to 2.59, $P<0.0001$).

When we looked at mortality after discharge alone, the intervention group had slightly higher mortality than the control group (2.01, 0.61 to 6.64, $P=0.23$). However, overall mortality at day 28 was lower in the intervention group than in controls (7% *v* 11%; 0.61, 0.40 to 0.95). The effect was strongest for the laboratory confirmed malaria cases (4% *v* 8%; 0.49, 0.25 to 0.95; table).

DISCUSSION

We found that a composite intervention—including standardised guidelines on the management of malaria, free emergency drugs for malaria, and modest financial incentives to the staff—reduced in-hospital mortality for patients with malaria by half, replicating the effect seen during the civil war between 1998-9 when these factors were present.⁴ Because all staff were trained before the study and randomised to the intervention or control wards, and all children received free emergency drugs, neither training nor free drugs alone affected the quality of management and subsequent survival.

The inclusion criteria for patients with malaria were based on clinical diagnosis, as is usually the case in low income countries. The intervention tended to be more beneficial in patients with confirmed malaria. This suggests that laboratory tests should be used when deciding whether or not to treat patients with anti-malarial drugs.

The study aimed to reduce in-hospital mortality, and the health staff could have discharged children earlier to avoid hospital deaths. Children in the intervention group had a shorter median length of hospital stay than those in the control group, yet they had lower cumulative mortality after one month. Care and attention given to the patients seems to influence how well they adhere to the advice of health personnel and increases their confidence in the health system, as twice as many children in the intervention group came to the hospital for the follow-up visit.

We cannot distinguish between the effect of supervising the implementation of guidelines and the effect of the financial incentive in reducing mortality. Both the intervention and the control wards were situated in the same building and the staff communicated with each other. There could have been contamination between the staff, from the two wards. However, this would have reduced the estimated effect.

Conclusions

We have shown that quality of care in the paediatric ward, based on impact indicators, depends not only on training and availability of drugs, but also on financial incentives. Our results are probably relevant to other national and district hospitals in developing countries that face the same conditions and problems—namely, low quality of care and staff with little motivation.¹⁵ Our results imply that consideration should be given to supporting health staff salaries, possibly on the basis of performance targets.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Health care in African hospitals is of low quality
Health personnel in African hospitals are poorly motivated

WHAT THIS STUDY ADDS

In poor countries, small financial incentives can contribute to a dramatic decrease in in-hospital mortality
Training and free drugs alone are not enough to reduce mortality

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Rapid tranquillisation in psychiatric emergency setting in India: pragmatic randomised controlled trial of intramuscular olanzapine versus intramuscular haloperidol plus promethazine

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ABSTRACT

Objective To compare the effect of intramuscular olanzapine with intramuscular haloperidol plus promethazine on rapid tranquillisation of agitated or violent adults with mental illness.

Design Pragmatic, allocation concealed, randomised controlled trial.

Setting Emergency services of a general hospital psychiatry department in Vellore, south India.

Participants 300 adults with agitated or violent behaviour as a result of mental illness; 150 randomised to intramuscular olanzapine and 150 randomised to intramuscular haloperidol plus promethazine.

Interventions Open treatment with intramuscular olanzapine or intramuscular haloperidol plus promethazine.

Main outcome measures Primary outcome was proportion of patients who were tranquil or asleep at 15 minutes and 240 minutes. Secondary outcomes were proportion of patients who were tranquil, asleep, restrained, absconding, or clinically improved at 15, 30, 60, 120, and 240 minutes; additional medical interventions and adverse effects over four hours; and compliance with oral drugs and adverse effects over two weeks.

Results Of 300 people randomised to receive either intramuscular olanzapine or intramuscular haloperidol plus promethazine, follow-up data were available for primary outcomes for 298 (99%). Both treatments resulted in similar proportions of people being tranquil or asleep at 15 minutes (olanzapine 131/150 (87%), haloperidol plus promethazine 136/150 (91%); relative risk 0.96, 95% confidence interval 0.34 to 1.47) and 240 minutes (olanzapine 144/150 (96%), haloperidol plus promethazine 145/150 (97%); relative risk 0.99, 0.95 to 1.03). However, more people given olanzapine than those given haloperidol plus promethazine required additional drugs over four hours (65/150 (43%) v 31/150

(21%); relative risk 2.07, 1.43 to 2.97). Adverse effects were uncommon with both treatments.

Conclusions Intramuscular olanzapine and intramuscular haloperidol plus promethazine were effective at rapidly tranquillising or sedating agitated or violent adults with mental illness but the combination resulted in fewer additional medical interventions within four hours of intervention.

Trial registration Clinical trials NCT00455234.

INTRODUCTION

As rates of mental illness are similar worldwide¹ it is reasonable to presume that the management of aggressive or violent behaviour is an important problem and a mental health priority in low and middle income countries, where most of the world's people live, and particularly in countries with large populations, such as India. Non-pharmacological strategies are recommended to manage violence in the emergency psychiatry setting, but rapid tranquillisation with drugs to reduce agitation may be unavoidable.²⁻⁴ Guidelines and clinical practice vary widely on the choice of drugs to manage violence in psychiatric emergencies.²⁻⁵

Two trials by the TREC Collaborative Group (tranquilização rápida-ensaio clínico [rapid tranquillisation-clinical trial]), carried out in India⁶ and Brazil,⁷ proved the efficacy and safety of combined intramuscular haloperidol and promethazine in agitated or violent people compared with intramuscular benzodiazepines. Although guidelines from the UK National Institute for Health and Clinical Excellence² commended the quality of the trials, it stopped short of recommending the routine use of combined haloperidol and promethazine in the United Kingdom owing to insufficient data, particularly on safety, and the preference for calming rather than for sedation. Intramuscular olanzapine is

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