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Effectiveness of blood transfusions and risk factors for mortality in children aged from 1 month to 4 years at the Bon Marché Hospital, Bunia, Democratic Republic of the Congo

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Abstract

OBJECTIVE To assess the effectiveness of blood transfusions in a hospital of north-eastern Democratic Republic of the Congo.

METHODS Prospective study of children admitted for severe anaemia. During admission, data were collected on clinical condition and haemoglobin levels, before and after blood transfusion. A linear regression model was built to explore factors associated with haemoglobin level after transfusion. Risk factors for mortality were explored through multivariate logistic regression.

RESULTS Haemoglobin level (Hb) was below 4 g/dl in 35% (230/657), between 4 and 6 g/dl in 58% (348/657) and at least 6 g/dl in another 6% (43/657) of the transfused children. A transfusion of 15 ml/kg of whole blood increased the Hb from 4.4 to 7.8 g/dl. Haemoglobin level after transfusion was associated with baseline Hb, quantity of delivered blood and history of previous transfusions. Overall case-fatality rate was 5.6% (37/657). Risk factors for deaths were co-morbidities such as chest infection, meningitis or malnutrition, Hb ≥ 6 g/dl, impaired consciousness or jugular venous distention on admission, and provenance.

CONCLUSION Transfusion was a frequent practice, the use of which could clearly have been rationalised. While indications should be restricted, quantities of transfused blood should be adapted to needs.

keywords blood transfusion, Democratic Republic of the Congo, paediatric, risk factors, mortality

Introduction

Severe anaemia is an important cause of morbidity and mortality in under-five children in Sub-Saharan Africa (Phiri *et al.* 2008). Severe anaemia has mainly been studied as a complication of severe malaria (Akech *et al.* 2008b), but other underlying factors are known to play a role, such as bacteremia, helminthic infections, HIV, G6PD deficiency, vitamin A and B12 deficiencies (Calis *et al.* 2008). While trends of severe anaemia over time show a decrease corresponding to the decrease in malaria incidence observed in many African settings (Pedro *et al.* 2010), similar decreasing trends are not observed in terms of case-fatality rates of children admitted with severe anaemia, which remain around 5–10% (Phiri *et al.* 2008; Pedro *et al.* 2010).

According to recommendations by the World Health Organization (WHO 2002), blood transfusion in children should be restricted to those with a haemoglobin (Hb) level below 4 g/dl, or between four and 6 g/dl with clinical features of acidosis such as dyspnoea or impaired consciousness, or hyperparasitaemia above 20%. This conservative approach to transfusion is based on the hazards related to this practice in developing countries, such as viral infection by human immunodeficiency virus (HIV), hepatitis B (HBV) or C (HCV) virus (Marcucci *et al.* 2004; Madjdpour & Spahn 2005), or bacterial contamination of the blood (Hassall *et al.* 2009). Withdrawing blood transfusion from patients with higher Hb levels has been shown to be safe in Kenya (Akech *et al.* 2008).

The quantity of blood to be transfused according to WHO is 5 ml/kg of red blood cells or 10 ml/kg of whole blood, which is said to be sufficient to relieve acute shortage of oxygen carrying capacity (WHO 2002), with an expected increase in haemoglobin concentration of approximately 2–3 g/dl, corresponding to 2 ml/kg of red blood cells to increase the haemoglobin by 1 g/dl. However, according to other sources, 3 ml/kg of red blood cells

are needed to increase the haemoglobin value of 1 g/dl (Dalmas & Wibaut 2003). A simple way to transfuse red blood cells only is to leave blood to settle down vertically before administration, to separate red blood cells from the plasma.

To evaluate the effectiveness and potential dangers of blood transfusions in an African medical context, we conducted a prospective study of children admitted for severe anaemia in north-eastern Democratic Republic of Congo.

Method

Setting

Bunia is the capital of the District of Ituri, located in the Eastern Province, in the north-eastern region of the Democratic Republic of the Congo (DRC). In 2003, the Swiss section of Médecins Sans Frontières (MSF-CH) set up 'Bon Marché Hospital', a secondary-level hospital, to treat victims of the internal conflict. Over time, the program shifted progressively towards general care, with a focus on paediatric services. At the time of the study, it contained 100 paediatric beds, with an average of 500 children admitted monthly (MSF 2009). In 2008, 350 transfusions were given on average each month. Malaria transmission is perennial, although there is a relative increase between June and December. According to a study on the causes of mortality conducted from May to July 2007 in the hospital paediatric service (Nackers 2007), severe anaemia (defined in this study as a level of haemoglobin <5 g/dl, or a decompensated anaemia) was the second most common reason for admission after severe malaria. Severe anaemia was implicated in 27% of the deaths. Deaths in anaemic children occurred rather late after admission (13/34 = 38% died more than 48 h after admission). Many children were transfused repeatedly, which put into question the efficiency of the transfusions.

Design

This prospective hospital-based cohort study included children from four neighbouring health zones (Bunia, Rwampara, Nizi and Lita) aged 1 month to 4 years, presenting with severe anaemia defined as a haemoglobin level below 4 g/dl or higher but associated with signs of cardio-respiratory distress. Informed written consent was obtained from the caretaker. The protocol was approved by the Ethics Committee of the University of Kinshasa, Democratic Republic of Congo and the Ethics Review Board of Médecins Sans Frontières.

During admission, data were collected on clinical condition and haemoglobin levels of the children before and after blood transfusion, 1 and 3 days after the transfusion and before discharge. Both donor and recipient blood were screened for hepatitis B surface antigen, anti-hepatitis C antibodies and syphilis by rapid treponemal test. Donor blood was systematically screened for HIV, and HIV screening was proposed to all transfusion recipients (opt-out approach). Haematocrit and reticulocyte count were measured. Thin blood smear was examined for hypochromia, micro or macrocytosis, and for parasite count in case of positive rapid test for malaria. The Emmel test was used to screen for sickle cell trait. Children were advised to come for follow-up visits at 1, 2 and 3 months after the transfusion. During follow-up visits, haemoglobin levels were checked and clinical condition assessed. In the event of missed appointments, a tracing visit to the community was organised. This study focuses on results of the hospitalisation phase.

Definitions

Transfusion was indicated in case of severe anaemia, defined as haemoglobin (Hb) below 4 g/dl, or in case of a moderate anaemia (Hb 4–6 g/dl) associated with signs of cardio-respiratory distress. It could be exceptionally justified above 6 g/dl in case of severe cardio-respiratory distress. Respiratory distress was defined by tachypnea and at least one of the following: dyspnoea with signs of distress (nasal flaring, chest indrawing and grunting), anxious restlessness or alteration in consciousness due to hypoxia or hypercapnia. Cardiocirculatory failure was defined as tachycardia (or bradycardia) and at least one of the following: a capillary refill time (CRT) ≥3 seconds with cold extremities or temperature gradient, weak pulse, jugular venous distention, oliguria, peripheral oedema or painful hepatomegaly.

Transfusion

According to the hospital guideline, children who needed a blood transfusion were transfused with 15 ml/kg of packed red blood cells, at a flow of 5 ml/kg/h (in case of major distress, blood was given rapidly over the first 30 min). Blood was either taken from voluntary donors or from a family donor if no other donor was available. Blood was collected with a penta-bag system, which allows direct preparation of four 100- to 125-ml bags from a 450-ml bag. Blood was stored vertically to allow for sedimentation of red blood cells and separation from the plasma. Blood cross matching was performed in the laboratory. To avoid gross errors, ABO-compatibility between patient and transfusion blood was repeated at bedside using the Bio_Rad card™. The transfusion was stopped after

infusion of the red blood cells, to avoid passage of plasma. Furosemide was only recommended in case of clinical signs of fluid overload.

Data collection and analysis

Data were collected on standardised case report forms, entered in EpiData (EpiData Association, Odense Denmark) and analysed with Stata 11 statistical software (Statacorp, College Station, TX, USA). In univariate analysis, categorical variables were compared using chi-square test, and continuous variables with *t*-test if normality could be assumed, else the rank test was used. Paired *t*-test was used if comparing observation from the same subject (for example before and after transfusion). Factors associated in the univariate analysis at a *P*-value below 0.10 were further explored in multivariate models. To explore factors associated with haemoglobin level after transfusion, a model was built using a linear regression model. Post-estimated standardised residuals were analysed to check the good fit of the model, leading to the exclusion of four observations from the final model (patients with very low initial haemoglobin (≤4.3 g/dl) and high haemoglobin after transfusion (≥12.1 g/dl), probably indicating a mistake for one of the two values). Risk factors for in-hospital mortality were explored through multivariate logistic regression. Goodness-of-fit was assessed by Hosmer–Lemeshow test. Lost-to-follow-up (LFU) during hospitalisation was counted as negative outcomes in the mortality analysis, but not included in raw case-fatality rates reported. Sensitivity analysis was carried out counting LFU either as alive or as negative outcome.

Results

Patient characteristics

In total, 657 children were included in the study between December 2009 and April 2010 (Table 1). The sex ratio (boy/girl) was 1.09. More than 80% of the children (539/657) were below the age of three and 34% (224/657) were below one. 22% (142/657) had received a blood transfusion in the past. Of these, most had been transfused once previously (82/142 = 57.7%). Median time since last transfusion was 4 months (interquartile range (IQR): 3–6 months).

On admission, haemoglobin level (Hb) was below 4 g/dl in 35% (230/657), between four and 6 g/dl in 58% (348/657) and at least 6 g/dl in another 6% (43/657) of the children. More than 90% (606/657) had an increased respiratory rate (tachypnoea) and 87.4% (574/657) fitted the definition of respiratory distress. Most frequently reported signs of respiratory distress were nostril flare (534/657 = 81.3%) and anxious restlessness (393/657 = 59.8%), while only 14.9% (98/657) showed chest indrawing. Impaired consciousness was reported for 20.2% (133/657). Increased heart rate was observed in 73.2% (481/657), and a weak pulse was described in 75.2% of the children (494/657). Other signs of cardiac failure were more rarely described. Agreement between clinicians and protocol definitions was poor (kappa 0.33 for respiratory distress, $\kappa = 0.15$ for cardiocirculatory failure). Clinicians tended particularly to overestimate cardiocirculatory failure, while they estimated more accurately the proportion of children with respiratory distress.

Co-morbidities

Malaria rapid test (CareStart) was positive in 86% of the cases. The proportion of parasitised red blood cells was above 5% in 53% (347/657) of the children. The most frequently diagnosed co-morbidities were respiratory infections (11%, 73/657), septicaemia (3%, 22/657) and meningitis (3%, 18/657). Overall, 40.6% of the children (267/657) had another final diagnosis that could at least partly explain the anaemia (malnutrition, HIV infection, tuberculosis, sickle cell disease, parasitic infection, digestive bleeding, intoxication with local products, pneumonia, meningitis, septicaemia or another bacterial infection). Even among the children with a positive rapid test for malaria, 36.8% (208/565) also had another diagnosis. Most co-morbidities were not identified during the initial assessment (for example, only 20 of the 73 patients with a final diagnosis of chest infection had the diagnosis made initially). Nutritional assessment based on weight for height was often incomplete (missing height for 207/657 = 31.5%). The Crofton score – for tuberculosis screening – was not performed systematically and its performance could not be evaluated. No chest radiography was done.

Transfusion practices

Median delay from admission to transfusion was 4 h (interquartile range, 2–10 h 30 min). 97 patients (14.8%) were transfused more than 24 h after admission. All subjects included were transfused. Red blood cell concentrate was left to sediment in 97% (638/657) of the cases before being administered. Bedside blood grouping was not performed for more than half of the patients (363/657 = 55.5%). Furosemide was almost systematically administered (630/657 = 96.3%), without it being a formal recommendation. The quantity of blood delivered by the laboratory was below the quantity recommended to

Table 1 Demographic and clinical characteristics of 657 children transfused for severe anaemia, Bon Marché Hospital, DRC, 2009–2010

	Total *N* = 657		Deaths or lost to follow-up *N* = 41		Alive *N* = 616		Crude OR	
	n	Column %	*n*	Row %	*n*	Row %		[95% CI]
Sex								
Male	342	(52.0)	20	(5.8)	322	(94.1)	1	
Female	315	(47.9)	21	(6.7)	294	(93.3)	1.15	[0.6; 2.2]
Age								
1–11 months	224	(34.1)	25	(11.2)	199	(88.8)	5.2	[1.5; 17.8]
12–23 months	188	(28.6)	10	(5.3)	178	(94.7)	2.3	[0.6; 8.7]
24–35 months	127	(19.3)	3	(2.4)	124	(97.6)	1.2	[0.2; 7.2]
36–47 months	73	(11.1)	2	(2.7)	71	(97.3)	1	
48–59 months	41	(6.2)	0	(0.0)	41	(100.0)	NA	
60 months and above	4	(0.6)	1	(25.0)	3	(75.0)	13.8	[1.0; 188.1]
Provenance (health zone)								
Bunia	261	39.7	23	(8.8)	238	(91.2)	1	
Rwampara	231	35.2	7	(3.0)	224	(97.0)	0.3	[0.1; 0.8]
Nizi	89	13.5	2	(2.2)	87	(97.7)	0.2	[0.0; 1.0]
Lita	76	11.6	9	(11.8)	67	(88.2)	1.4	[0.6; 3.1]
History of previous transfusion	142	(21.6)	5	(3.5)	137	(96.5)	0.5	[0.2; 1.3]
Haemoglobin (mean; standard deviation)	4.4	1.1						
≤4 g/dl	230	(35.0)	18	(7.8)	212	(92.2)	1.8	[0.9; 3.6]
>4 and ≤6 g/dl	384	(58.4)	17	(4.4)	367	(95.6)	1	
>6 g/dl	43	(6.5)	6	(13.9)	37	(86.0)	3.5	[1.3; 9.5]
Signs of respiratory distress								
Tachypnea*	606	(92.2)	37	(6.1)	569	(93.9)	1.3	[0.4; 3.8]
Nasal flaring	534	(81.3)	31	(5.8)	503	(94.2)	0.6	[0.3; 1.4]
Chest indrawing	98	(14.9)	10	(10.2)	88	(89.8)	1.8	[1.1; 2.8]
Anxious restlessness	393	(59.8)	28	(7.1)	365	(92.9)	1.5	[0.7; 2.9]
Impaired consciousness	133	(20.2)	15	(11.3)	118	(88.7)	2.4	[1.2; 4.7]
Tachypnea and at least 1 sign	565	(86.0)	37	(6.5)	528	(93.4)	1.5	[0.5; 4.4]
Respiratory distress according to clinician	552	(84.0)	37	(6.7)	515	(93.3)	4.5	[0.6; 33.8]
Signs of cardiocirculatory failure								
Tachycardia	481	(73.2)	31	(6.4)	450	(93.6)	0.9	[0.4; 1.8]
Weak pulse†	494	(75.2)	22	(4.4)	472	(95.5)	0.3	[0.2; 0.6]
Capillary refill time ≥3 s‡	219	(33.3)	13	(5.9)	206	(94.1)	0.9	[0.3; 3.0]
Peripheral oedema	79	(12.0)	2	(2.5)	77	(97.5)	0.4	[0.1; 1.5]
Painful hepatomegaly	127	(19.3)	6	(4.7)	121	(95.3)	0.7	[0.3; 1.7]
Jugular venous distention	181	(27.5)	16	(8.8)	165	(91.2)	1.7	[0.9; 3.3]
Oliguria	28	(4.3)	1	(3.6)	27	(96.4)	0.5	[0.1; 4.1]
Tachycardia and at least 1 sign	423	(64.4)	28	(6.6)	395	(93.4)	1.2	[0.6; 2.4]
Cardiocirculatory failure according to clinician	552	(84.0)	36	(6.5)	516	(93.5)	1.8	[0.5; 6.1]
CareStart malaria test positive	565	(86.0)	31	(5.5)	534	(94.5)	1	
CareStart malaria test negative	80	(12.2)	9	(11.2)	71	(88.7)	2.2	[1.0; 4.8]
Parasitaemia								
<0.1% (negative)	86	(13.1)	9	(10.5)	77	(89.5)	1	
0.1–1.9%	149	(22.7)	11	(7.4)	138	(92.6)	0.7	[0.3; 1.7]
2.0–4.9%	59	(9.0)	5	(8.5)	54	(91.5)	0.8	[0.2; 2.5]
5.0–9.9%	116	(17.7)	6	(5.2)	110	(94.8)	0.5	[0.2; 1.4]
10.0% and above	234	(35.6)	9	(3.8)	225	(96.1)	0.3	[0.1; 0.9]

Table 1 *(Continued)*

	Total *N* = 657		Deaths or lost to follow-up *N* = 41		Alive *N* = 616		Crude OR	
	n	Column %	*n*	Row %	*n*	Row %		[95% CI]
Co-morbidities								
Clinical malnutrition	31	(4.7)	8	(25.8)	23	(74.2)	6.2	[2.6; 15.3]
Chest infection	73	(11.1)	30	(41.1)	43	(58.9)	36.3	[15.1; 87.7]
Meningitis	20	(3.0)	4	(20.0)	16	(80.0)	4.0	[1.3; 12.8]
Septicaemia	22	(3.3)	1	(4.5)	21	(95.4)	0.7	[0.1; 5.4]

*Tachypnea: respiratory rate (RR) >55 beats per minute (bpm)/min if age below 2 months, RR >45 bpm if age 2–11 months, RR > 35 bpm if at least 1 year old.
†Tachycardia: heart rate (HR) > 170 bpm if age below 2 months, HR >150 bpm if aged 2–24 months, HR >125 bpm if aged >24 months.
‡375 missing values.

correct the haemoglobin (30 ml/kg of whole blood or 15 ml/kg of packed red blood cells), with 96% of the children receiving <30 ml/kg of whole blood and 24% receiving <20 ml/kg. Children received a mean of 15 ml/kg of whole blood (SD, 6 ml/kg), corresponding to 7.5 ml/kg of packed red blood cells. The haemoglobin level increased significantly from 4.4 before transfusion to 7.8 g/dl on day 1 ($P < 0.001$). Increasing the haemoglobin value of 1 g/dl required 4.4 ml/kg of whole blood (or 2.2 ml/kg of red blood cells, taking a conservative estimate of half the quantity of whole blood being constituted by red blood cells). During transfusion, the occurrence of an adverse event did not automatically lead to interruption of the transfusion. Only six transfusions were stopped, for 74 recorded events other than fever. The transfusion was stopped in two cases of urticarial rash without general symptoms, two cases of malaise without rash (all recovered), one urticarial rash with malaise and restlessness, in whom the transfusion was stopped within 1 h. He received dexamethazone and promethazine without success and died thereafter. Another child died during the transfusion, with no apparent signs of adverse reaction.

Evolution during admission

Clinical parameters such as heart rate and respiratory rate improved after transfusion. However, only 22% of the children were discharged with a corrected anaemia (defined as haemoglobin above 9 g/dl without signs of cardio-respiratory distress). Multivariate analysis through linear regression model showed that haemoglobin level after transfusion was higher if baseline haemoglobin (coeff, 0.56; 95% CI 0.45, 0.67) and quantity of delivered blood in ml/kg (0.04; 95% CI 0.02, 0.06) were higher (Table 2). However, patients with a history of previous transfusions had lower haemoglobin levels after transfusion (−0.37; 95%CI −0.66, −0.08). Transfusion became more efficient during the course of the study (coeff, 0.01; 95% CI 0.01, 0.02).

Table 2 Multivariate analysis of factors associated with haemoglobin levels after transfusion, under-five children transfused for severe anaemia, Hôpital Bon Marché, DRC, 2009–2010. Linear regression model (*N* = 627)

	Coefficient	95% CI	*P*-value
Haemoglobin level on admission (in g/dl)	0.56	0.45, 0.67	<0.001
History of previous transfusions	−0.37	−0.66, −0.08	0.012
Quantity of whole blood delivered (in ml/kg)	0.04	0.02, 0.06	<0.001
Date of admission, (in days)	0.01	0.01, 0.02	<0.001

Mortality

The overall case-fatality rate was 5.6% (37/657; Table 3), highest in the group of children with the highest haemoglobin on admission (13.9% (6/43) for a Hb ≥ 6 g/dl compared with 4.2% (16/384) and 6.5% (15/230) for children with a Hb between 4 g/dl and 6 g/dl, and below 4 g/dl, respectively). Most children died more than 24 h after admission (24/37 = 65%). Case-fatality was also highest in both the youngest and oldest age group (21/224 = 9.4% and 1/4 = 25%, respectively).

Lost-to-follow-up cases ($n = 4$) were included as negative outcomes in the mortality analysis. Clinical signs associated with a negative outcome (death or

Table 3 Respiratory distress, cardiocirculatory failure and case-fatality rate by haemoglobin level in 657 children transfused for severe anaemia, Hôpital Bon Marché, DRC, 2009–2010

	No signs of distress		Both respiratory distress and cardiocirculatory failure		Cardiocirculatory failure only		Respiratory distress only		Total		Case-fatality rate	
	n	(%)	*n*	(%)	*n*	(%)	*n*	(%)	*N*	(%)	*n*	%
Haemoglobin												
≤4 g/dl	16	(7.0)	135	(58.7)	14	(6.1)	65	(28.2)	230	(100.0)	15	(6.5)
>4 and ≤6 g/dl	24	(6.2)	232	(60.4)	20	(5.2)	108	(28.1)	384	(100.0)	16	(4.2)
>6 g/dl	6	(13.9)	19	(44.2)	3	(7.0)	15	(34.9)	43	(100.0)	6	(13.9)
Total	46	(7.0)	386	(58.7)	37	(5.6)	188	(28.6)	657	(100.0)	37	(5.6)

Respiratory distress was defined by tachypnea (respiratory rate (RR) >55 beats per minute (bpm)/min if age below 2 months, RR > 45 bpm if age 2–11 months, RR > 35 bpm if at least 1 year old) and at least one of the following: dyspnea with signs of distress (flaring of nostrils, intercostal indrawing, xyphoidian depression), anxious restlessness or alteration in consciousness. Cardiac failure was defined as tachycardia (heart rate (HR) >170 bpm if age below 2 months, HR >150 bpm if aged 2–24 months, HR >125 bpm if aged >24 months) and at least one of the following: weak pulse, a capillary refill time (CRT) ≥3 s, peripheral edema, painful hepatomegaly, jugular turgescence or rare urine.

Table 4 Multivariate model of risk factors for hospital mortality among under-five children transfused for severe anaemia, Hôpital Bon Marché, DRC, 2009–2010 (41 deceased or lost-to-follow-up for a total of 650 patients)

	Adjusted OR	95% CI	*P*-value
Haemoglobin level			
≤4 g/dl	2.2	0.9; 5.3	0.084
>4 and ≤6 g/dl	1		
>6 g/dl	5.2	1.4; 20.1	0.016
Provenance (health zone)			
Rwampara	1		
Bunia	4.2	1.5, 12.1	0.007
Nizi	0.9	0.1, 5.6	0.937
Lita	3.8	1.1, 14.0	0.04
Impaired consciousness	2.5	1.0, 6.0	0.047
Jugular veinous distention	3.0	1.2, 7.4	0.016
Chest infection	39.3	16.1; 95.8	<0.001
Meningitis	10.5	2.3, 48.9	0.003
Clinical malnutrition	5.4	1.6, 18.4	0.007

Logistic regression model Goodness-of-fit according to Hosmer-Lemeshow test with 10 probability groups: chi2 with 8 degrees of freedom 5.21; $P = 0.735$.

loss-to-follow-up; Table 1) in univariate analysis were chest indrawing (crude OR, 1.8; 95% CI 1.1, 2.8) and impaired consciousness (crude OR, 2.4; 95% CI 1.2, 3.9). All children who died had at least one sign of respiratory distress. Among signs of cardiac distress, there was a trend for jugular venous distention to be associated with mortality (crude OR, 1.7; 95% CI 0.9, 3.3), while the occurrence of a weak pulse seemed to be protective (crude OR, 0.3; 95% CI 0.1, 0.6).

In the multivariate analysis (Table 4), diagnoses of co-morbidities such as chest infection (adjusted OR, 39.3; 95% CI 16.1–95.8), meningitis (adjusted OR, 10.5; 95% CI 2.3–48.9) or malnutrition (adjusted OR, 5.4; 95% CI 1.6–18.4) were associated with negative outcome. Other independent risk factors were a Hb ≥6 g/dl on admission, compared with a haemoglobin between 4 and 6 g/dl (adjusted OR, 5.2; 95% CI 1.4–20.1), presence of impaired consciousness on admission (adjusted OR, 2.5; 95% CI 1.0–6.0) or jugular venous distention (adjusted OR, 3.0; 95% CI 1.2–7.4), provenance from Bunia or Lita (adjusted OR, 4.2 (95% CI 1.5, 12.1) and 3.8 (95% CI 1.1, 14.0), respectively), compared with Rwampara. Age, chest indrawing and weak pulse were not associated with mortality after adjusting for the other factors. Levels of parasitaemia seemed associated with reduced mortality based on the univariate analysis, but there was no more association after adjusting for other factors such as co-morbidities.

Discussion

Our results confirm that severe anaemia is a disease of very young children (often infants and toddlers up to 3 years old). We were surprised to record such a high proportion of children (almost one of four) reporting a previous history of transfusions. This shows that severe anaemia is a recurrent problem for some children, as has been shown in Malawi (Phiri *et al.* 2008). This should lead to an active search for co-morbidities or underlying factors in children with recurrent anaemia. The frequency of repeated transfusions should be taken into account in transfusion

guidelines, because the risk of alloimmunisation increases with repeated transfusions. Unfortunately, there are no simple tests to detect irregular antibodies adapted to remote settings.

It may seem counterintuitive that patients living in close proximity to the hospital (Bunia health zone) were at higher risk of death than those coming from further away (Rwampara and Nizi health zones). This possibly reflects the fact that severely ill children do not even reach the hospital when they live further away.

The issue of severe anaemia goes beyond severe malaria only. Only half of the children in our cohort had high levels of parasitaemia (above 5%). Neither the presence of malaria nor levels of parasitaemia played a role in terms of outcome. However, the study took place in a hospital where severe malaria was probably well managed. Still, the presence of a positive malaria test should not prevent the physicians from considering co-morbidities, whether acute or chronic, especially when quantitative blood smears are not done.

In practice, children received half of the recommended amount of blood. This was probably favoured by the use of the penta-bag system, to save blood for more recipients. The quantity of transfused blood had an impact on haemoglobin level after transfusion but, probably because the quantities were small overall, we could not show an effect in terms of mortality or need for retransfusion. Children with severe anaemia who do need blood transfusion should receive an adequate volume. Transfusion of insufficient quantities of blood can lead to the need for repeated transfusions, often from different donors. This increases the risk both of infection and alloimmunisation. Current WHO recommendations of transfusing 5 ml/kg of red blood cells do not seem adequate, as this would only increase the haemoglobin value by <2.5 g/dl according to our results.

While leaving blood to sediment is an easy way to concentrate red blood cells in low-resource settings, it makes it difficult to estimate precisely the amount of red blood cells given, as the infusion bags are not graduated. Also, it is optimistic to assume that half of the volume of whole blood corresponds to red blood cells, as normal haematocrit is usually below 50%.

The average haemoglobin level before transfusion among our population of transfused children can be considered to be rather high. Many children seem to have been transfused because of signs of vital distress attributed to the anaemia without looking for the presence other co-morbidities or underlying factors. The study was performed where blood was rather easily available compared with other African contexts, and this seems to have led to the over-prescription of blood transfusion. However, as shown by the high case-fatality of children with a high haemoglobin level, transfusion was not the correct answer in those children. Decrease in in-hospital mortality of children with anaemia requires better management of co-morbidities, based on an in-depth analysis of clinical signs and physiopathological reasoning.

As all signs of respiratory distress were relatively frequent, it was difficult to identify which ones were most associated with mortality. Impaired consciousness was reported frequently and interpreted as a sign of respiratory failure, although in most cases, this may point to an additional diagnosis such as cerebral malaria or meningitis and is not a marker of the severity of the anaemia. Weak pulse is a subjective criterion that may easily be overestimated, explaining some of our unexpected results. Clinicians had difficulty strictly applying definitions of cardiac and/or respiratory distress. In the context of severe anaemia, these definitions should be standardised and simplified, in order for physicians to correctly identify children in need of blood. For example, use of the capillary refill time, which has been shown to be a prognostic factor in severe malaria (Evans *et al.* 2006), should be actively promoted. Also, distinction between anaemia and pneumonia as the cause of the respiratory distress can be difficult in the initial assessment. This ultimately leads to many transfusions being given to children with non-severe anaemia.

Our study questions not only issues concerning transfusions, but most of all, the overall level of care for paediatric emergencies. While emergency paediatric care represents a major part of the activity of most hospitals in developing countries, specific training of physicians and nursing staff on emergency paediatric care has been neglected. The implementation of simple triage measures and training in better recognition and case management of paediatrics emergencies including severe anaemia and shock can make a significant difference in terms of patient outcomes (Molyneux *et al.* 2006). Recently, MSF has started such trainings, with very good results and encouraging feedbacks both from expatriate and national staff.

Although blood transfusion is a frequent procedure, rules of good transfusion practice such as bedside grouping should not be overlooked, even in very busy wards. More attention should be given to recognition and management of adverse reactions. It is particularly in such contexts, when there is not much time to think, that precautionary rules prevent accidents.

Conclusion

In Bunia Hospital, blood transfusions were frequent, the use of which could clearly be rationalised. Cases of severe

anaemia were found to be complex. Severe malaria was only one contributing factor to anaemia, while other co-morbidities and or underlying conditions played an important part in terms of mortality. Such cases call for global and integrated management. While indications should be restricted, quantities of transfused blood should be adapted to needs, to ensure efficiency and lower the risks associated with blood transfusions from multiple donors.

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