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Treatment of severe malnutrition with 2-day intramuscular ceftriaxone *vs* 5-day amoxicillin

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Abstract

Background. Systemic antibiotics are routinely prescribed for severe acute malnutrition (SAM). However, there is no consensus regarding the most suitable regimen. In a therapeutic feeding centre in Khartoum, Sudan, a randomised, unblinded, superiority-controlled trial was conducted, comparing once daily intramuscular injection with ceftriaxone for 2 days with oral amoxicillin twice daily for 5 days in children aged 6–59 months with SAM.

Methods. Commencing with the first measured weight gain (WG) following admission, the risk difference and 95% confidence interval (95% CI) for children with a WG ⩾10 g/kg/day were calculated over a 14-day period. The recovery rate and case fatality ratio (CFR) between the two groups were also calculated.

Results. In an intention-to-treat analysis of 458 children, 53.5% (123/230) in the amoxicillin group and 55.7% (127/228, difference 2.2%, 95% CI −6.9–11.3) in the ceftriaxone group had a WG ⩾10 g/kg/day during a 14-day period. Recovery rate was 70% (161/230) in the amoxicillin group and 74.6% (170/228) in the ceftriaxone group ($p=0.27$). CFR was 3.9% (9/230) and 3.1% (7/228), respectively ($p=0.67$). Most deaths occurred within the 1st 2 weeks of admission.

Conclusion. In the absence of severe complications, either ceftriaxone or amoxicillin is appropriate for malnourished children. However, in ambulatory programmes, especially where there are large numbers of admissions, ceftriaxone should facilitate the work of medical personnel.

Introduction

A high incidence of mortality among children with severe acute malnutrition (SAM) occurs particularly during nutritional crises.[1,2] The care of children with SAM in a therapeutic feeding centre (TFC) or hospital is based on provision of nutritional rehabilitation and the treatment of associated complications, mainly infections, hypoglycaemia, hypothermia and dehydration.[3] Over the last 20 years, the use of standardised protocols has helped to reduce case fatality ratios (CFR) among children with SAM.[4,5] In South Africa, an in-hospital CFR decreased from 20% to 6% after the introduction of a standardised nutrition rehabilitation protocol which included an antibiotic regimen of ampicillin and gentamicin.[6]

There is general agreement that administration of systemic broad-spectrum antibiotic therapy on admission improves the outcome of SAM.[7] The World Health Organization recommends that all patients with complicated SAM routinely receive either erythromycin or ampicillin and gentamicin to reduce mortality and improve

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nutritional response to feeding.[8] However, there is no clear agreement on the most suitable antimicrobial regimen. Amoxicillin has been used routinely in TFCs as first-line antibiotic therapy but little is known about the response and its toxicity in children with SAM. The amoxicillin regimen is not ideal because of its duration (5 days, ten doses) and the potential risks of poor absorption and resistance.[9] Emergence of antibiotic resistance, a factor rarely controlled for in resource-poor settings, might also seriously impair the use of broad-spectrum antibiotics. A hospital study among malnourished children in Kenya described increased resistance to commonly used antibiotics such as erythromycin, ampicillin, cotrimoxazole, chloramphenicol and even oxacillin.[10]

A short course of intramuscular (IM) ceftriaxone might be an alternative to a 5-day regimen of an oral antibiotic. Ceftriaxone has the longest half-life of the cephalosporins. In the treatment of paediatric acute otitis media (AOM), a single IM injection of ceftriaxone 50 mg/kg has been shown to be as efficient as 10-day oral amoxicillin clavulanate at 12.5 mg three times a day.[11] In an urban emergency department (Boston Children's Hospital), two IM injections of ceftriaxone (50 mg/kg) were given to febrile outpatient infants with no source of infection detected on physical examination. It was a successful alternative to hospital admission.[12]

This study compares the effectiveness of two systematic antimicrobial treatments administered on admission to children with SAM: once daily injection of IM ceftriaxone for 2 days *vs* twice daily oral amoxicillin over 5 days (ten doses). Weight gain (WG) was used as the primary outcome because poor response to treatment of infection is likely to delay WG and prolong admission.

Patients and Methods

A randomised, unblinded, superiority-controlled trial comparing the two treatment regimens was conducted.

Patients were enrolled between January 2002 and September 2003 at the Mayo TFC, 15 km south of Khartoum, Sudan. The population comprised internally displaced populations mainly from southern Sudan. The study site was chosen because the working conditions were satisfactory, the centre adhered to international standards of nutritional rehabilitation programmes, and the political situation was stable.[8] TFC staff provided 24-hour care for admitted children.

Patients eligible for the study met the following anthropometric criteria: weight-for-height percentage index (W-H%) $<70\%$ of the reference median (using the NHCS/CDC 1977 growth reference curves) and/or presence of bilateral oedema (defined as bilateral pitting persisting after 3 seconds of thumb pressure on the dorsum of both feet) and/or mid-upper-arm circumference (MUAC) <110 mm. Children had to weigh $\geqslant 5$ kg on admission and have a height of >65 cm and $\leqslant 109.9$ cm (usually corresponding to children aged 6–59 months).

Those with any of the following characteristics were excluded: parents who refused permission to participate; treatment with any of the study drugs in the 7 days before admission; admission in the last 7 days to any health facility for severe malnutrition; known hypersensitivity to amoxicillin or ceftriaxone; decision by the physician to use a different antimicrobial drug on admission; on-going vomiting; history of a convulsion or impaired consciousness in the 24 hours preceding admission; and AOM diagnosed on admission. Children diagnosed with AOM were excluded because the TFC treatment protocol for AOM was a 10-day oral amoxicillin regimen which conflicted with the study's 5-day regimen.

On admission, weight was measured by trained TFC staff using a 25 kg Salter® scale (100 g precision). Height was measured using standard UNICEF measuring boards (0.1 cm precision). MUAC was measured using MUAC armbands reading at 2 mm. Information on medical history and clinical

examination including vital signs (temperature, heart rate, respiratory rate) was recorded. Haemoglobin was measured using a haemoglobinometer (Lovibond). A Paracheck-Pf® malaria rapid test for the diagnosis of *Plasmodium falciparum* was performed on all admitted children.

Nutritional rehabilitation took place in three phases. Phase I (stabilisation) consisted of a nutritional intake of 100 kcal/kg/day divided between eight meals in the form of therapeutic milk F-100 (Nutriset®) diluted at 130 ml/100 kcal. When the patients' appetites had been restored, oedema had begun to resolve and medical complications were controlled, they were moved to a transitional phase consisting of a nutritional intake of 130 kcal/kg/day using F-100 diluted at 100 ml/100 kcal. Phase II (rehabilitation) started when WG occurred and oedema had disappeared. In this phase, the daily nutritional intake was 200–300 kcal/kg/day divided between six meals in the form of F-100 (diluted at 100 ml/100 kcal), Plumpy'nut® (enriched peanut butter, Nutriset, 500 kcal/92 g) or therapeutic food biscuit BP100 (Compact, 527 kcal/100 g).

In addition to the study drug, patients were offered the standard treatment administered at the TFC that consisted of vitamin A, mebendazole for children weighing >8 kg, folic acid and iron supplementation, the latter given 2 weeks after admission. Dehydration was treated according to the rehydration guidelines for SAM using rehydration solution salts for the severely malnourished (ReSoMal, Nutriset). Vaccinations were also completed according to the Sudanese national immunisation schedule.

On enrolment, children were assigned to receive one of the two treatments. A computer-generated randomisation list of a 20-patient block (ten in the ceftriaxone group, ten in the amoxicillin group) was drawn up by a statistician. A research assistant allocated the next available number to each child on entry to the trial and each number corresponded to a sealed envelope containing the allocated treatment. A nurse administered the treatment under supervision by the research assistant. Medical staff and patients' guardians were not blinded to the allocated treatment.

Children were randomly assigned to receive either a single dose of 75 mg/kg bodyweight/day of IM ceftriaxone for 2 days (1 g vials for injections, Combino Pharm, S.L.) or 80 mg/kg/day of amoxicillin in two doses for 5 days (250 mg tablets, Biochemie or 125 mg/5 ml syrup Ospamox®, Novartis-Biochemie).

Following programme procedures, participating children remained in the centre until they had maintained a W-H% ⩾85% of the reference median for 7 consecutive days. Thereafter they were considered to have recovered (TFC exit criteria). Weight was recorded daily and MUAC and height were measured weekly and fortnightly, respectively.

The primary outcome was the proportion of children with a WG increase of at least 10 g/kg/day, calculated over a 14-day period beginning with the 1st day of WG after admission. WG was calculated as follows:

$$WG = \frac{w_2 - w_1}{W_1 \; x \; 14 \; days}$$

W_1 (kg) and w_1 (g) were the weights measured on the 1st day of an increased weight curve and w_2 (g) was the weight measured 14 days after w_1.

Treatment was defined as successful when children had gained ⩾10 g/kg/day by the 14th day of WG (primary outcome) or when they were were discharged before 14 days of WG because they had met the TFC exit criteria for recovery.

Other outcome measures included (i) recovery rate (TFC exit criteria) for children discharged, (ii) the overall CFR (the proportion of children who died during their stay in the TFC), (iii) defaulter rate (proportion of children absent from the TFC after 3 consecutive days) and (iv) the referral rate (proportion of children referred

to another medical facility who did not return to the TFC after 3 days).

For children discharged from the TFC as having recovered, we calculated length of stay (days) in the TFC from admission to exit and WG (g/kg/day) at discharge calculated from the 1st day of WG to the day of discharge. Proportions of adverse events were also compared between treatment groups.

Before commencing the study, ethical approval was obtained from the Ethical Review Committee of the Federal Ministry of Health of The Republic of Sudan and the Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale (CCPPRB). Parents or guardians gave written, informed consent.

Statistical analysis

The primary objective of the study was to discover whether routine administration of a 2-day regimen of IM ceftriaxone improved WG during the 1st 14 days of WG by at least 10% compared with a regimen of 5 days of amoxicillin. Given a success rate of 80% in children receiving amoxicillin and 90% in those receiving ceftriaxone, and with a power of 80% and a one-sided significance level of 5%, the required sample size was calculated to be 177 children per group (a total of 354). We increased the sample size by 10% to adjust for losses to follow-up and for children who died or left the TFC before 14 days of WG because of default or referral to other sites (no primary outcome calculable). The final sample included 230 children in each group.

We conducted an intention-to-treat (ITT) analysis of all children in the study who had received at least one dose of the study drug. In this analysis, the definition of failure included children with WG $<$10 g/kg/day over a 14-day period, our primary outcome, and children who died, defaulted or were referred to other sites before achieving the WG goal.

In the per-protocol (PP) analysis, we excluded from the denominator (i) children who defaulted before the primary outcome was measurable, (ii) children in whom the trial drug failed and had to be replaced by another antimicrobial drug (rescue treatment) and/or (iii) children who received one or more additional antimicrobial drug(s) (concomitant treatment) before they reached 14 days of WG (ceftriaxone, chloramphenicol, cotrimoxazole, amoxicillin or metronidazole).

In the ITT and PP analyses, we also looked at success rates by anthropometric admission criteria (i.e. W-H% $<$70% or bilateral oedema, or MUAC $<$110 mm) and by age group (6–23 and 24–59 months). In the ITT analysis, we looked at mean WG calculated 14 days after the first weight increase.

We planned an interim analysis of the primary outcome when 100 children were included in each arm of the study. The trial was to be stopped if a significant difference between the study groups ($p=0.029$) were identified in primary outcome success rates.[13]

For primary outcome, we calculated the risk difference and 95% confidence interval (95% CI). Differences in proportions between groups in the distribution of baseline characteristics on admission and for secondary outcomes were tested using the χ^2 or Fisher's Exact test for categorical variables. For means and 95% CIs, the *t*-test (continuous variables, normal distribution) or Mann–Whitney U non-parametric test (continuous variables, distribution not normal) was used.

Data entry and analysis were undertaken using EpiInfo 6.04dfr (Centers for Disease Control and Prevention, Atlanta, GA, USA) and Stata/SE 9.0 (College Station, Texas, USA).

Results

Of the 1288 children screened for enrolment between January 2002 and September 2003, 460 (35.7%) met the eligibility criteria. Of

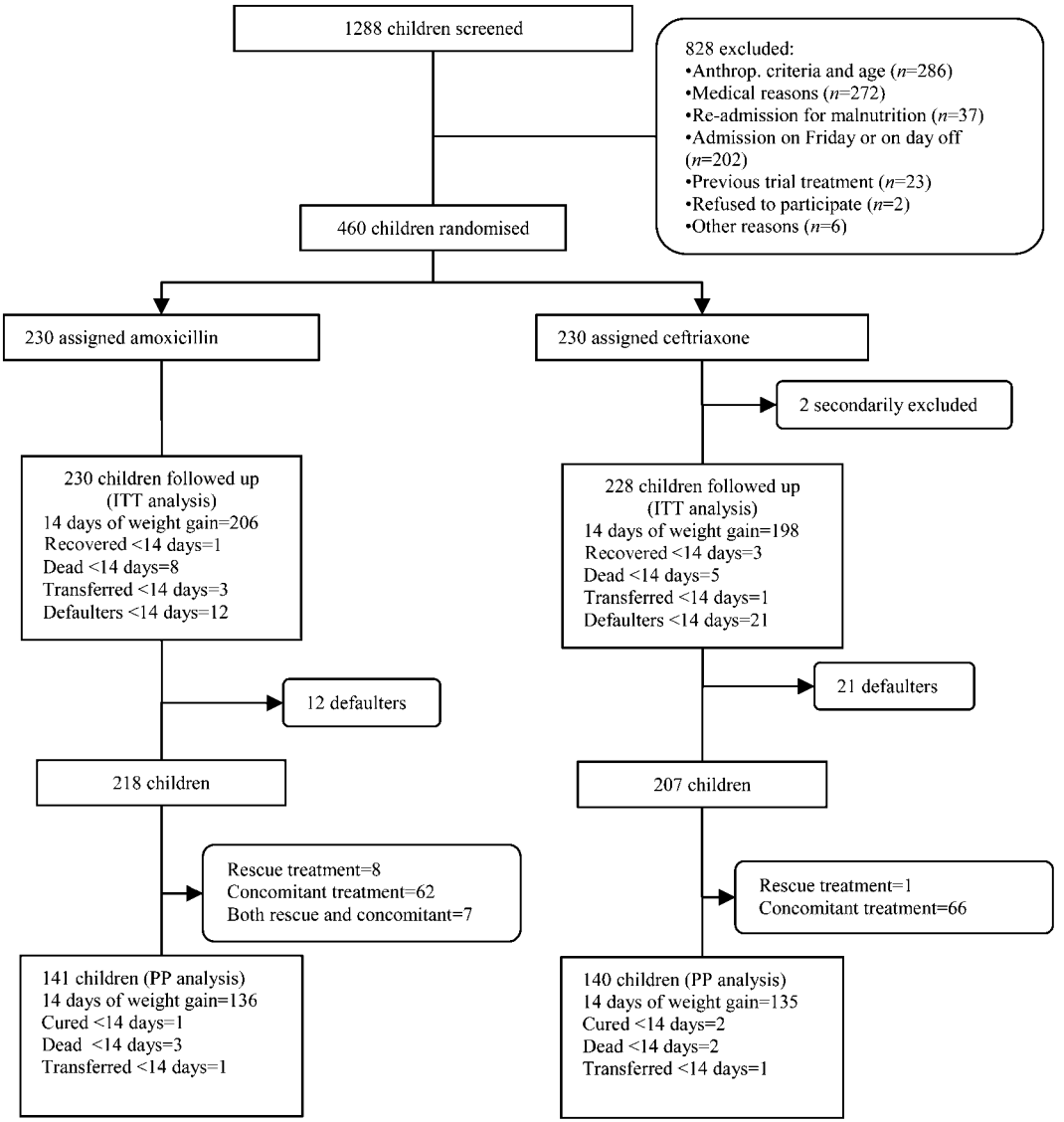

FIG. 1. Trial profile.

these, 230 were randomised to the amoxicillin group and 230 to the ceftriaxone group. Reasons for primary exclusions are shown in Fig. 1. Medical reasons included children with AOM or severe complications diagnosed at entry such as on-going vomiting, one episode of convulsion in the 24 hours preceding admission, impaired consciousness, respiratory distress and shock (hypovolaemic or septic).

Included in the ITT analysis were 230 children assigned to the amoxicillin group and 228 assigned to the ceftriaxone group. Two children allocated to the latter did not receive the first treatment dose, in one case because the mother withdrew her child from the study before the first injection and in the other because AOM was secondarily diagnosed. Twenty-four children in the amoxicillin group and 30 in the ceftriaxone group

left the TFC before 14 days of WG because they recovered, died, defaulted or were referred to other sites (Fig. 1).

Included in the PP analysis were 141 children assigned to the amoxicillin group and 140 assigned to the ceftriaxone group. Twelve children in the amoxicillin group and 21 in the ceftriaxone group were excluded because they defaulted before reaching 14 days of WG. In addition, we excluded 77 children in the amoxicillin group and 67 in the ceftriaxone group because the trial treatment was interrupted and/or they received an additional treatment before reaching 14 days of WG (Fig. 1). Treatment interruption was significantly more common in the amoxicillin group (17/230, 7.4%) than in the ceftriaxone group (1/228, 0.4%) ($p<0.001$). There were no significant differences in the administration of an additional treatment before 14 days of WG.

The distribution of baseline socio-demographic, anthropometric and clinical characteristics did not differ significantly between the groups. In the amoxicillin group, 12.2% were admitted with bilateral oedema and 10.1% in the ceftriaxone group. Table 1 presents baseline characteristics for children in the ITT and PP analyses. In both groups, the median time from admission to 1st WG was 1 day ($p=0.33$). The median time spent in phase I was 5 days in the amoxicillin group and 4 days in the ceftriaxone group ($p=0.7$).

In the ITT analysis, overall success rates in the amoxcillin and ceftriaxone groups were 53.5% (123/230) and 55.7% (127/228), respectively (difference 2.2%, 95% CI −6.9–11.3). In the PP analysis, success rates in the amoxicillin and ceftriaxone groups were 63.1% (89/141) and 62.9% (88/140), respectively (difference −0.2%, 95% CI −11.5–11.0) (Table 2).

There were no statistical differences in success rates when the admission criterion was W-H% <70% ($p=0.51$) or MUAC <110 mm ($p=0.47$). The success rate in children admitted with bilateral oedema was higher in the amoxicillin group ($p=0.04$). It was not influenced by age (Table 3). WG calculated 14 days after first increase did not differ between the groups (ITT analysis) (Table 4).

We calculated secondary outcomes for the 458 children (Table 4) in the ITT analysis. The recovery rate was 70% (161/230) in the amoxicillin group and 74.6% (170/228) in

TABLE 1. *Baseline socio-demographic, anthropometric and clinical characteristics by treatment group.*

	Intention-to-treat analysis*		Per-protocol analysis*	
	Amoxicillin, $n=230$	Ceftriaxone, $n=228$	Amoxicillin, $n=141$	Ceftriaxone, $n=140$
Age (mths):				
Mean (SD)	18 (8)	17 (7)	18 (7)	17 (7)
Median (IQR)	18 (12–23)	16 (12–20)	18 (12–23)	16 (12–19)
Male	127 (55.2%)	119 (52.2%)	66 (46.8%)	73 (52.1%)
W-H% <70%[†]	166 (72.1%)	169 (74.1%)	109 (77.3%)	109 (77.6%)
Bilateral oedema	28 (12.2%)	23 (10.1%)	13 (9.2%)	12 (8.6%)
MUAC <110 mm[§]	36 (15.7%)	36 (15.8%)	19 (13.5%)	19 (13.6%)
Fever[‡]	67 (29.1%)	70 (30.7%)	35 (24.8%)	43 (30.7%)
Abnormal respiratory rate**	40 (17.4%)	41 (18.0%)	20 (14.2%)	24 (17.1%)
Moderate dehydration	23 (10.1%)	33 (14.5%)	10 (7.1%)	19 (13.6%)
Paracheck positive	2 (0.9%)	4 (1.9%)	2 (1.4%)	3 (2.1%)
Hb <8 g/dl	41 (18.1%)	37 (16.4%)	21 (15.0%)	21 (15.0%)

* Quantitative data are mean (SD) or median (interquartile range, IQR), categoricals are numbers (%); [†] no bilateral oedema; [§] no bilateral oedema and W−H% ⩾70%; [‡] ⩾37.5°C (axillary); ** respiratory rate >50 for children 6–11 months, >40 for children 12–59 months.

the ceftriaxone group ($p=0.27$). Length of stay and WG calculated on discharge for children who recovered did not differ between groups (Table 5).

During follow-up, 3.9% (9/230) of children in the amoxicillin group and 3.1% (7/228) in the ceftriaxone group died ($p=0.62$). This is an overall CFR of 3.5% (16/458). Thirteen (81%) deaths occurred during the 1st 2 weeks after admission, eight in the amoxicillin group and five in the ceftriaxone group. Five children died of septic shock, three of lower respiratory tract infections, four from fluid overload and one from severe dehydration. Three children died later, on the 26th (ceftriaxone), 30th

TABLE 2. *Proportion of primary outcome (success rate).*

	Amoxicillin		Ceftriaxone			
	n (%)	Total	*n* (%)	Total	Difference, % (95% CI)	*p*-value
Intention to treat	123 (53.5)	230	127 (55.7)	228	2.2 (−6.9–11.3)	0.63
Per protocol	89 (63.1)	141	88 (62.9)	140	−0.2 (−11.5–11.0)	0.96

TABLE 3. *Proportion of primary outcome by anthropometric criteria and age group.*

	Amoxicillin		Ceftriaxone			
	n (%)	Total	*n* (%)	Total	Difference, % (95% CI)	*p*-value
Intention to treat						
W-H% <70%⋆	98 (59.0)	166	107 (63.3)	169	4.3 (−6.1–14.7)	0.51
Bilateral oedema	11 (39.3)	28	3 (13.0)	23	−26.2 (−49.0–3.5)	**0.04**
MUAC <110 mm†	14 (38.9)	36	17 (47.2)	36	8.3 (−14.5–31.1)	0.47
Age 6–23 mths	90 (51.4)	175	103 (57.2)	180	5.8 (−4.5–16.1)	0.27
Age 24–59 mths	33 (60.0)	55	24 (50.0)	48	10.0 (−29.2–9.2)	0.31
Per protocol						
W-H% <70%⋆	73 (67.0)	109	76 (69.7)	109	2.7 (−9.6–15.1)	0.74
Bilateral oedema	8 (61.5)	13	2 (16.7)	12	−44.9 (−78.7–11.0)	**0.02**
MUAC <110 mm†	8 (42.1)	19	10 (52.6)	19	−10.5 (−21.0–42.1)	0.52
Age 6–23 mths	62 (58.5)	106	71 (62.8)	113	4.3 (−8.5–17.3)	0.52
Age 24–59 mths	27 (77.1)	35	17 (63.0)	27	−14.2 (−37.1–8.7)	0.16

⋆ No bilateral oedema; † no bilateral oedema and W-H% ⩾70%.

TABLE 4. *Weight gain (WG, g/kg/day) calculated 14 days after first WG by anthropometric criteria and age group (intention-to-treat analysis).*

	Mean WG day 14 (95% CI)		
	Amoxicillin	Ceftriaxone	*p*-value
W-H% <70%⋆	12.0 (11.0–13.0)	12.4 (11.4–13.3)	0.72
Bilateral oedema	8.6 (5.1–12.1)	5.5 (3.3–7.7)	0.08
MUAC <110 mm†	8.7 (6.8–10.6)	9.8 (7.8–11.8)	0.79
Age 6–23 mths	10.5 (9.6–11.4)	11.5 (10.6–12.4)	0.94
Age 24–59 mths	12.9 (10.9–14.9)	10.7 (8.4–13.0)	0.07
Overall	11.2 (10.2–11.9)	11.4 (10.5–12.2)	0.69

⋆ No bilateral oedema; † no bilateral oedema and W−H% ⩾70%.

(amoxicillin) and 50th days (ceftriaxone) after admission, from meningo-encephalitis syndrome of unknown origin, severe respiratory infection and pulmonary TB, respectively.

Two adverse events in the ceftriaxone group and eight in the amoxicillin group ($p=0.05$) were reported and attributed to the drug tested. In the ceftriaxone group, one child presented with vomiting and another with diarrhoea. Six children in the amoxicillin group presented with diarrhoea, one with vomiting and one with an allergic reaction (facial oedema). The child who developed facial oedema was treated with dexamethasone. Amoxicillin was stopped and replaced by ceftriaxone, except for one case of diarrhoea in whom amoxicillin was replaced by cotrimoxazole. None of the adverse events could be associated with the trial intervention with any certainty. Neither infection at injection site nor post-injection local pain was reported by the guardians or medical staff in the ceftriaxone group.

Discussion

The results of our study did not demonstrate that a 2-day IM ceftriaxone regimen is superior to a 5-day amoxicillin regimen in children admitted to a TFC with SAM when mean WG was the primary focus. In both groups, mean daily WG was >10 g/kg/day in the 2 weeks after first WG increase, except in children admitted solely for bilateral oedema or with a MUAC <110 mm.

The CFR in both groups was <5%. Most deaths (81%) occurred within the 1st 2 weeks of admission. We excluded patients with severe complications such as severe infections, on-going vomiting, a history of impaired consciousness or convulsions in the 24 hours before admission.

Some limitations might have contributed to the absence of an expected difference. The primary outcome (mean daily WG) was measured from the 1st day of WG. When weight began to increase, children might have already recovered from infections and therefore the primary outcome might no longer have depended on antibiotic treatment. However, the delay between admission and first WG did not differ between the two treatment groups either.

More than 25% of children in each group received a second antimicrobial treatment (ceftriaxone, chloramphenicol, cotrimoxazole, amoxicillin or metronidazole) before reaching 14 days of WG. Prescriptions were in accordance with TFC treatment protocols. Where bacteriological analyses are not available (culture and drug susceptibility), the presence or nature of infection cannot be verified. In addition, centre-acquired infections are a frequent source of complications.[14] Staff members might therefore be over-cautious and over-prescribe antibiotics when they suspect severe bacterial infections, which could attenuate any difference in the ITT analysis. In such a context,

TABLE 5. *Exit criteria, length of stay in TFC until recovery (days) and WG at exit (g/kg/day)* (n=*458*).

	Amoxicillin, $n=230$ (%)	Ceftriaxone, $n=228$ (%)	p-value
Exit criteria			
Recovered	161 (70.0)	170 (74.6)	0.27
Deceased	9 (3.9)	7 (3.1)	0.62
Defaulted	39 (17.0)	43 (18.9)	0.59
Referred	4 (1.7)	2 (0.9)	0.68
Other criteria*			
Length of stay	33.5 (31.5–35.5)	31.4 (29.4–33.3)	0.07
WG at exit	10.2 (9.4–11.0)	10.2 (9.7–10.7)	0.50

* Quantitative data are means (95% CI).

results of the PP analyses do not reflect the actual situation in the TFC where treatment for complications associated with SAM requires frequent adjustment.

In 14 patients, amoxicillin was interrupted and replaced by ceftriaxone, in the majority because of respiratory infection, septic shock and allergy. In the absence of blinding, it is not unlikely that this stemmed from a lack of trust in amoxicillin. This switch to ceftriaxone in 14 children might also have contributed to the reduced difference in the ITT analysis.

Cases with bilateral oedema were different from others (Tables 3 and 4) and the data might indicate that amoxicillin is superior in patients with bilateral oedema. Nonetheless, WG is confounded by oedema and its use as an outcome in settings where kwashiorkor is the dominant manifestation of malnutrition has serious limitations. In our study, however, this group represented only 11% of all cases.

The study also indicates that when precautionary methods and safe injection protocols are used, infection from injections is uncommon. Short-course IM ceftriaxone could facilitate the management of children in emergency situations when operational considerations are central. The cost of ceftriaxone, though still more than that of amoxicillin, has greatly reduced in recent years. In this study, the cost of treating one child weighing 10 kg was €1.6 for ceftriaxone and €0.2 for amoxicillin.

The results have to be considered in the larger context of new treatment strategies for malnutrition in complex emergencies. Progressively ambulatory or home-based treatment is preferred to standard inpatient centre-based programmes.[15] In ambulatory programmes, only children with complicated SAM require to be treated in an inpatient structure.[16] There are several benefits: mothers do not have to stay several weeks in the TFC and patients have a lower risk of centre-acquired infections. A CFR of 1.7%, close to that in this study, was documented in children with SAM treated at home in Niger. In the same programme, CFR in children with complicated SAM treated in an in-patient structure was dramatically higher, 18.9%.[17] A short course of ceftriaxone could be considered for children with uncomplicated SAM before they are sent home. The resulting benefit might be better compliance compared with a 5-day regimen of amoxicillin, though this would need to be documented.

When studies are conducted in such difficult clinical settings, it is likely that methodological and population-based error will occur. Drop-out will be more likely and failure to comply more frequent, and there is the problem of 'blinding' to the analysis. It is therefore imperative that such studies be replicated in various field situations.

In the absence of superiority of ceftriaxone over amoxicillin, the choice might relate mainly to operational considerations. We believe that either treatment is appropriate for children with uncomplicated SAM. In ambulatory programmes and/or when large numbers of children present with SAM, the use of short-course ceftriaxone should facilitate the work of medical personnel and improve adherence.

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