Food and Chemical Toxicology 50 (2012) 1517–1523

Contents lists available at SciVerse ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Control of konzo in DRC using the wetting method on cassava flour

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ARTICLE INFO

Article history:
Received 2 November 2011
Accepted 1 February 2012
Available online 10 February 2012

Keywords:
Konzo
Wetting method
Cassava flour
Cyanide
Urinary thiocyanate
S-containing amino acids

ABSTRACT

Fifty konzo cases were identified in four villages in Popokabaka Health Zone, DRC. One third of people had only one meal per day, mainly of cassava flour consumed as a thick porridge (fufu) and pounded, boiled cassava leaves. Retention of cyanogens in flour resulted from short soaking of cassava roots. A 1.5 years intervention was made in the largest village Kay Kalenge, where the wetting method was taught to all women of the village, who accepted it willingly. The total cyanide content of cassava flour was reduced to below 10 ppm. Fufu from treated flour tasted and stored better than fufu from untreated flour. The mean urinary thiocyanate content of 100 school children reduced from 332 to 130 μmole/L and the number of samples exceeding 350 μmole/L decreased from 26 to 0 during the intervention. No new konzo cases occurred, which included two dry seasons when konzo peaks. Konzo was first identified by Dr. Trolli in 1938 in Popokabaka Health Zone and it has now been prevented for the first time in the same area. The methodology is now in use in Boko Health Zone and we believe it is the most effective way to control konzo in tropical Africa.

1. Introduction

Konzo is an upper motor neuron disease which causes irreversible paralysis mainly in children and women of child bearing age, due to high cyanide intake from consumption of a monotonous diet of bitter cassava (Cliff et al., 1985; Howlett et al., 1990). Konzo occurs amongst very poor rural people in Democratic Republic of Congo (DRC), Mozambique, Tanzania, Cameroon, Central African Republic and has recently been reported in Angola (Allen, 2010). Konzo epidemics occur as a result of (1) war such as the recent civil war in DRC, where people were forced from their homes and had to eat poorly processed bitter cassava from the bush, (2) drought (Cliff et al., 2011; Mlingi et al., 2011) which stresses the cassava plant and causes it to produce much more cyanogen than normal (Bokanga et al., 1994) and (3) as a result of short cut processing methods (Banea et al., 1992). Persistent konzo also occurs in very deprived areas in Mozambique, DRC and Tanzania (Ernesto et al., 2002; Bonmarin et al., 2002; Howlett, 1994).

The total number of reported cases of konzo up to December 2009 from five African countries is 6768, with the largest incidence (3459) in DRC. However this greatly underestimates the true number, given that konzo often occurs during crises such as war and drought and in isolated areas (Cliff, 2010). In 2000 the Ministry of Health in DRC estimated that the total number of konzo cases in DRC was 100,000 (Diasolua Ngudi, 2005). There are 11 provinces in DRC and konzo is present in four, viz Bandundu, Kasai Oriental, Kasai Occidental and South Kivu (Chabwine et al., 2011).

The universal mechanism in animals to detoxify cyanide (CN) is its conversion catalysed by the enzyme rhodanese, to produce thiocyanate (SCN), which is water soluble and removed in the urine. The reaction consumes essential S-containing amino acids methionine and cysteine (cystine) which must be obtained from ingested protein. If there is a shortfall of protein in the diet, such as occurs in these very poor communities where many people have only one meal per day, then priority removal of essential S-containing amino acids to detoxify ingested poisonous cyanide may lead to protein malnutrition and stunting, as has been observed in DRC (Banea Mayambu et al., 2000). Furthermore, if there is a shortage of S-containing amino acids to detoxify ingested cyanide, then this would lead to an increase in the concentration of cyanide in the blood which could cause konzo (Cliff et al., 1985; Cardoso et al., 2004), perhaps via formation of the neurotoxin cyanate (Tor-Agbidye et al., 1999). This is probably the explanation of the occurrence of konzo in areas where people did not have access to animal protein, yet within 5 km there were people of the same ethnic group who did not get konzo because they had access to animal protein from forested areas (Banea Mayambu, 1993) or had access to fish from Lake Victoria (Howlett et al., 1992) or from the sea (Ministry of Health Mozambique, 1984).

A simple wetting method was developed which reduced 3–6-fold the total cyanide content of cassava flour (Bradbury,

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doi:10.1016/j.fct.2012.02.001

2006; Cumbana et al., 2007), and involved mixing the flour with water and standing in the shade for 5 h or in the sun for 2 h (Bradbury and Denton, 2010). This method was acceptable to rural women in field trials in Mozambique in 2005 and required no extra work or equipment (Muquingue et al., 2005; Nhassico et al., 2008). Subsequently the wetting method was taught to 216 rural women in konzo-prone villages in Tanzania using illustrated, laminated posters that explained the wetting method in Kiswahili (Mlingi et al., 2011; Bradbury et al., 2011).

The wetting method is not a substitute for traditional methods used to remove cyanogens from cassava (Cardoso et al., 2005), but should be used in addition to those traditional methods. For example, when total cyanide levels in cassava flour soared during a drought in Mozambique, women processors faced with cyanide intoxication, changed from simple sun drying to heap fermentation, shown to reduce the total cyanide content 2-fold (Cardoso et al., 2005). This change in processing was not sufficient to prevent the occurrence of konzo (Ernesto et al., 2002), however if the wetting method could have been used in villages where there was a peak in the number of cases in 1998–1999 (it was discovered in 2005, Bradbury, 2006), it would have reduced greatly the total cyanide content of flour and may have prevented konzo at that time. The wetting method may also be used where there is doubt about the origin and total cyanide content of cassava roots or cassava flour (Karumba et al., 2009; Bradbury et al., 2011).

In this paper we report a 1.5 years intervention in Kay Kalenge village in Popokabaka Health Zone in Bandundu Province, DRC, where konzo was first reported more than 70 years ago (Trolli, 1938). A preliminary survey of four villages was made in September 2009 and the wetting method was introduced and used by the women of Kay Kalenge in March 2010. Since then there have been no new cases of konzo and urinary thiocyanate levels in the school children have decreased to safe levels.

2. Materials and methods

2.1. Study area

A survey was undertaken in four villages (Kay Kalenge, Indaba, Bilungu and Munkoki) with a total of 2206 inhabitants in the Imbela health area, Popokabaka Health Zone, Bandundu Province, see Fig. 1. The annual rainfall is about 1200 mm and the main dry season is May to September. Konzo was first reported in Popokabaka Health Zone by Trolli (1938) and konzo epidemics have recently been notified in Kahemba (Bonmarin et al., 2002) Feshi, Popokabaka, Boko, Masinanimba and Bulungu Health Zones within Bandundu province.

2.2. Survey of four villages

In September 2009 after discussion with the health zone team and permission of the chiefs of the villages a survey was conducted in four adjacent villages in Popokabaka Health Zone, the largest Kay Kalenge (see Fig. 1) and three others with a total population of 2206, see Table 1. Suspect cases of konzo were examined using the WHO protocol (WHO, 1996). Focus groups carried out a survey of the foods consumed over a period of 1 week, and also obtained information on processing of cassava and its consumption.

2.3. Extended trial in Kay Kalenge

An extended trial was carried out over 1.5 years which included two dry seasons when konzo peaks in the largest village Kay Kalenge. In March 2010 the combined team from PRONANUT in Kinshasa and from Caritas Popokabaka made their second visit to Kay Kalenge and subsequent visits by the combined team were made in August and December 2010 and in May and September 2011. Between visits of the combined team, monthly visits were made by the Caritas team from Popokabaka to support the women of Kay Kalenge. In March 2010 medical examinations were made of the 34 konzo cases in Kay Kalenge village by two physicians. Twenty-eight patients were given antiinflammatories and multi vitamins.

The wetting method (Bradbury, 2006; Cumbana et al., 2007) for the removal of cyanogens from cassava flour involved adding cassava flour to a bowl and marking the level on the inside of the bowl. Water was added with mixing until the level of the wet flour reached the mark on the bowl. The wet flour was then spread in a layer not greater than 1 cm thick on a basket to allow hydrogen cyanide gas to escape to the air and left in the sun for about 2 h (Bradbury and Denton, 2010) or in the shade for about 5 h. In the traditional way the damp flour was mixed with boiling water to produce a thick porridge (fufu) which was eaten with something to give flavour such as pounded, boiled cassava leaves (saka saka). Twelve women leaders of the village were trained to use the wetting method and they each trained 15–20 women of the village. Small training sessions were carried out very early in the morning before the women went to the fields. Each group identified a woman who was responsible for collecting the flour after treatment and in the evening all 12 groups prepared fufu from their treated flour. Illustrated, laminated posters in Kiyaka that describe the wetting method and supplied from Australia were distributed (Bradbury et al., 2011; http://online.anu.edu.au/BoZo/CCDN/). The women accepted the method spontaneously. Concerns raised related to (1) the time required to do the treatment that delayed food preparation for the family, (2) the need for a knife, pan or plastic basin and large plate and (3) the need for additional water which was required if the wet flour was exposed to 2 h in the sun. Very little water was lost by evaporation if the wet flour was left in the shade for 5 h. Water is a very precious commodity in Kay Kalenge. A committee of 12 leading women ensured that every woman in the village was reached and used the wetting method. During the August 2010 visit 10 new women leaders were trained in the wetting method and they trained others. A further training session was carried out in December 2010 and in this way the women of all 320 households in the village learned to use the wetting method. Seventeen focus groups and individual interviews were made involving 303 women to find out their opinions on the properties of fufu prepared from treated and untreated flour and 270 small basins were distributed to households in Kay Kalenge.

2.4. Urinary thiocyanate analysis

One hundred samples of urine were collected randomly from school age children and a record made of their age, sex and whether they were living in a family with a case of konzo or not. Over the five visits there were approximately equal numbers of males and females with more children in the 3–9 age group (65–80 children) than in the 10–14 age bracket. These samples were analysed in Kay Kalenge using the simple picrate kit D1, developed by Haque and Bradbury (1999) and subsequently field tested in Mozambique (Ernesto et al., 2002; http://online.anu.edu.au/BoZo/CCDN/). A colour chart was used with 10 shades of colour from yellow to brown, which correspond to a range of 0–100 mg thiocyanate/L urine = ppm. The results in ppm were multiplied by 17.2 to convert them to μmole thiocyanate/L urine (Haque and Bradbury, 1999).

2.5. Total cyanide analysis

In August 2010 cassava flour samples were taken for analysis just before the use of the flour to prepare fufu from households that had not used the wetting method and from those that had used the wetting method. In subsequent visits flour samples were taken for analysis, just before they were used to prepare fufu. The analyses were done using a simple picrate kit B2 to determine the total cyanide content of cassava flour (Egan et al., 1998; Bradbury et al., 1999) which was subsequently field tested in Mozambique (Cardoso et al., 1998). A protocol was followed that was supplied with the kit (http://online.anu.edu.au/BoZo/CCDN/). A colour chart was used with 10 shades from yellow to brown corresponding to 0–800 mg HCN equivalents/kg cassava flour = ppm.

3. Results

3.1. Survey of four villages

The population and number of konzo cases in the four villages of the survey is shown in Table 1. The total number of konzo cases was 50 in a total population of 2206 with a prevalence rate of 2.3%. Konzo occurred abruptly in less than one day in 90% of cases and over 2–7 days with the remainder. There were no cases of partial improvement after attack and 86% said their condition became worse over time. Some konzo patients were unable to walk (12%), 32% walked with one stick and 56% were visibly spastic but did not use a stick; 14% had difficulty in speaking and 22% had eye trouble. Knee jerk bilateral reflexes occurred in 98% of patients and ankle reflexes were exaggerated bilaterally in 96% of patients. Seventy-eight percent of patients had at least one person with konzo alive or dead in their family. Children over 4 years old and women were most affected; 72% were female; 28% male. The age of onset of the disease was typically 4–15 years. With women, 33% were nursing a baby at the time of the konzo attack. The

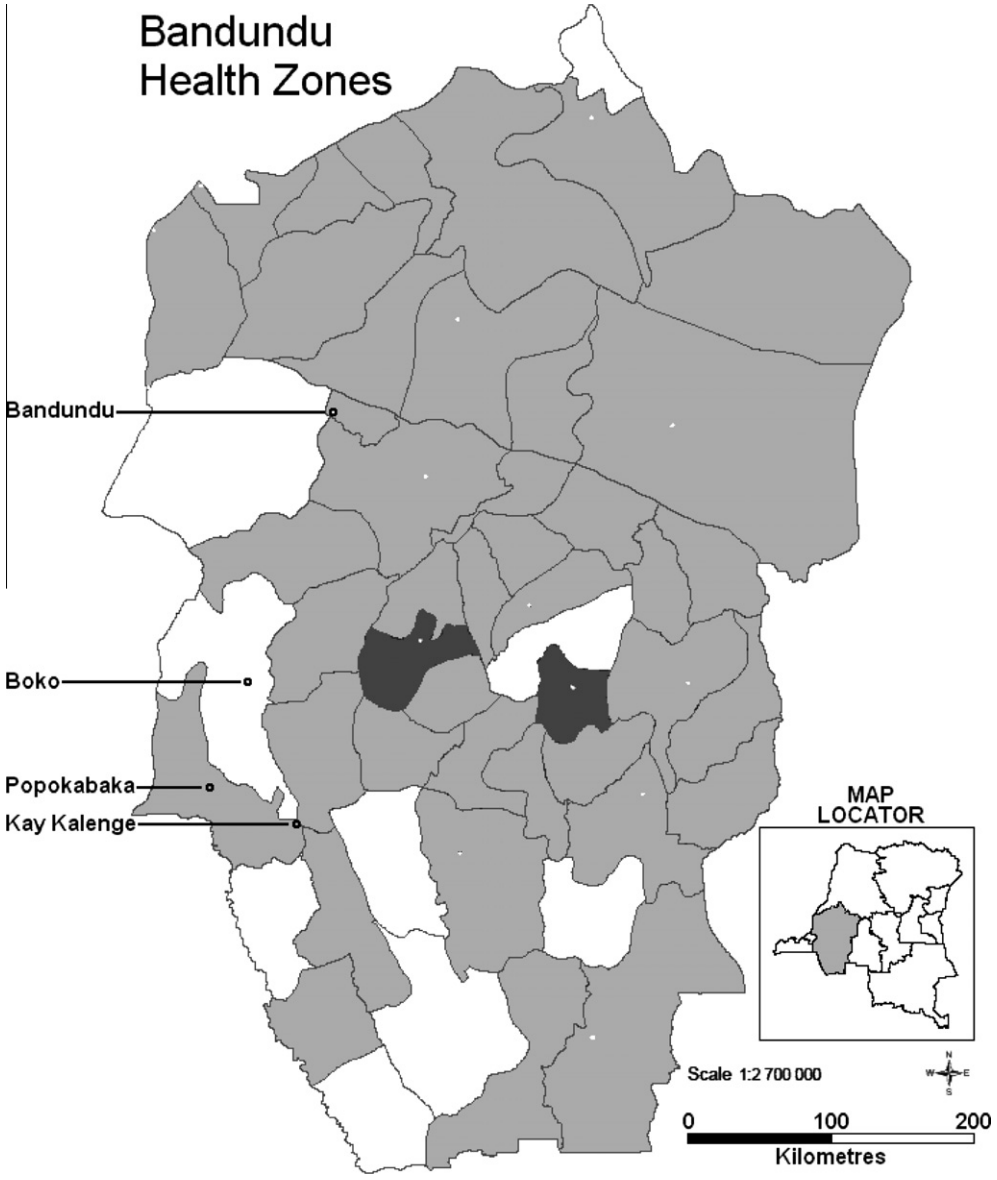

Fig. 1. Map showing health zones of Bandundu Province, DRC, modified from (http://reliefweb.int/sites/reliefweb.int/files/resources/3A4632031B94F342852572DC006BFC2E-ocha_REF_cod070508.pdf), which includes Popokabaka and Boko Health Zones.

Table 1
Number of konzo cases and its prevalence in four villages surveyed.

Village	Population	Number of konzo cases	% Prevalence of konzo
Kay Kalenge	1250	34	2.7
Indamba	511	10	1.9
Bilungu	270	5	1.8
Munkoki	175	1	0.6
Total	2206	50	2.3

annual distribution of konzo cases over the years is shown in Fig. 2 and the seasonal distribution in Fig. 3.

The results of a focus group survey of food consumption and methods of processing showed that one third of households consumed only one meal per day and that cassava is the dominant food source, with very high consumption of fufu made from cassava flour and of pounded, boiled cassava leaves (saka saka). The method of processing cassava roots was to immerse them in a pond of water for only 1–2 days which was thought to be sufficient time to remove cyanogens. People distinguished konzo from other types of paralysis, but most people thought that konzo came from sorcery, although some knew that cyanide from cassava was the cause.

3.2. Extended trial in Kay Kalenge

Throughout the 1.5 years trial (March 2010 to September 2011), there were no new cases of konzo. Since March 2010, 12 women gave birth, and none of them contracted konzo after childbirth. In December 2010, 303 village women were involved in focus group discussions and unstructured interviews to assess the quality of fufu from flour made by the wetting method, see Table 2. In August 2010 the mean total cyanide content (standard deviation in brackets) of nine cassava flour samples from households not using the wetting method was 22(12) ppm, compared with 10(9) ppm from 15 households using the wetting method, a significant reduction ($P < 0.05$) from using the wetting method. Cyanide analyses of 15–30 cassava flour samples after the wetting treatment in December 2010, May 2011 and September 2011 gave mean total cyanide contents of 4(8), 8(7) and 7(5), respectively. The mean urinary thiocyanate contents of school children are given in Table 3 and

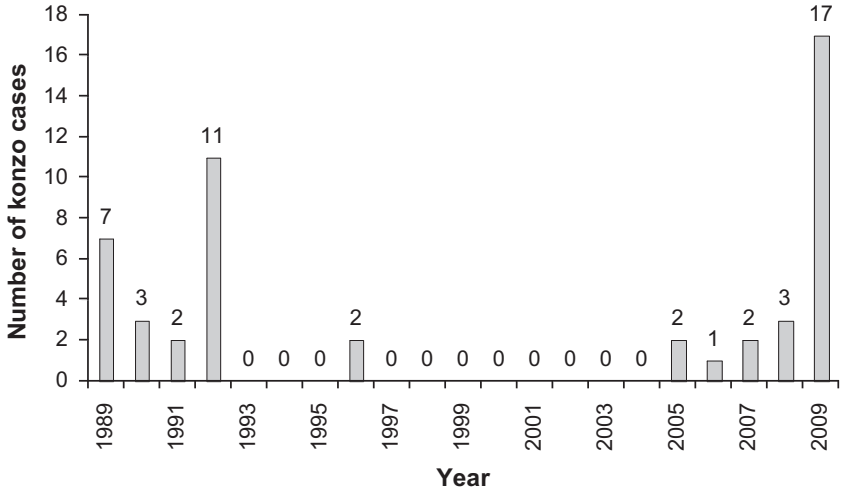

Fig. 2. Annual distribution of konzo cases from 1989 to 2009 in the four villages surveyed.

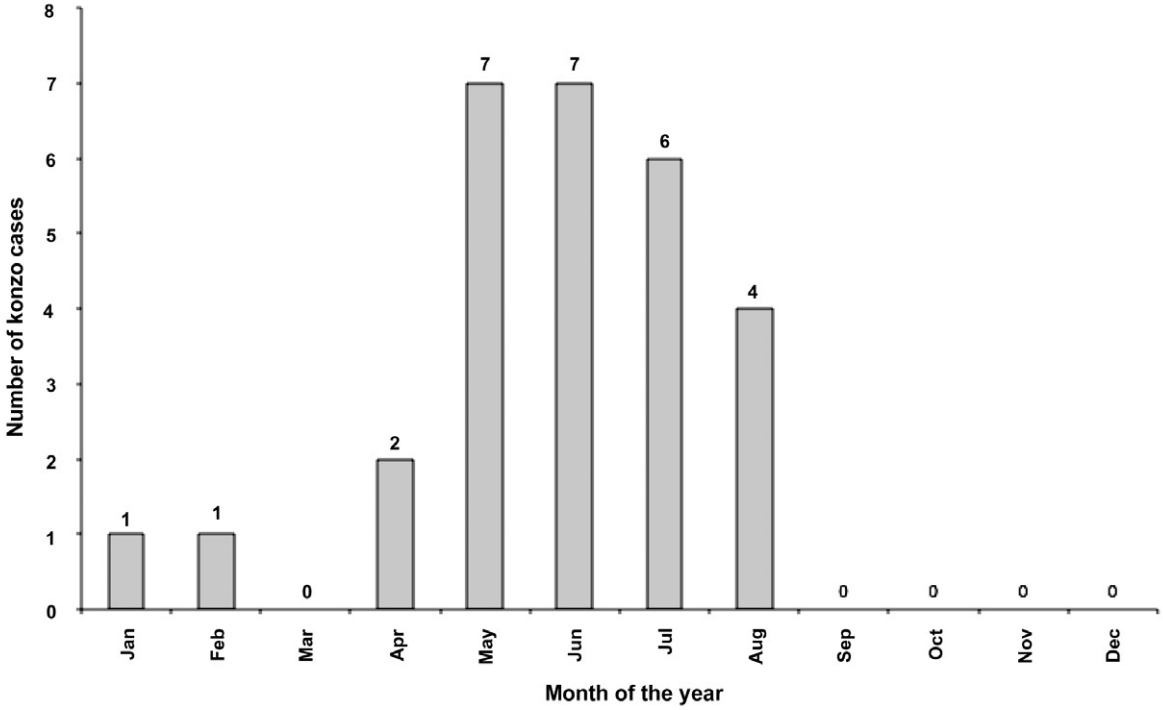

Fig. 3. Seasonal distribution of konzo cases in the four villages surveyed.

the numbers of children with particular levels of urinary thiocyanate content are shown in Table 4 and Fig. 4.

4. Discussion

4.1. Survey of four villages

In September 2009 we made a survey of four villages in Popokabaka Health Zone, the area where konzo was first discovered by Trolli (1938), and found 50 cases of konzo with 12% severely disabled (unable to walk), 32% moderately disabled (needed one stick to walk) and 56% mildly disabled (did not need a stick but had visible spasticity). Another study in Popokabaka Health Zone of 43 konzo cases gave 16% severe, 9% moderate and 74% mild (Diasolua Ngudi et al., 2011). A study of 237 konzo cases in nearby Kahemba zone gave 5% severe, 25% moderate and 70% mild (Bonmarin et al., 2002). Among 116 patients in Tanzania 5% of cases were severe, 28% moderate and 67% mild (Howlett et al., 1992). Because of

Table 2
Quality characteristics of "old fufu" and "new fufu".[a]

Old fufu	New fufu
Bad taste[b]	Good taste
Heavy	Light
Rubbery	Not rubbery
Not comparable with chikwangue[c]	Similar to chikwangue[c]
Can be stored for only 6–12 h	Stored for up to 3 days

[a] Fufu prepared from cassava flour after the wetting method treatment is called "new fufu"and that from cassava flour not treated by the wetting method is called "old fufu".
[b] Because of a bitter taste due to residual linamarin present, which is bitter (King and Bradbury, 1995).
[c] Chikwangue is made by soaking roots in water for 3–5 days, squeezing to remove water, pounding, removing fibres, wrapping the mash in leaves and steaming. It can be stored for up to 1 week (Banea et al., 1992).

Table 3
Mean urinary thiocyanate content (μmole/L urine) of 100 school children, March 2010 to September 2011.

Date of visit	Mean thiocyanate content of urine (μmole/L urine)[a]
March 2010	332 (280)
August 2010	213 (172)
December 2010	101 (139)
May 2011	132 (89)
September 2011	130 (84)

[a] Standard deviation shown in brackets.

Table 4
Numbers of urinary thiocyanate samples in each level, from 100 Kay Kalenge school children.[a]

Urinary thiocyanate (μmole/L)	Numbers of school children in				
	March 2010	August 2010	December 2010	May 2011	September 2011
0	1	1	16	6	3
17	4	3	26	6	7
34	6	6	8	7	7
69	2	9	7	9	13
103	13	15	19	25	24
172	25	38	13	37	38
344	25	21	8	10	8
688	18	6	3	0	0
1032	6	1	0	0	0

[a] At each visit 100 urine samples were analysed from 100 school children.

the reasonable agreement between these four sets of results mean values and standard deviations in brackets, were calculated as follows: severely disabled 10(5)%, moderately disabled 24(10)% and mildly disabled 66(8)%. The age of onset of konzo was typically 4–15 years for children who were most affected, as were women of child bearing age. Overall there were 72% females and 28% males, which agrees with 77% females (Diasolua Ngudi et al., 2011). However the ratio of females to males is very variable which was considered by Howlett (1994) to be due to local unknown factors (Mlingi et al., 2011). With young women, 33% were nursing a baby at the time they contracted konzo. In Kahemba, 36 of the 37 women for whom information was available developed konzo within a year of delivery and only one developed konzo during pregnancy (Bonmarin et al., 2002).

The incidence of konzo over the years (Fig. 2) shows an absence of cases between 1997 and 2004 and peaks in 1992 and 2009, which is quite different from other results for Popokabaka Health Zone which peak in 1998 and show small numbers from 1980 to 2003 (Diasolua Ngudi et al., 2011). Konzo incidence over the years appears to be very dependent on local factors. These results, together with those of Bonmarin et al., (2002) for Kahemba and Chabwine et al., (2011) for Burhinyi in South Kivu, show that persistent konzo is occurring over the years in Bandundu and South Kivu provinces in DRC. In Fig. 3, konzo is shown to occur mainly from April to August which corresponds with the dry season and the peak harvesting of cassava (Bonmarin et al., 2002; Chabwine et al., 2011). The good correlation between peak consumption of cassava, (hence peak cyanogen intake) and incidence of konzo was a foundational argument linking the incidence of konzo with cyanide overload (Ministry of Health Mozambique, 1984).

The food consumption of these very poor rural people, one third of whom have only one meal per day, show an overwhelming reliance on cassava roots processed to flour and consumed as a thick porridge (fufu) and pounded, boiled cassava leaves (saka saka). A protein source used much less frequently was ground nuts. The high protein, vitamin and mineral content of cassava leaves makes a good nutritional balance with the very starchy cassava root product (fufu) (Achidi et al., 2005; Bradbury and Denton, 2011), but the protein is deficient in S-containing amino acids, methionine and cysteine (Diasolua Ngudi et al., 2003), that are needed to detoxify cyanide to thiocyanate. Furthermore these key nutrients are partially decomposed by boiling of pounded cassava leaves in water, which is used to remove cyanogens (Diasolua Ngudi et al., 2003; Bradbury and Denton, 2011). Diasolua Ngudi et al. (2011) also found a very great reliance on cassava in the form of fufu and saka saka. The combination of high cyanogen intake and shortage of S-containing amino acids needed to detoxify cyanide, increases the blood cyanide level and very likely triggers konzo (Cliff et al., 1985).

4.2. Extended trial in Kay Kalenge

In March 2010 the wetting method to remove cyanogens from flour was taught to the women of Kay Kalenge village and was readily accepted, although its use did cause some time delay in food preparation and required a bowl, 270 of which were supplied later. Two more training sessions were given later, so that all 320 households learned the wetting method. Visits of the full team every four months and intervening monthly visits by the Caritas team ensured continued use of the wetting method. To ensure success of the wetting method in controlling konzo it is important that (1) the women understand that konzo comes from cyanogens (poisons) present in cassava flour, (2) they are trained to use the wetting method to remove cyanogens and (3) they are commited to using it on a regular basis.

There were no new cases of konzo in the village during the extended trial, which included two dry seasons when konzo peaks (Fig. 3). This compares very favourably with the situation in 2009 when there were many cases of konzo (Fig. 2) and there would have been at least one case of konzo after childbirth.

An attractive feature of the fufu made from flour treated by the wetting method (new fufu) is that it has a much better flavour than fufu made from untreated flour (old fufu), which has a bitter taste due to residual bitter linamarin in the fufu (King and Bradbury, 1995). In Table 2 a comparison is made of the quality characteristics of old and new fufu. New fufu tastes good, is not "heavy" or "rubbery", is similar to chikwangue and may be stored for up to 3 days, hence the wetting method does not need to be used every day.

The wetting method produced a considerable reduction in the mean total cyanide content (Section 3.2) as was previously observed in Tanzania (Mlingi et al., 2011). Furthermore, the mean total cyanide contents of cassava flour samples after the introduction of the wetting treatment method were all lower than the FAO/WHO safe limit of 10 ppm (FAO/WHO, 1991). The short cut immersion in water for only 1–2 days resulted in cassava flour with a high cyanide content that leads to the onset of konzo (Banea et al.,

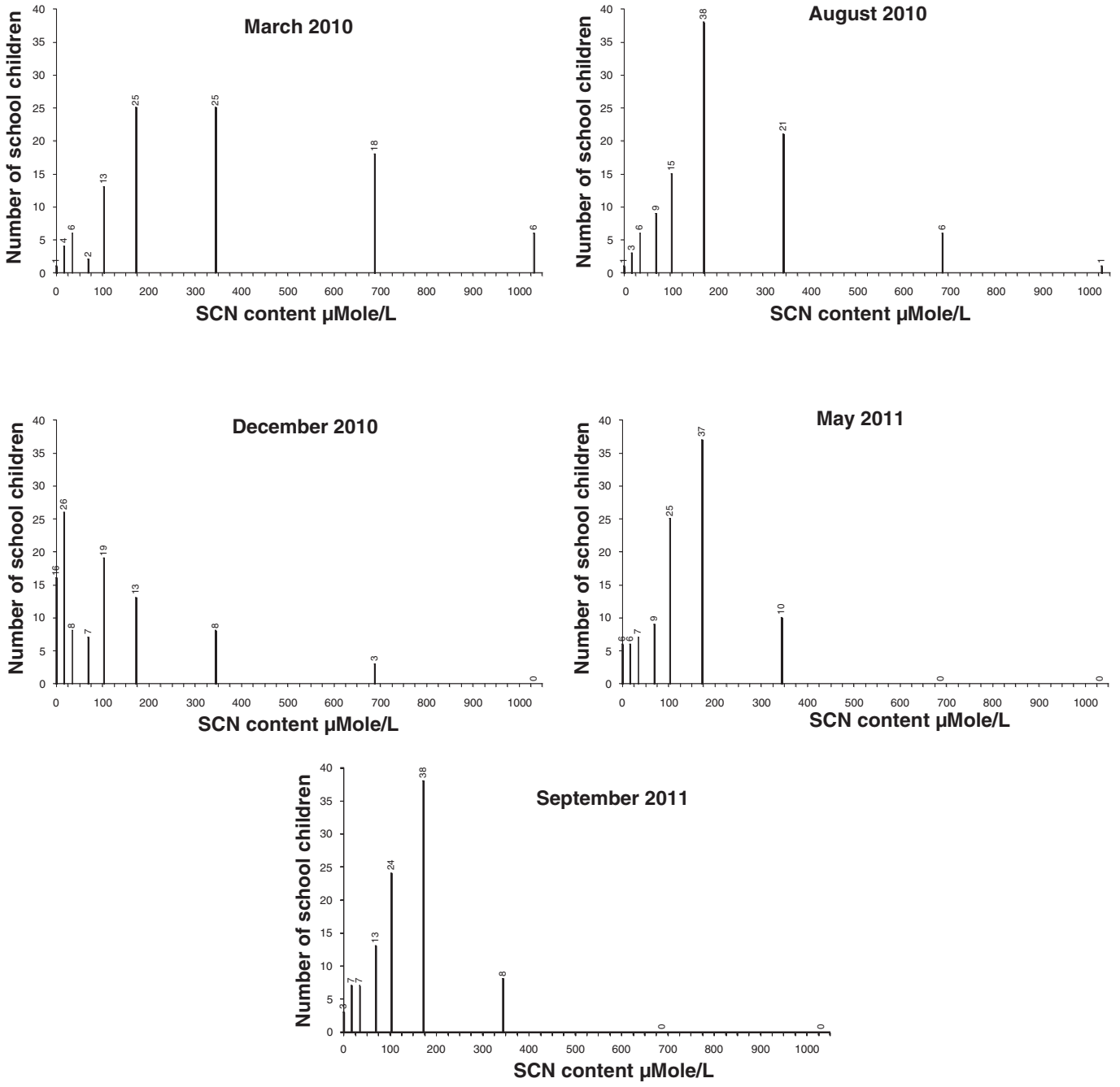

Fig. 4. Graphs of the thiocyanate content (µmole/L urine) of 100 samples of urine of school children from Kay Kalenge village in March, August and December 2010 and May and September 2011.

1992). This was also observed in a recent study in three villages in Boko Health Zone.

Urinary thiocyanate results on urine samples from 100 Kay Kalenge school children, showed that there were no consistent differences in mean thiocyanate levels between (1) children who came from families with a case of konzo as compared with children from families with no case of konzo, (2) boys and girls and (3) lower age (3–9 years) and older age (10–14 years) children. Mean urinary thiocyanate results (Table 3) from 100 school children showed that in March 2010 (before the intervention) the value of 332 µmole/L urine was typical of that found in a konzo outbreak in Mozambique (Ernesto et al., 2002). A reduction occurred during the intervention to 100 µmole/L in December 2010, because many children were not eating cassava during the rainy season, (Diasolua Ngudi et al., 2011), followed by an increase to 130 µmole/L in May and September 2011. The results in Table 4 and Fig. 4 show that the number of school children with levels >350 µmole/L has decreased from 24 before the intervention in March 2010 to 0 by May 2011, and the removal of school children with very dangerous levels of 1032 µmole/L by December 2010.

The geographical spread of konzo is increasing in (1) DRC, where it had not previously been reported in South Kivu (Chabwine et al., 2011), (2) Mozambique, where it has spread to Zambezia province (Cliff et al., 2011), (3) Tanzania where it was first found in Mara region in the north and more recently in Mtwara and Ruvuma regions in the south (Mlingi et al., 2011), (4) Central African Republic and Cameroon (Ciglenecki et al., 2011) and (5) Angola, just recently reported (Allen, 2010). The

spread of konzo in Africa is related to increased production of cassava to feed a rapidly increasing population, its replacement of other crops because of its agricultural advantages and its introduction into new areas where people have no knowledge of the processing required to remove cyanogens (Nhassico et al., 2008). It is important that the spread of konzo in Africa be stopped and the disease eliminated. The methodology to do this is now available.

5. Conclusion

The use of the wetting method on cassava flour by the women of Kay Kalenge village over 1.5 years including two dry seasons has resulted in lowering the cyanide content of cassava flour to safe levels, produced tastier fufu, reduced the thiocyanate content of urine from school children to safe levels and prevented new cases of konzo. Konzo was first identified in 1938 in Popokabaka Health Zone (Trolli, 1938) and it has now been prevented for the first time in the same area. This methodology is being used in three villages where konzo is prevalent in Boko Health Zone (see Fig. 1) with funding from the Australian Agency for International Aid (AusAID), and we believe it is the way to control konzo.

Conflict of Interest

The authors declare that there are no conflicts of interest.

Acknowledgements

We thank the women of Kay Kalenge Village for wholeheartedly accepting and using the wetting method to remove cyanide from cassava flour which has prevented the occurrence of new cases of konzo. We thank also the health care staff of Popokabaka Health Zone and Masina Health Centre for their collaboration and encouragement of the women of Kay Kalenge.

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