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Persistent konzo and cyanogen toxicity from cassava in northern Mozambique

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Abstract

We aimed to detect new cases of konzo and monitor cyanogen exposure from cassava flour in communities previously affected by konzo epidemics in Nampula Province, northern Mozambique. Other objectives were to detect subclinical upper motor neuron damage in schoolchildren and test a new kit to measure urinary thiocyanate concentration. In 1999 and 2000, we carried out active and passive case detection for konzo in Memba and Mogincual Districts. In July and October, 1999, we collected cassava flour from 30 houses in three communities and measured cyanogen concentrations with a picrate kit. In October 1999, we examined all schoolchildren in three communities for ankle clonus and measured urinary thiocyanate concentration in thirty schoolchildren in each of five communities with a picrate kit. We found 27 new cases of konzo in Mogincual District. Mean total cyanogen concentrations in cassava flour varied between both seasons and years, but were always high, ranging from 26 to 186 ppm. Very high mean levels at three sites in November 1998 and July 1999 were probably due to low rainfall in the 1997–1998 season. The proportion of schoolchildren with ankle clonus varied from 8 to 17%. The new picrate kit for urinary thiocyanate worked well; mean concentrations in schoolchildren ranged from 225 to 384 μmol l^{-1}. Konzo and sub-clinical upper motor neuron damage persist in poor rural communities in northern Mozambique, associated with high cyanogen concentrations in cassava flour and high urinary thiocyanate concentrations in schoolchildren.

Keywords: Konzo; Ankle clonus; Cyanogens; Cassava; Thiocyanates; Picrate; Mozambique

1. Introduction

Konzo, an upper motor neuron disease characterized by irreversible spastic paraparesis, was first

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observed in the former Belgian Congo (Trolli, 1938). In 1981, epidemic konzo emerged in northern Mozambique, associated with consumption of bitter cassava during a severe drought (Ministry of Health, Mozambique, 1984). In 1992–1993, war caused a further large konzo epidemic in the same province (Cliff et al., 1997). Konzo has now also been reported from Tanzania, the D.R. Congo, Central African Republic, and Cameroon (Howlett et al., 1990; Tylleskar et al., 1992, 1994; Lantum, 1998).

In all these reports, konzo has been associated with high and sustained cyanogen intake at sublethal concentrations from cassava flour. The major cyanogen in cassava is the cyanogenic glucoside (linamarin). During processing, linamarin is rapidly hydrolysed (catalyzed by the enzyme linamarase that is also made by the plant) to glucose and acetone cyanohydrin. The latter is unstable in neutral/alkaline solution and breaks down to hydrogen cyanide and acetone. Less than one half of ingested linamarin is broken down to cyanide in the body and converted to thiocyanate, which is excreted in the urine together with unchanged linamarin (Carlsson et al., 1999). Ingested acetone cyanohydrin is broken down in the gut to cyanide.

Measurement of the total cyanogen and acetone cyanohydrin contents of cassava flour gives a measure of cyanogen hazard, whilst urinary thiocyanate concentration indicates the recent intake of cyanogen by the individual (Carlsson et al., 1999). These measurements have been greatly expedited by the recent development of simple kits (Egan et al., 1998; Bradbury et al., 1999; Haque and Bradbury, 1999).

We aimed to detect new cases of konzo and monitor cyanide exposure from cassava flour in selected communities previously affected by konzo epidemics. These communities are still dependent on bitter cassava as their main staple, which they harvest from August to October. Other objectives were to detect subclinical upper motor neuron damage, as manifested by ankle clonus, in schoolchildren and to test a new picrate kit for measuring urinary thiocyanate concentration (Haque and Bradbury, 1999).

2. Materials and methods

2.1. Konzo case detection

In October 1999, we visited Memba and Mogincual Districts in Nampula Province, as they had reported most cases in the 1981–1982 drought-related and 1992–1993 war-related konzo epidemics, respectively (see Fig. 1). In Memba, we chose Cava and Acordos de Lusaka and in Mogincual, Mujocojo, for case detection, as these communities had previously reported a high konzo incidence. In Mogincual, we added Maculani and Namichire, as they had recently reported new cases. In July 2000, we visited the Mogincual sites again to bring patients in to a rehabilitation center in Liupo, the district capital. In November 2000, we examined patients in this center.

2.2. Cassava flour collection

In July 1999, we collected 30 cassava flour samples from houses in Mujocojo and Terrene-A in Mogincual District and Acordos de Lusaka in Memba District. All these sites had been previously monitored. In November 1998 and October 1999 collections were also made at Cava in Memba District. We used the same house selection method and questionnaire as previously (Cardoso et al., 1998).

2.3. Ankle clonus measurement and urine collection in schoolchildren

All school children in Mujocojo (84), Acordos de Lusaka (149), and Cava (142) were examined for ankle clonus by two examiners using the same methods as previously (Cliff et al., 1999). Urine samples for thiocyanate analysis were obtained from all students with ankle clonus. Children were lined up by height in two queues, according to sex. To obtain controls without clonus, we chose the next child of the same sex. To collect a total of thirty samples we chose additional controls of the same sex and similar

height. Urine samples were also obtained from thirty school children at both Terrene-A and Namichire.

2.4. Laboratory methods

Cassava flour samples were analyzed for total cyanogen using the picrate kit method (Egan et al., 1998; Bradbury et al., 1999) which we have used previously in the same communities (Cardoso et al., 1998, 1999; Ernesto et al., 2000). Those collected in October 1999 were also analyzed for (acetone cyanohydrin + HCN/CN^-). Urine samples were stored at room temperature for up to 30 h and refrigerated at 2–4 °C for up to 24 h before analysis and the thiocyanate content was stable under these conditions (Haque and Bradbury, 1999). Single analyses of thiocyanate in urine samples were made using a new picrate kit method and the thiocyanate content (μmol l^{-1}) obtained by multiplying the thiocyanate content in ppm by 17.2 (Haque and Bradbury, 1999).

3. Results

3.1. Konzo case detection

Twenty seven new konzo cases, with onset since 1996, were found in Mogincual District: Liupo (3), Maculani (8), Mujocojo (7), Namichire (9). Onset was spread over the months and years, beginning in December 1996. Seventeen cases were in children (including 5-year-old male identical twins), eight in women of child-bearing age and two in adult men. Patients all had the characteristic clinical features of konzo.

3.2. Total cyanogen and (acetone cyanohydrin + HCN/CN^-) contents of cassava flour

The mean values for total cyanogen over 30 samples at each location are shown in Table 1 together with the data from our previous monitoring. In October 1999, the total cyanogen content in Mujocojo is significantly lower than that at

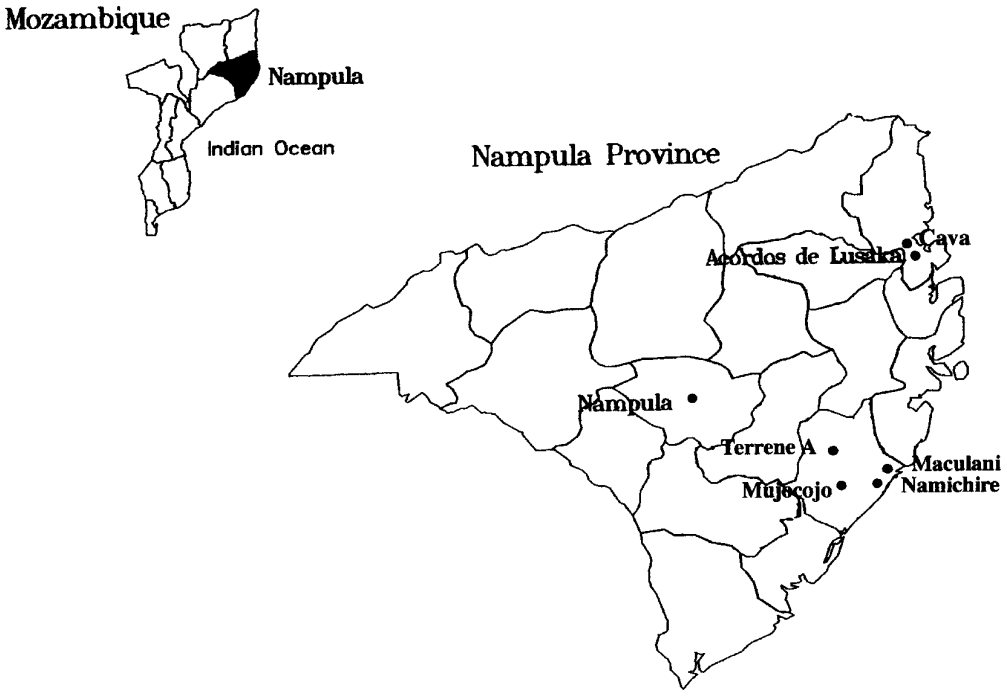

Fig. 1. Map of Mozambique (inset) and of Nampula Province showing the location of study sites.

Table 1
Total cyanogen and (acetone cyanohydrin + HCN/CN^-) results in mg HCN equivalents/kg flour(ppm) for cassava flour from four locations over 1996–1999

Year and month[a]	Total cyanogen results in ppm			
	Mujocojo	Terrene-A	Acordos de Lusaka	Cava
1996 October[b]	49(29)	43(30)	–	–
1997 September[c]	26(23)	13(19)	67(39)	–
1998 November[d]	109(71)	42(38)	138(69)	110(71)
1999 July	164(96)	186(79)	94(85)	–
1999 October	26(20)	38(37)	57(53)	42(28)
1999 October (Acetone cyanohydrin + HCN/CN^-; ppm)	8(8)	9(9)	7(9)	8(5)

All results are the mean of 30 samples; standard deviations in brackets.
[a] Annual rainfall in Mogincual District (at Liupo) was 880 mm in 1997–1998 compared with an average annual rainfall of 1100 mm.
[b] Cardoso et al., (1998).
[c] Ernesto et al., (2000).
[d] Cardoso et al., (1999).

Acordos de Lusaka and Cava. The amount of (acetone cyanohydrin + HCN/CN^-) is uniformly low in all flour samples analyzed in October 1999 and amounts to about 20% of the total cyanogen present.

Cardoso et al. (1998) reported that the two major processing methods of peeled cut roots in these communities are sun drying and heap fermentation. In this study, 78 sun dried and 34 heap fermentation samples gave mean total cyanogen contents of 46(42) and 28(27) ppm, respectively ($P = 0.015$). The results in Table 2 show that there was a strong preference for heap fermentation in July, whereas in October there was a preference for sun drying.

3.3. Ankle clonus and urinary thiocyanate in schoolchildren

The proportion of school children with ankle clonus varied from 8–17%. The picrate kit method for urinary thiocyanate worked well. Mean urinary thiocyanate concentrations (μmol l^{-1} with standard deviations in brackets) in schoolchildren from Acordos de Lusaka, Cava, Mujocojo, Terrene-A and Namichire were 362(346), 339(358), 225(190), 384(230) and 298(168), respectively. These high values were consistent with chronic cyanogen exposure. The overall mean urinary thiocyanate concentrations in children with and without clonus were not significantly different.

4. Discussion

Konzo has re-emerged and is now persistent in parts of Mogincual District. Persistent or sporadic

Table 2
Numbers of cassava flour samples processed by sun drying and heap fermentation in July and October 1999

Location	Processing method	Number of flour samples processed	
		July	October
Mujocojo	Sun drying	4	17
	Heap fermentation	26	13
Terrene-A	Sun drying	1	26
	Heap fermentation	28	4
Acordos de Lusaka	Sun drying	9	23
	Heap fermentation	19	7

Processing methods defined as sun drying and heap fermentation using the classification given in Cardoso et al., (1998).

konzo has also been reported from Cameroon, Central African Republic, and Tanzania (Lantum, 1998; Tylleskar et al., 1994; Howlett, 1994). Previously, konzo has been mostly epidemic in Mozambique, although sporadic cases have also been reported (Cliff, 1994; Cliff et al., 1997). The onset throughout the year contrasts to epidemic konzo, which peaks at the time of the cassava harvest (Ministry of Health, 1984; Cliff et al., 1997). Possibly, the retrospective histories were unreliable regarding the month of onset. Persistent konzo may, however, be partly due to patients consuming cassava with a high cyanogen content outside the harvest season.

The reasons for the reemergence of konzo in Mogincual District after some years without case reports are not clear. Possibly, konzo had continued unnoticed in these rural communities in the intervening years. Konzo may, however, have reemerged, because of adverse agricultural conditions. Isolated rural communities in Mogincual have received few inputs to help them recover from the devastating effects of war. A project to teach better cassava processing methods had functioned in the District from 1994 to 1996, when funding stopped.

The mean values of total cyanogen in cassava flour are high in all locations (Table 1), compared with the World Health Organization safe level of 10 ppm (FAO/WHO, 1991). The large variability over time is probably due to variations in rainfall and processing methods. Low rainfall increases the cyanogen content of cassava roots (Bokanga et al., 1994) and processing by sun drying removes less cyanogens than does heap fermentation (Essers et al., 1995; Cardoso et al., 1998; Ernesto et al., 2000).

Concentrations were lower in the harvest months (August to October) of 1996, 1997 and 1999, years of normal or high rainfall during the previous rainy season. The very high concentrations found in November 1998 and July 1999 are most probably due to the fact that the roots from which the flour was produced were grown during a period of low rainfall (Cardoso et al., 1999).

Processing methods also varied with the seasons. In October 1999, the lower total cyanogen content in cassava flour in Mujocojo than at Acordos de Lusaka and Terrene-A may be due to the greater use of heap fermentation rather than sun drying at Mujocojo. Mujocojo was the only one of these sites in which konzo cases with onset in the previous 2 years were found. Perhaps this had caused flour producers in Mujocojo to be more careful to remove cyanogen during processing rather than reverting to sun drying in October (Table 2).

The presence of ankle clonus in 8–17% of schoolchildren suggests that subclinical upper motor neuron damage persists in these communities. Urinary thiocyanate concentrations in schoolchildren were also high, consistent with chronic cyanide intoxication.

In conclusion, this study has shown that konzo and signs of subclinical upper motor neuron damage persist in poor rural communities consuming cassava flour containing high amounts of cyanogen. These communities should be targets of strategies to eliminate konzo and poverty in Africa.

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