Konzo and continuing cyanide intoxication from cassava in Mozambique

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Abstract

In Mozambique, epidemics of the cassava-associated paralytic disease, konzo, have been reported in association with drought or war: over 1100 cases in 1981, over 600 cases in 1992–1993, and over 100 cases in 2005. Smaller epidemics and sporadic cases have also been reported. Large epidemics have occurred at times of agricultural crisis, during the cassava harvest, when the population has been dependent on a diet of insufficiently processed bitter cassava. Konzo mostly affects women of child-bearing age and children over 2 years of age.

When measured, serum or urinary thiocyanate concentrations, indicative of cyanide poisoning, have been high in konzo patients during epidemics and in succeeding years. Monitoring of urinary thiocyanate concentrations in schoolchildren in konzo areas has shown persistently high concentrations at the time of the cassava harvest. Inorganic sulphate concentrations have been low during and soon after epidemics.

Programmes to prevent konzo have focused on distributing less toxic varieties of cassava and disseminating new processing methods, such as grating and the flour wetting method. Attention should be given to the wider question of agricultural development and food security in the regions of Africa where dependence on bitter cassava results in chronic cyanide intoxication and persistent and emerging konzo.

1. Introduction

Konzo is characterized by the sudden onset of irreversible spastic paraparesis, associated with prolonged high dietary cyanogenic glucoside consumption and a diet deficient in sulphur amino acids (Howlett et al., 1990; Tylleskär et al., 1993). The cyanogenic glucosides originate from insufficiently processed roots of bitter cassava. Since 1981, poor rural communities in some cassava staple areas of Mozambique have suffered from konzo both in epidemic and persistent form.

2. Material and methods

This review of konzo in Mozambique draws on the published literature and unpublished data, gathered by the authors. Methods used to determine urinary thiocyanate concentration and ankle clonus in schoolchildren are detailed in the cited papers (Casadei et al., 1990; Cliff et al., 1985, 1999; Ernesto et al., 2002). Variations around the mean were expressed in different ways in the different data sets and were not always available. Since 1999, we have used a picrate kit to measure urinary thiocyanate (Haque and Bradbury, 1999) and the total cyanogenic potential in cassava products (Egan et al., 1998; Bradbury et al., 1999).

3. Konzo in Mozambique

3.1. Occurrence and patient characteristics

The Ministry of Health (1984) first reported konzo in Mozambique in 1981, when a large epidemic of over 1100 cases occurred in northern Nampula Province. District health authorities also reported cases in neighbouring Chiure in Cabo Delgado Province. The epidemic was associated with a severe drought.

Following this larger epidemic, smaller epidemics were reported through the 1980s in the same and other districts of Nampula (Essers et al., 1992; Cliff, 1994). From 1984 to 1992, war engulfed Nampula, and documentation of the epidemics was incomplete.

In 1992–1993, a further large epidemic of over 600 cases occurred further south in the province (Cliff et al., 1997). In 1992, the disease affected communities displaced by war, and in 1993, those returning home after the war ended.

New cases of konzo continued to be reported in previously affected areas of Nampula (Ernesto et al., 2002). In 2005, an outbreak of 13 cases occurred in Membia District, associated with drought. Konzo is now persistent in Nampula, with sporadic cases still being reported.
In 2000, konzo emerged in Zambézia Province, further south, when 10 cases were reported from Ile District. In 2005, an epidemic with over 100 reported cases occurred in a large area in the central part of the province. The epidemic was associated with drought. Zambézia continues to report sporadic cases.

Over the 28 years since it was first reported in Mozambique, konzo has extended its geographical range. Fig. 1 shows that konzo has been reported from more districts in the decade 2000–2009 than in the decade 1980–1989.

In all epidemics, the clinical picture has been monotonous, with a presentation of irreversible non-progressive symmetrical spastic paraparesis of acute onset and varying severity.

Konzo has predominantly affected women of child-bearing age and children over 2 years of age. Multiple cases often occur in the same household and now cases are passing down through generations.

Serum or urinary thiocyanate concentrations have always been high in konzo patients at the time of epidemics. In the 1981 epidemic, the mean serum concentration ± SEM registered in 246 specimens was 329 ± 8 μmol/l (Ministry of Health, 1984). In Murrupula in 1982, a mean ± SD of 195 ± 39 μmol/l was registered in December, 2 months after the epidemic peak (Essers et al., 1992).

Table 1 shows the urinary thiocyanate concentrations in patients with konzo in two districts in Nampula Province and two sites in Mocuba District in Zambézia Province between 2005 and 2006. In 2005, a drought year, all the patients had recently acquired konzo. In 2006, there was no drought and no new cases were found. Nonetheless, the patients still had high concentrations of urinary thiocyanate. The highest mean ± SEM concentration of 479 ± 70 μmol/l was found in 12 patients in Mogincual District in 2006. This district has suffered from persistent konzo since the war-induced epidemic of 1992–1993.

3.2. Underlying causes of konzo

Epidemics have mostly occurred during agricultural crises, peaking at the time of the cassava harvest, when the population has been dependent on a diet of insufficiently processed bitter cassava.

Cassava is the main staple in these areas and is harvested from August to October. Bitter cassava, which is high in cyanogenic glucoside content, predominates. Communities process the root to lower the cyanogenic glucoside content using a variety of methods. The bulk of the harvest is processed by sun-drying for several weeks, but concentrations remain high as it is an inefficient method. Heap fermentation is also used. The roots are then pounded to produce flour, which is cooked as a stiff porridge. Although the resulting flour has lower total cyanogenic potential, it is still unsafe when the initial concentration in the root is high (Cardoso et al., 2005). Our previous studies have shown average total cyanogenic potential of 40–46 mg HCN equivalents/kg flour (fresh weight) in normal years (Cardoso et al., 1998). In years of low rainfall, the average total cyanogenic potential of cassava flour increases to >100 mg HCN equivalents/kg (fresh weight) (Cardoso et al., 2005), more than 10 times the WHO safe level of 10 mg total HCN/kg (FAO/WHO, 1991).

The underlying causes of the konzo epidemics in Mozambique have varied. When due to drought, as in the first large epidemic, the cassava root contains a higher concentration of cyanogenic glucosides. Women take short cuts in processing, as they are hungry and do not have time to sun-dry for several weeks. They may shorten the sun-drying time or use the inefficient method of pounding and sun-drying the pieces for 1 day. Because other crops fail in drought, communities become more dependent on cassava, as it is often the only crop to survive (Ministry of Health, 1984).

In the most recent epidemics in Zambézia and Nampula, both drought and commercialization have contributed. In Zambézia, communities sold their cassava to neighbouring drought-stricken Malawi, and were then caught short when their own crop failed. Our investigation of these cases showed that many families had purchased dried roots in local markets. In Nampula, in nine households with konzo cases, who had purchased roots or flour, the mean total cyanogenic potential of the flour was 145 mg HCN equivalents/kg (fresh weight). When due to war, lack of other foods and shortcuts in processing contributed (Cliff et al., 1997).

3.3. Cyanide intoxication in konzo-affected communities

In the first large epidemic in Mozambique, 22 community controls also had high serum thiocyanate concentrations, with a mean of 288 μmol/l (Ministry of Health, 1984). This is well above the mean concentration of 42.5 μmol/l recorded in normal Swedish non-smokers (Lundquist et al., 1979).

Cyanide intoxication in the community at the time of the cassava harvest has persisted along the years. Monitoring of urinary thiocyanate concentration in schoolchildren has consistently shown high levels.

Fig. 2 shows the mean urinary thiocyanate concentrations in schoolchildren in the village of Miaja (also known as Acordos de Lusaka) along the years from June 1982 to October 2003 (Casadei et al., 1990; Cliff et al., 1986, 1999; Ernesto et al., 2002, unpublished data). The village had first been chosen for study as it was severely affected in the 1981 epidemic with an incidence rate of 34 cases/1000 (Ministry of Health, 1984). Four cases were detected in 1982, when the mean concentration of 1175 μmol/l in September was extremely high, compared to a mean, in normal Swedish non-smokers, of 43.0 μmol/l (Lundquist et al., 1979). Values peaked again at the time of the cassava harvest the following year, with a high of 673 μmol/l. No new cases were reported, probably because the drought had passed and the community had access to other food sources. By 1984, concentrations had fallen to near normal values.

No measurements were taken for the next 9 years, owing to war. In July 1993, before the harvest, the geometric mean concentration was 113 μmol/l (Cliff et al., 1999), a concentration still indicative of cyanide intoxication. When next measured in October 1997, the mean concentration was high at 512 μmol/l. Over the next 5 years, concentrations fell to 130 μmol/l in October 2003. The fall coincided with a decline in cassava consumption due to an epidemic of brown streak virus in cassava. No new cases have been reported in this village since the 1980s.
Table 2 shows that urinary thiocyanate concentrations have been high in schoolchildren in other konzo-affected sites, both during and after konzo outbreaks. In 1993, the year of a konzo outbreak in Mogincual District, the concentration of linamarin, the main cyanogenic glucoside present in cassava, was also measured and was high at 80 ± 9 µmol/l (Cliff et al., 1997).

Table 3 shows that mean urinary inorganic sulphate concentrations in schoolchildren in konzo-affected areas are low, particularly during epidemics. In 1983, the concentrations in the previously

Table 1

<table>
<thead>
<tr>
<th>Location</th>
<th>Konzo occurrence</th>
<th>Urinary thiocyanate concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Year (month)</td>
<td>Mean ± SEM (µmol/l)</td>
</tr>
<tr>
<td>Nampula Province</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 12)</td>
<td></td>
<td>479 ± 70</td>
</tr>
<tr>
<td>(n = 12)</td>
<td></td>
<td>528 ± 137</td>
</tr>
<tr>
<td>(n = 10)</td>
<td></td>
<td>380 ± 98</td>
</tr>
<tr>
<td>Zambézia Province, Mocuba District</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caiave (n = 27)</td>
<td>Epidemic 2005</td>
<td>2005</td>
</tr>
<tr>
<td></td>
<td></td>
<td>272 ± 33</td>
</tr>
<tr>
<td>Caiave (n = 25)</td>
<td>Epidemic 2005</td>
<td>2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>289 ± 27</td>
</tr>
<tr>
<td>Sassamange (n = 20)</td>
<td>Epidemic 2005</td>
<td>2005</td>
</tr>
<tr>
<td></td>
<td></td>
<td>379 ± 71</td>
</tr>
<tr>
<td>Sassamange (n = 30)</td>
<td>Epidemic 2005</td>
<td>2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>321 ± 23</td>
</tr>
</tbody>
</table>

3.4. Low inorganic sulphate concentration in konzo-affected communities

Table 3 shows that mean urinary inorganic sulphate concentrations in schoolchildren in konzo-affected areas are low, particularly during epidemics. In 1983, the concentrations in the previously
konzo-affected village of Miaja were compared with control schoolchildren in the district capital and Swedish children. Mean concentrations ± SEM expressed as mmol/mol creatinine were 0.73 ± 0.08, 1.34 ± 0.17 and 1.36 ± 0.10, respectively (Cliff et al., 1985). The mean concentration of total urinary sulphate was measured in six patients in a small epidemic in 1982 (Essers et al., 1992). The concentration of 0.81 (0.34, SD) was low when compared to Swedish children (range 1–3.3). The low concentrations shown in Table 3 reflect low sulphur amino acid intake. The detoxification of cyanide in the body by conversion to thiocyanate is dependent on sulphur-containing amino acids. Decreased intake may impair cyanide detoxification, and at the same time detoxification uses up these amino acids (Cardoso et al., 2004).

3.5. Subclinical pathology

Studies showed that a proportion of schoolchildren (4–22%) in konzo-affected communities had ankle clonus, a sign of upper motor neuron damage (Cliff et al., 1986, 1999; Ernesto et al., 2002). In the first two studies, carried out in 1983 and 1993, there was an association between ankle clonus and urinary thiocyanate concentration.

3.6. Preventive programmes

Programmes to prevent konzo have focused on distributing less toxic varieties of cassava, and disseminating root processing methods, such as extended wetting, wet or dry fermentation, grating and roasting, and, more recently, the flour wetting method (Bradbury, 2006; Cumbana et al., 2007). Field testing showed that this method was acceptable to rural women (Muquingue et al., 2005) and the method is now being more widely taught by the Ministry of Health. Community rehabilitation programmes have provided basic physiotherapy and walking aids to patients.

Konzo-affected communities need support to improve their agricultural practices and diversify their diet. More attention should therefore be given to agricultural extension and development and food security in these communities.

4. Conclusions

Konzo is spreading to new areas in Mozambique, as rural poverty extends (Hanlon and Smart, 2008) and cassava cultivation increases. Konzo is now occurring outside major agricultural crises, with persistent cases and smaller epidemics. Affected communities continue to suffer cyanide intoxication at the time of the cassava harvest. The rural poor in cassava staple areas are vulnerable to occasional cases of konzo and small epidemics, and to large epidemics at times of crisis. They are also vulnerable to the possible long term impact of disease due to chronic cyanide intoxication. Increasing impoverishment of the rural poor, a neglect of food production, and climate change may all increase the likelihood of further cases of konzo.

**Conflict of interest**

The authors declare that there are no conflicts of interest.

**Acknowledgments**

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**References**


**Table 3**

<table>
<thead>
<tr>
<th>Location</th>
<th>Konzo occurrence</th>
<th>Urinary inorganic sulphate concentration</th>
<th>Year</th>
<th>Mean ± SEM (mmol/l)</th>
<th>Mean ± SEM (mol/mol creatinine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membia District: Mija (n = 30)</td>
<td>Epidemics 1981–1982</td>
<td>1982</td>
<td>3.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.41 ± 0.04</td>
<td></td>
</tr>
<tr>
<td>Membia District: Mija (n = 31)</td>
<td>Epidemics 1981–1982</td>
<td>1983</td>
<td>5.0&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.73 ± 0.08</td>
<td></td>
</tr>
<tr>
<td>Membia District: Mija (n = 26)</td>
<td>Epidemics 1981–1982</td>
<td>1993</td>
<td>7.0 (5.3, 9.3)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mungincual District: Mocone, Mujocojo, Terrence A&lt;sup&gt;-&lt;/sup&gt; (n = 77)</td>
<td>Persistent</td>
<td>1993</td>
<td>4.9 ± 0.4</td>
<td></td>
<td></td>
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</tbody>
</table>

<sup>a</sup> Cliff et al. (1985).  
<sup>b</sup> Cliff et al. (1999).  
<sup>c</sup> Cliff et al. (1997).  
<sup>d</sup> Recalculated by authors.  
<sup>e</sup> Geometric mean (95% confidence intervals).