Lignocaine and chlorhexidine toxicity in children resulting from mouth paint ingestion: A bottling problem

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Background: A pharmaceutical product was marketed in Australia for ‘teething’ in an almost identical container to a popular paediatric paracetamol preparation. The product contained lignocaine and chlorhexidine. The similarity of the packaging resulted in large number of therapeutic errors in which the ‘teething’ preparation was given in error for paracetamol. As the exact dose of the erroneously administered mouth paint was known this provided an opportunity for outcome assessment of lignocaine ingestion.

Methods: Calls to two state poison information centres regarding this product were prospectively followed up. Information collected included: demographics, type of exposure, details of the exposure and adverse effects. A systematic review of the literature was used to identify all previous reported cases of lignocaine and chlorhexidine ingestion.

Results: There were 28 cases with complete follow up where the product was given in therapeutic errors (10 girls and 18 boys; median age 11 months; range 2 months–4 years). The mean ingested dose of lignocaine was 2.7 mg/kg (standard deviation 1.3 mg) and chlorhexidine was 0.06 mg/kg (standard deviation 0.03 mg). The largest ingested lignocaine dose was 5.9 mg/kg. Two children developed minor symptoms: one vomited twice and the other was reported to have increased salivation and difficulty with solid food for 20 min. No other adverse effects were reported. The literature review suggested that severe effects occurred with doses more than 15 mg/kg.

Conclusion: No major adverse effects occurred with lignocaine ingestions of less than 6 mg/kg and it would be appropriate to observe these patients at home. Chlorhexidine did not appear to cause clinical effects in this low concentration.

Key words: chlorhexidine; lignocaine; toxicity.
involved the measurement of exact doses, this provided a unique opportunity to study lignocaine and chlorhexidine toxicity in a paediatric population. We report a series of ingestions of lignocaine and chlorhexidine mouth paint (containing lignocaine, 200 mg and chlorhexidine, 5 mg per 10 mL) in a paediatric population as well as a review of the literature regarding toxicity of lignocaine and chlorhexidine ingestion in children.

Methods

From June 2001 to July 2003 calls regarding ingestion of the WCH mouth paint were identified from both the New South Wales Poisons Information Centre (NSW PIC) and the Western Australian Poison Information Centre (WA PIC). Both PICs provide information to medical professionals as well as the general public. NSW PIC is the largest PIC in Australia and is the only 24-h centre in Australia. It receives approximately 110 000 calls per year. WA PIC is the second largest PIC in Australia and operates from 8.00 hours to 22.00 hours and receives approximately 50 000 calls per year. Ethics approval for the prospective recruitment and follow up of cases was obtained for the NSW PIC from the ethics committee of The Children’s Hospital at Westmead and the Clinical Audits committee at Sir Charles Gairdner Hospital.

Routine information from each call was reviewed including demographics (age, sex and weight), type of exposure (unintentional or therapeutic error), details of the exposure (time of ingestion and ingested dose) and clinical effects. Cases from the NSW PIC were recruited prospectively and subjects were interviewed over the phone at either the time of the call or within 24 h and were followed up by phone until all clinical effects had resolved. In this group further information was collected on further clinical effects and duration of effects.

Based on an initial analysis of cases prospectively followed up from the NSW PIC, it became evident that all clinical effects occurred and resolved within 1–2 h. This is consistent with the known pharmacokinetics of lignocaine.2,4 We therefore analysed calls from the WA PIC that were telephoned through two or more hours after ingestion. Detailed clinical information is recorded at the time of the call. These cases were considered to have complete follow up and were included in the analysis of clinical effects.

A systematic review of the literature was used to identify all previous reported cases of lignocaine and chlorhexidine ingestion. MEDLINE (1966–August 2005), OLD MEDLINE (1951–1965) and EMBASE (1980–August 2005) were searched using the following search terms ‘lignocaine’, ‘lidocaine’, ‘p(a)ediatric’, ‘chlorhexidine’, ‘ingestion’, ‘toxicity’, ‘overdose’. Reference lists of all relevant articles identified were also searched.

For descriptive statistics, means and standard deviations are quoted for normally distributed data, whereas medians and inter-quartile ranges are used for non-parametric data. All statistical analysis was performed using GraphPad InStat (version 3.02 for Windows 95, GraphPad Software, San Diego, CA, USA).

Results

Over the time period (June 2001–July 2003) there were 198 calls regarding the WCH mouth paint. WA PIC received 164 calls and NSW PIC received 34 calls. This is consistent with the fact that the product was only marketed in South Australia, which is serviced during the day by the WA PIC and overnight by the NSW PIC. Of these, 162 cases (82%) were given in error for paracetamol. In total, 36 cases (18%) were unintentional ingestions. Cases were excluded from the analysis if the exact dose of ingestion was not known.

Cases with Clinical Follow Up

There were 28 cases with complete follow up, 10 girls and 18 boys. The demographics of the cases are included in Table 1. The median age was 11 months (range 2 months–4 years). The mean ingested dose of lignocaine was 2.7 mg/kg (standard deviation 1.2) and the largest ingested dose was 5.9 mg/kg. The mean ingested dose of chlorhexidine was 0.06 mg/kg (standard deviation 0.03) and the largest was 0.15 mg/kg.

There were two children (7%) who developed adverse effects. The first was an 8-month-old boy (weight 7.3 kg) who was given 1.5 mL of the mouth paint. Total ingested dose was 4.1 mg/kg of lignocaine and 0.1 mg/kg of chlorhexidine. The child was distressed and unsettled and was noted to have increased salivation and difficulty with solid food for 20 min, but no further adverse effects. The second child was a 7-month-old girl (weight 9 kg) who was given 1.5 mL of the mouth paint. Total ingested dose was 3.3 mg/kg of lignocaine and 0.08 mg/kg of chlorhexidine. This child vomited twice within 30 min of ingestion, but had no other adverse effects. No other adverse effects were reported. In particular, there were no reports of seizures or arrhythmias.

Literature Review

There were 10 reports of lignocaine ingestion in children1,4,6,9-13 (Table 2). The dose ingested ranged from 14 to 50 mg/kg. The major
Clinical effects were seizures and respiratory arrest with one report of the death of a 13-month-old boy following ingestion of an unknown amount of lignocaine.13

Review of chlorhexidine toxicity revealed a series of five newborn babies who were accidentally fed a dilute antiseptic solution (containing chlorhexidine 0.05% and cetrimide 1%).14 Clinical effects consisted of caustic burns to the lips, mouth and tongue. One child developed pulmonary oedema thought to be related to the cetrimide. All recovered without complications. There is also a report of one 12-h-old newborn with exposure to 2.5 mg of chlorhexidine over a 24-h period from the application of chlorhexidine spray to the mother’s nipple, which occurred with every feed for 48 h.15 The child was found to have cyanotic spells associated with bradycardia, occasionally requiring doses of atropine, which resolved after cessation of the chlorhexidine spray. Exposure was confirmed by analysis of chlorhexidine in the neonate’s blood.

### Discussion

Doses for lignocaine ingestion under 6 mg/kg are highly unlikely to cause significant symptoms. They can be managed at home or safely discharged from hospital. Doses more than 6 mg/kg are likely to cause symptoms and require observation, but severe toxicity is unlikely unless doses more than 15 mg/kg are ingested. Clinical effects would be expected to occur within the first 1–2 h following ingestion.

Lignocaine is rapidly absorbed from the gastrointestinal tract8,10 with peak plasma concentrations occurring within 30 min.2,6–10 It is rapidly metabolised by the liver and undergoes extensive first-pass metabolism2,3,9 with only 30–35% of the dose reaching the systemic circulation.1,3,6,10 Its elimination half-life is approximately 90 min.1,2,10 Toxic effects are likely to occur rapidly and resolve quickly with these pharmacokinetics and is consistent with our study with the only two symptomatic children developing symptoms within 30 min of ingestion.

In our study the largest ingested dose of lignocaine was 5.9 mg/kg with no children developing significant clinical effects. It could be reasoned that based on the fact that the therapeutic intravenous dose of lignocaine is 5 mg/kg and that the oral bioavailability is only approximately 30%, the toxic dose for oral ingestion of lignocaine may be as high as 16 mg/kg. All previous case reports of severe effects following lignocaine ingestion in children were in the range 25–50 mg/kg with only one case of 14 mg/kg.1,4,6,9–13 Based on this and the results of our study it would be reasonable to observe

### Table 1  Characteristics of the sample and lignocaine/chlorhexidine exposures

<table>
<thead>
<tr>
<th></th>
<th>NSW PIC</th>
<th>WA PIC</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. cases</td>
<td>19</td>
<td>9</td>
<td>28</td>
</tr>
<tr>
<td>Sex</td>
<td>9 girls</td>
<td>1 girl</td>
<td>10 girls</td>
</tr>
<tr>
<td>10 boys</td>
<td></td>
<td>8 boys</td>
<td>18 boys</td>
</tr>
<tr>
<td>Median age (months) (range)</td>
<td>11 (7 months–4 years)</td>
<td>10 (2 months–2 years)</td>
<td>11 (2 months–4 years)</td>
</tr>
<tr>
<td>Mean ingested dose of lignocaine (mg/kg) (SD)</td>
<td>2.7 (1.3)</td>
<td>2.8 (1.1)</td>
<td>2.7 (1.2)</td>
</tr>
<tr>
<td>Maximum ingested dose of lignocaine (mg/kg)</td>
<td>5.9</td>
<td>4.2</td>
<td>5.9</td>
</tr>
<tr>
<td>Mean ingested dose of chlorhexidine (mg/kg) (SD)</td>
<td>0.06 (0.03)</td>
<td>0.06 (0.03)</td>
<td>0.06 (0.03)</td>
</tr>
<tr>
<td>Maximum dose of chlorhexidine ingested (mg/kg)</td>
<td>0.15</td>
<td>0.10</td>
<td>0.15</td>
</tr>
<tr>
<td>Children who developed symptoms</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

NSW PIC, New South Wales Poisons Information Centre; SD, standard deviation; WA PIC, Western Australia Poison Information Centre.

### Table 2  Summary of previously reported cases of oral lignocaine exposure, dosage and clinical effects

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Weight (kg)</th>
<th>Ingested dose</th>
<th>Dose (mg/kg)</th>
<th>Clinical effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>22 months10</td>
<td>Female</td>
<td>10.0</td>
<td>20–25 mL</td>
<td>40–50</td>
<td>Repeated seizures, cyanosis respiratory arrest; recovered</td>
</tr>
<tr>
<td>3.5 years9</td>
<td>Female</td>
<td>14.0</td>
<td>2 tablespoons over 4 h</td>
<td>29 × 2 doses</td>
<td>Seizures for 1 h, respiratory distress; recovered</td>
</tr>
<tr>
<td>15 months9</td>
<td>Male</td>
<td>8.0</td>
<td>0.5 tablespoon × 2 over 8–10 h</td>
<td>25 × 2 doses</td>
<td>Seizures for 9 h, apnoea; recovered</td>
</tr>
<tr>
<td>1 year9</td>
<td>Female</td>
<td>10.0</td>
<td>8–9 tablespoons over 8–9 h</td>
<td>40 × 8–9 doses</td>
<td>Repeated seizures for 1.5 h; recovered</td>
</tr>
<tr>
<td>5 months7</td>
<td>Male</td>
<td>7.2</td>
<td>1 teaspoon</td>
<td>14</td>
<td>One seizure; recovered</td>
</tr>
<tr>
<td>13 months13</td>
<td>Male</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Cardiorespiratory arrest; died</td>
</tr>
<tr>
<td>15 months8</td>
<td>Male</td>
<td>11.4</td>
<td>1.5 teaspoons every 3 h for 5 days</td>
<td>7.5 per dose over 5 days</td>
<td>Six generalised tonic clonic seizure, central cyanosis, intubated; recovered</td>
</tr>
<tr>
<td>20 months12</td>
<td>Female</td>
<td>10.6</td>
<td>One ounce of 2% viscous lidocaine</td>
<td>Aspirated, clonic seizures, 1</td>
<td></td>
</tr>
<tr>
<td>5 months1</td>
<td>Male</td>
<td>6.5</td>
<td>80 mL of 2% lidocaine over 24 h (3–4 mL every 4–6 h)</td>
<td>Tonic-clonic seizures, decreased level of consciousness, intubated; recovered</td>
<td></td>
</tr>
<tr>
<td>14 months11</td>
<td>Female</td>
<td>7.9</td>
<td>15 mL × 6 doses within 24 h</td>
<td>37.9 × 6 doses over 24 h</td>
<td>Generalised seizure × 2; recovered</td>
</tr>
</tbody>
</table>
children at home who have ingested less than 6 mg/kg. It could be reasoned that minor effects may be expected up to 15 mg/kg with severe effects at doses greater than 15 mg/kg.

This product also contained chlorhexidine in a very small concentration (0.05%). Review of the literature suggests that chlorhexidine concentrations above 20% produce corrosive symptoms. There are only two reports of chlorhexidine ingestion in children. One was related to repeated exposures and in the other case the clinical effects were thought to be related to another ingredient.

One limitation of this study was that patients were not examined and only a description of the clinical effects was obtained by telephone. However, standardised questions were used to ensure consistent data collection. In addition, all 28 cases were followed up until all symptoms had resolved. The use of PICs allowed larger numbers of cases to be recruited. In addition, many of the cases in this study may never have presented to hospital because of the lack of symptoms.

This study raises interesting public health issues. The use of very similar containers for common paediatric pharmaceutical mixtures is of great concern. The high error rate indicates that parents pay little attention to the product label. As a result of feedback provided by the NSW and WA PICs to the health department a trial of change of lid colour from white to blue was attempted. However, there were still significant numbers of cases following this and the product now has been withdrawn from the market. These errors are even more concerning in light of evidence that infant ‘teething’ usually causes few symptoms that would require treatment in the first place.

Acknowledgements

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References

14. Mucklow ES. Accidental feeding of a dilute antiseptic solution (Chlorhexidine 0.05% with cetrimide 1%) to five babies. Hum. Toxicol. 1988; 7: 567–9.