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Presentation and outcome of severe anticholinesterase insecticide poisoning

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Aims: To document the patterns of presentation and outcome of severe anticholinesterase insecticide poisoning in children requiring intensive care.
Methods: Retrospective case note review of all 5541 children admitted to the paediatric intensive care unit (PICU) of a university hospital during the 10 years from January 1990 to May 2000. Fifty four children (1%) with anticholinesterase insecticide poisoning were identified. Presenting features, route of exposure, treatment, complications, and mortality were recorded. Data were analysed by the Fisher's exact and Mann–Whitney tests.
Results: More children than expected were from a rural area (46% versus 25%). Decontamination occurred in 50% of children prior to PICU admission. Enteral exposure was most common (n = 27; 50%). Median pseudocholinesterase level was 185 IU/l (range 75–7404). Median total dose of atropine required to maintain mydriasis was 0.3 mg/kg (range 0.03–16.7) over a median of 10 hours (range 1–160). Complications included coma (31%), seizures (30%), shock (9%), arrhythmias (9%), and respiratory failure requiring ventilation (35%). No significant differences were detected in incidence of seizures, cardiac arrhythmias, respiratory failure, mortality, duration of ventilation, or PICU stay, according to route of exposure, or state of decontamination. Four children died (7%). Mortality was associated with the presence of a cardiac arrhythmia (likelihood ratio 8.3) and respiratory failure (likelihood ratio 3.3).
Conclusion: The mortality and morbidity of severe anticholinesterase insecticide poisoning in childhood is not related to route of exposure, or to delay in decontamination. However, the presence of either a cardiac arrhythmia or respiratory failure is associated with a poor prognosis.

A ccidental poisoning by acetylcholinesterase inhibitor (anticholinesterase) insecticides such as the organophosphates and carbamates remains an important public health problem in regions where these agents are in common usage.[1] Effective treatment may be delayed as the constellation of nicotinic and muscarinic signs and symptoms is often incomplete, and may mimic a variety of other conditions in childhood.[2]

It has been suggested that the clinical manifestations of childhood anticholinesterase insecticide poisoning differ from those in adults, with a predominance of central nervous system effects.[3 4] Mortality is also reported to be lower in childhood.[2–4] However, contrary to previous reports, it has been our impression that children with severe anticholinesterase exposure follow a similar course to that reported in adults.[3 4] We speculated that both morbidity and mortality in this condition are more closely related to the degree of toxin exposure than to patient age. The route of contamination (enteral or transcutaneous), or delay in decontamination, might thus influence outcome by affecting the degree of toxin exposure.

We present a retrospective observational study of severe anticholinesterase insecticide poisoning, with particular reference to mode of presentation and outcome, in children requiring intensive care over a 10 year period.

METHODS

This was a retrospective case note review set in an 11 bed paediatric intensive care unit (PICU) serving metropolitan Cape Town and the Western Cape province of South Africa. Discharge records of all 5541 children admitted to the PICU during the period January 1990 to May 2000 were reviewed; 54 children (1%) with anticholinesterase insecticide poisoning were identified.

Anticholinesterase poisoning was defined as the presence of nicotinic and/or muscarinic clinical features in combination with either (a) a history of exposure to an organophosphate or carbamate insecticide, or (b) a decreased level of serum pseudocholinesterase. Severe poisoning was defined as that requiring admission to intensive care.

The following data were collected.

- *Circumstances of poisoning.* Urban or rural place of residence; summer crop spraying season (September to February) or winter (March to August); identity of insecticide; route of contamination; accidental or intentional poisoning.

- *PICU admission data.* Direct or out of hospital referral; referral diagnosis; preadmission decontamination of the skin and/or gastrointestinal tract.

- *Clinical features.* Pupil size; level of consciousness; seizure activity; confusion; agitation; core temperature; bronchorrhoea; lacrimation; salivation; sweating; abdominal pain; diarrhoea; vomiting; urinary incontinence; blood pressure; heart rate; hypotonia; fasciculations. Hyperthermia was defined as a central body temperature >38.5°C, and hypothermia as a central body temperature <35°C. Hypotension, hypertension, bradycardia, and tachycardia were defined as values falling 2 standard deviations above or below the age appropriate mean.[5]

- *Investigation and treatment.* Serum pseudocholinesterase levels on admission; dose of obidoxime; total dose of atropine and duration of atropine administration in order to maintain mydriasis.

- *Complications and mortality.* Seizures; coma (defined as Glasgow coma scale <8); brady- or tachyarrhythmias; shock (defined as hypotension or poor peripheral perfusion responsive to either inotropic support or fluid therapy); respiratory failure (defined as a requirement for mechanical

Table 1 Mode of anticholinesterase insecticide exposure (n=54)

	No. (%)
Unknown	14 (26)
Mixed enteral and transcutaneous exposure	5 (9)
Insecticide container	3
House fumigation/contaminated food	1
Near drowning in tank of sheep dip	1
Enteral only	27 (50)
Insecticide container	19
Insecticide container (non-accidental)	1
Contaminated food	6
Contaminated milk feed (non-accidental)	1
Transcutaneous only	8 (15)
House fumigation	6
Agricultural spraying	1
Topical application as "traditional remedy"	1

Table 2 Presenting clinical features of anticholinesterase poisoning

Clinical feature	No. (%)
Miosis	31 (57)
Bronchorrhoea	30 (56)
Sinus tachycardia	20 (37)
Respiratory failure	19 (35)
Salivation	18 (33)
Depressed level of consciousness (GCS <8)	17 (31)
Seizures	30 (30)
Vomiting	15 (28)
Hypotonia	15 (28)
Hypertension	11 (20)
Fasciculations	11 (20)
Confusion	8 (15)
Abdominal pain	6 (11)
Agitation	5 (9)
Diarrhoea	5 (9)
Hypothermia	4 (7)
Urinary incontinence	4 (7)
Hypotension	5 (9)
Hyperthermia	3 (6)
Lacrimation	3 (6)
Bradyarrhythmia	3 (6)
Sinus bradycardia	2 (4)
Tachyarrhythmia	2 (4)
Sweating	2 (4)

ventilation); duration (days) of ventilation, PICU stay, and hospital stay in survivors; time (days) to death in non-survivors; mortality.

All data were collected retrospectively and therefore institutional ethics committee approval was not obtained.

Data are presented as median (range) and analysed using the Fisher's exact and Mann–Whitney tests for non-parametric data.

RESULTS
Demographics
The 54 children included 37 boys (69%) and 17 girls (31%), with median age 44 months (range 5–168) and median weight 15 kg (range 7–36).

Circumstances of poisoning
Twenty nine children (54%) lived in an urban area and 25 (46%) in a rural area, significantly more than expected from our historical referral pattern (25% rural; p = 0.008) (unpublished data). Twenty nine (54%) poisonings occurred in the summer crop spraying season and 25 (46%) in winter.

The specific anticholinesterase insecticides were identified in only 14 children and included parathion (n = 1), diazinon (n = 2), chlorpyrifos (n = 6), fenthion (n = 1), thiophosphate (n = 2), monocrotophos (n = 1), and gramazon (n = 1).

The route of contamination was documented in 40 children, of whom five suffered mixed enteral and transcutaneous exposure, and 35 were contaminated via a single route. Enteral exposure was more common (n = 27; 50%) than transcutaneous exposure (n = 8; 15%). Contamination was non-accidental in two children, including forced ingestion from an insecticide container (n = 1) and intentional contamination of milk feed by a caregiver (n = 1). Table 1 shows modes of exposure and table 2 lists presenting clinical features of anticholinesterase poisoning.

PICU admission data
The diagnosis of anticholinesterase insecticide poisoning had been made prior to PICU admission in 40 of the 54 children (74%). Other diagnoses considered included head injury (n = 2), unspecified toxin ingestion (n = 2), suspected spider bite (n = 1), status epilepticus (n = 5), unspecified encephalopathy (n = 2), and pneumonia (n = 2).

Twenty eight children (52%) had undergone decontamination, of either the gastrointestinal tract (gastric lavage, bowel lavage, and activated charcoal administration) or skin (removal of clothing, washing), or both, prior to PICU admission.

Investigation and management
Plasma pseudocholinesterase levels were measured in all children. The median pseudocholinesterase was 185 IU/l (75–7404), with a reference range for our laboratory given as 3070–8483 IU/l. Pseudocholinesterase levels were within the reference range in three children, two of whom had ingested the insecticide in front of witnesses, and one of whom had been playing in a field recently sprayed with a carbamate insecticide. All other children had levels of less than 50% of the lower limit of normal.

The median total atropine dose to achieve mydriasis was 0.30 mg/kg (0.03–16.70). Atropine administration, either by repeated bolus (n = 46) or by continuous infusion (n = 8), was required for a median of 10 hours (1–160) to maintain mydriasis. Fifty three children received obidoxime, median total dose 10 mg/kg (2.6–132.0 mg/kg).

Complications and mortality
Generalised tonic–clonic seizures were documented in 16 (30%), and coma in 17 children (31%). Five children (9%) were shocked, including two who were hypotensive secondary to a cardiac arrhythmia.

Cardiac arrhythmias were noted in five children (9%) (bradyarrhythmia, n = 3; tachyarrhythmia, n = 2). The median total atropine dose required was greater in children who developed an arrhythmia (1.0 mg/kg; range 0.10–16.70 mg/kg) than in those who did not (0.27 mg/kg; range 0.03–9.97) (p = 0.03).

Nineteen children (35%) required ventilation. Two children developed pulmonary oedema and one child developed acute respiratory distress syndrome (ARDS). The median duration of ventilation in survivors (n = 15/19) was 2 days (1–39).

The clinical finding of miosis on admission was not related to the incidence of complications such as cardiac arrhythmia (p = 0.27), respiratory failure (p = 1.0), or seizures (p = 0.37), nor was it associated with increased mortality (p = 0.13).

Table 3   Incidence of complications in survivors and non-survivors

	Survivors (n=50) No. (%)	Non-survivors (n=4) No. (%)	p value
Seizure	13 (26)	3 (75)	0.07
Coma	15 (30)	2 (50)	0.58
Respiratory failure	15 (30)	4 (100)	0.01
Cardiac arrhythmia	3 (6)	2 (50)	0.04

Table 4   Route of anticholinesterase contamination

	Enteral only (n=27)	Transcutaneous only (n=8)	p value
Pseudocholinesterase (IU/l)	495 (82–7404)	180 (83–6200)	0.17
Total atropine dose (mg/kg)	0.48 (0.09–1.30)	0.20 (0.08–16.70)	0.63
Seizures (no.) (%)	11 (41)	2 (25)	0.68
Ventilation (no.) (%)	13 (48)	2 (25)	0.42
Cardiac arrhythmia (no.) (%)	4 (15)	0 (0)	0.55
Mortality (no.) (%)	3 (11)	0 (0)	1.00
Duration of ventilation (survivors)	2 days (2–3)	1 day (1–39)	0.69
Duration of ICU (survivors)	4 days (2–9)	2 days (1–83)	0.15

Table 5   Preadmission decontamination

	Not decontaminated (n=26)	Decontaminated (n=28)	p value
Pseudocholinesterase (IU/l)	190 (75–6200)	185 (91–7404)	0.78
Total atropine dose (mg/kg)	0.26 (0.03–6.50)	0.48 (0.09–16.70)	0.16
Cardiac arrhythmia (no.) (%)	2 (8)	3 (11)	1.00
Seizures (no.) (%)	7 (27)	9 (32)	0.22
Ventilation (no.) (%)	7 (27)	12 (43)	0.15
Mortality (no.) (%)	3 (12)	1 (4)	0.34
Duration of ventilation (survivors)	2 days (1–2)	2 days (1–39)	0.24
Duration of ICU stay (survivors)	4 days (1–83)	3 days (1–6)	0.09

The median ICU stay in the 50 survivors (93%) was 3 days (1–83), and median duration of hospital stay was 4 days (2–83).

Four children (7%) died. Median time to death in non-survivors was 2 days (2–9). Causes of death were refractory shock (n = 2), acute respiratory distress syndrome (n = 1), and multiorgan failure (n = 1).

Table 3 shows the incidence of complications in survivors and non-survivors. There were significant associations between the presence of a cardiac arrhythmia (sensitivity 50%, specificity 94%, likelihood ratio 8.3), and respiratory failure requiring ventilation (sensitivity 100%, specificity 70%, likelihood ratio 3.3), and mortality. The presence of seizures was associated with a trend towards increased mortality, which did not reach statistical significance (sensitivity 75%, specificity 74%, likelihood ratio 2.9).

Subgroup analysis

Pseudocholinesterase levels. Pseudocholinesterase levels were no different in survivors compared to non-survivors (median 180 IU/l (75–7404) versus 301 IU/l (82–360), p = 0.51). There was a trend for children requiring ventilation to have lower levels than those who did not require ventilation (median 180 IU/l (82–366) versus 284 IU/l (75–7404)), although this did not reach statistical significance (p = 0.09).

Route of contamination. Table 4 compares those who had ingested the agent (n = 27) to those who received only transcutaneous exposure (n = 8).

Preadmission decontamination. Table 5 compares children who were not decontaminated prior to admission (n = 26) to those who were decontaminated (n = 28).

Forty one of the 54 cases (76%) were notified to the Department of Health and Social Services. A total of 122 children with either organophosphate or carbamate insecticide poisoning were notified throughout the Western Cape province during the study period.

DISCUSSION

We have shown that anticholinesterase insecticide poisoning in children is an important cause of morbidity and mortality, as well as a burden on tertiary healthcare resources (almost 1% of PICU admissions) in this region. The magnitude of this problem may be even greater given the evidence of under reporting, even in our own tertiary institution.

Although the adult experience is largely of intentional ingestion, contamination in childhood is usually accidental and as might be expected, boys living in rural areas are at greater risk of exposure.[6–9] There were no seasonal differences in the incidence of anticholinesterase poisoning, which suggests that the rural preponderance is related to availability rather than agricultural exposure. Only two children were directly affected by agricultural use of these agents, whereas almost 50% of poisonings occurred by accidental exposure to the contents of an insecticide container. This finding highlights the need for greater public awareness of the dangers of these agents, which should be stored only in appropriately labelled childproof containers.

Previous reports in the paediatric age group have documented the high frequency of muscarinic signs and symptoms at presentation, including miosis, salivation, and bronchorrhoea, while others have described a predominance of central nervous system complications.[2–4] By contrast, cardiovascular and respiratory morbidity is commonly seen in adults.[6–10]

Our patients manifested not only muscarinic signs and symptoms, but also nicotinic features such as sinus tachycardia, hypertension, hypotonia, and muscle fasciculations. It is notable that although central nervous system effects, including a depressed level of consciousness and seizures, were common, there was also an appreciable incidence of cardiorespiratory complications such as brady- and tachyarrhythmias, shock, and respiratory failure. In our experience the clinical features and complications of childhood poisoning are not as different from adults as previous authors have suggested.[3 4]

It is of some concern that despite the relatively high incidence of anticholinesterase insecticide poisoning, the presumptive diagnosis was not made in more than a quarter of children referred for intensive care. We had hypothesised that children who did not undergo decontamination prior to ICU admission would have ongoing skin or gut absorption, greater toxin exposure, and therefore a worse outcome. However, other than a trend towards a longer ICU stay, we were not able to show any difference in mortality or markers of morbidity between these children and those who did undergo early decontamination. It is possible that toxin exposure of such a degree, that requires intensive care support, is so extensive that efforts at decontamination are quantitatively ineffective.

We had also speculated that direct ingestion might result in heavier anticholinesterase contamination than transcutaneous exposure, and thus affect outcome. Indeed the adult experience of predominantly intentional or accidental ingestion appears to be associated with relatively high mortality (12–50%).[6–9] However, although there were no deaths among children who received only transcutaneous exposure, the route of contamination was not significantly associated with either mortality or morbidity, possibly because of the small number of children involved.

Despite the frequent occurrence of complications such as seizures (30%), coma (31%), cardiac arrhythmias (9%), shock (9%), and respiratory failure (35%), children admitted with anticholinesterase insecticide poisoning required a relatively brief duration of ventilation, intensive care, and hospital stay. However, the presence of either a cardiac arrhythmia or respiratory failure was associated with a poor outcome.

Overall mortality (7%), although higher than reported in other paediatric series, compares favourably with that of recent adult and mixed paediatric/adult studies.[2–4 6–9] Therefore, we would continue to advocate early skin and gut decontamination, combined with the aggressive use of atropine aimed at mydriasis, in the management of children with suspected anticholinesterase insecticide poisoning.

Conclusion

Severe anticholinesterase insecticide poisoning remains an important cause of morbidity and mortality in children, with boys in rural areas most at risk. Neither mortality nor morbidity is related to the route of exposure, or to delay in decontamination. Although mortality is lower in childhood, the cardiorespiratory complications are similar to the adult experience. The presence of a cardiac arrhythmia or respiratory failure is associated with a poor prognosis.

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