Paediatric organophosphate poisoning – a rural hospital experience

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Objectives. To document the presentation and course of organophosphate poisoning (OPP) in children and to record the frequency of atropine toxicity during treatment.

Design. A retrospective observational study was conducted of all recorded paediatric cases of OPP admitted to a regional hospital over a 5-year period from 1 June 1996 to 31 May 2001.

Setting. The study was conducted at Eben Donges Hospital, a regional hospital in the Boland/Overberg area of the Western Cape, where pesticide-intensive fruit farming remains the largest revenue generator.

Subjects. The study included all children aged 12 years or less (as per health services classification) with confirmed OPP.

Results. There were 23 patients. Most of the cases came from the De Doorns area (35%), with poisoning by ingestion accounting for 61% of cases. A distinct seasonal predominance was found that coincided with the summer harvest. Mode of presentation was variable and was not related to the initial pseudocholinesterase level. Evidence of atropine toxicity occurred in 8 of the 18 cases treated with atropine. No statistically significant risk factor was found for atropine toxicity. The average duration of hospitalisation was 5.05 days, with 2 children requiring transfer to tertiary facilities.

Conclusions. The high number of referrals from a specific geographical area, combined with a 61% accidental ingestion rate, illustrates an area where legislation has failed to limit unnecessary exposure. Awareness of the seasonal predominance could prove pivotal to the success of future preventive strategies. Initial presentation and serum pseudocholinesterase levels did not correlate with duration of stay. The decision to transfer to a tertiary facility should only be explored once the patient has been stabilised with atropine. Atropine treatment is effective but carries a risk of toxicity. Glycopyrrolate may constitute an alternative treatment option.

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Eben Donges Hospital (EDH) is a regional hospital in the Boland/Overberg region of the Western Cape. It serves a diverse community whose economic stability is reliant on the intensive fruit-farming industry. This farming is heavily dependent on organophosphate (OP)-containing insecticides for pest control, often to the detriment of labourers' health. The combination of accessibility, limited legislation and lack of education has resulted in frequent OP exposure, including among children.

Acetylcholine, the neurotransmitter at postganglionic parasympathetic, preganglionic sympathetic and parasympathetic, somatic striated skeletal and central nervous system (CNS) receptors, is rapidly hydrolysed by an enzyme in the synaptic cleft, acetylcholinesterase.[1] OP compounds form covalent bonds with the latter resulting in an excess of acetylcholine, which produces hyperstimulation and the myriad of symptoms and signs characteristic of organophosphate poisoning (OPP).[2-6]

Anticholinergics, in particular atropine, have been the cornerstone of OPP treatment for decades.[7] Atropine's role as a competitive antagonist at the muscarinic receptors in the peripheral and CNS allows rapid control of the bradycardia, hypotension, bronchospasm, excessive secretions and gastrointestinal complications of OPP, allowing for stabilisation of the patient.[3] Atropine does not reverse the effects of OPP at the nicotinic and all CNS receptors and patients may require additional support for respiratory muscle paralysis/weakness and convulsions, etc.[3]

Atropine's biochemical structure allows it to pass through the blood-brain barrier, potentially reversing some of the CNS effects of the OPP; however it can also produce symptoms indistinguishable from the very condition the clinician is trying to treat, namely nervousness, drowsiness, mental confusion and agitation. These symptoms appear to be dose related and are a complication of treating OPP.[5]

Currently there is no literature documenting the incidence of CNS atropine toxicity in children during OPP treatment.

Objectives

The study aimed to document the presentation and course of OPP among children treated for this condition and to record the frequency of CNS atropine toxicity.

Method

A retrospective folder review was undertaken of all paediatric patients (age 12 years and younger) admitted to EDH with confirmed OPP over a 5-year period from 1 June 1996 to 31

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May 2001. The diagnosis of OPP was based on a combination of history of suspected poisoning, presenting symptoms and signs (Table I) and definitive confirmation using serum pseudocholinesterase levels. Participants' folders were reviewed for data on age, sex, geographical district/area of exposure to poison, presenting symptoms and signs, pseudocholinesterase level, mode of treatment, duration of hospital stay and documented evidence of CNS atropine toxicity. Atropine toxicity was defined as the persistence of symptoms of excessive nervousness, drowsiness, mental confusion, agitation or excitement after 24 hours in a child with dilated pupils and a clear record of repeated doses of atropine administration; once documented special investigations excluded mimicking conditions such as repoisoning with OP from fat stores and septicaemia. Folders with incomplete data and uncertain cases were excluded from the review.

This study has the potential to improve preventive strategies and community awareness of the OPP problem.

Statistical analysis

Categorical variables were compared using the Fisher's exact test, and groups were compared using the Mann-Whitney U-test. A level of significance of less than 0.05 was used throughout.

Results

During the study period 23 paediatric patients were treated for OPP at EDH. The demographics of these patients showed a male-to-female ratio of 12:11, with a median age of 4 years and a range of 1 - 12 years. Children from the De Doorns area in the Hexriver Valley accounted for 35% (N = 8) of poisonings, children from Worcester for 17% (N = 4), Breërivier and Robertson for 9% (N = 2) each respectively, and the remaining drainage areas had incidental cases. The documented sources of poisoning were as follows: 61% (N = 14) accidental ingestion of OPs, with unwashed freshly sprayed fruit or poorly marked storage containers as possible sources, 22% (N = 5) skin and inhalation exposure as a result of recent use of OPs for pest control in and around homes, and 17% (N = 4) unknown or unconfirmed source of poisoning. There appeared to be a definite seasonal predominance, with cases peaking between October and January, accounting for 70% (N = 16) of all cases (Fig. 1).

Table I. Symptoms and signs of organophosphate poisoning

Muscarinic effects
Cardiovascular system: bradycardia and hypotension
Gastrointestinal tract: salivation, nausea and vomiting, diarrhoea and abdominal pain, tenesmus and faecal incontinence
Respiratory system: bronchospasm, bronchorrhea
Eyes: miosis
Other: lacrimation, diaphoresis and urination
Nicotinic effects
Musculoskeletal: fasciculation, weakness, paralysis, cramps and respiratory paralysis
Cardiovascular system: tachycardia and hypertension
Central nervous system effects
Altered level of consciousness, agitation and confusion, delirium, coma, seizures, ataxia, dysarthria and respiratory depression

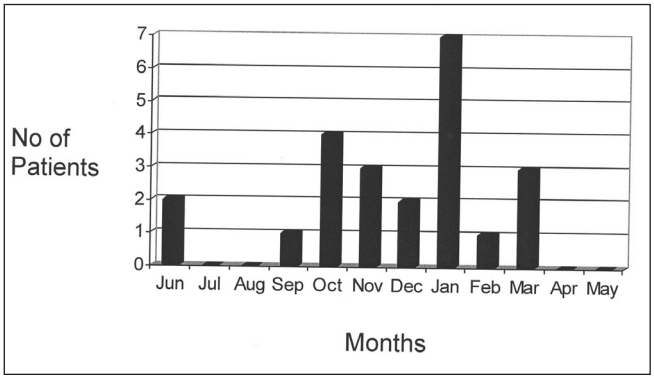

Fig. 1. Seasonal OPP incidence.

Presenting symptoms and signs were in keeping with those described by other authors, with abnormal pupils (78%) and excessive secretions (65%) the most common features (Table II).[7]

Table II. Summary of presenting symptoms and signs

	N (%)
Pin-point pupils	18 (78)
Excessive secretions	15 (65)
Decreased level of consciousness	9 (39)
Vomiting	9 (39)
Diarrhoea	7 (30)
Tachycardia	6 (26)
Confusion	6 (26)
Fasciculations	5 (22)
Respiratory failure	3 (13)
Apathy	3 (13)
Muscle weakness	2 (8)
Shock	2 (8)
Abdominal pain	2 (8)
'Garlic' odour	2 (8)
Irritability	1 (4)
Ingestion of poison	14 (61)
Skin and inhalation exposure	5 (22)
Unknown source of poisoning	4 (17)

All patients admitted were treated in the same way. Initial conservative therapy included gastric lavage and use of activated charcoal (for suspected ingestion cases), declothing and full-body wash, and cardiovascular and respiratory stabilisation. A single dose of obidoxime, a cholinesterase reactivator, was used in 9 cases on admission. Of the 23 cases, 20 received atropine (according to the recommended OPP dosage), 2 treated conservatively and 1 case received a glycopyrrolate (Robinul) infusion (Fig. 2).

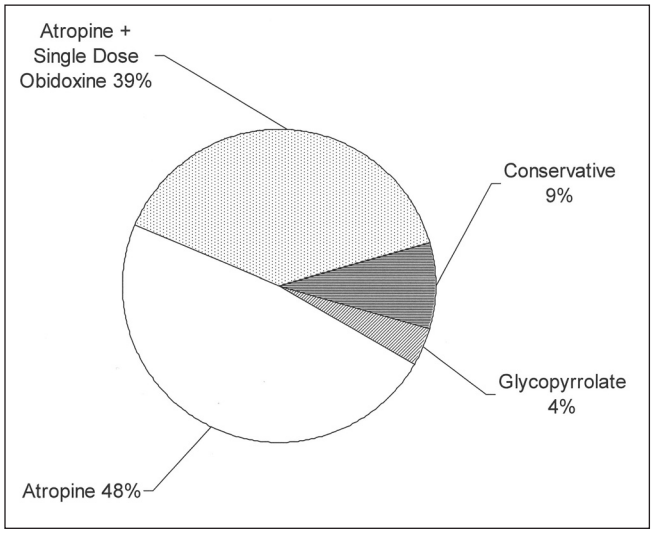

Fig. 2. Treatment summary.

Intubation was required in 4 children, of whom 2 received short-term (less than 24 hours) ventilation. The remaining 2 children were transferred to a tertiary facility, 1 for intractable seizures not controllable with conventional anticonvulsants and requiring a Thiopentone infusion, and the other for hypoxic cerebral damage from respiratory failure and cardiovascular collapse. The former child survived with neurological impairment and the latter died 10 days after presentation.

Documented evidence of CNS atropine toxicity occurred in 8 of the 18 cases (excluding the 2 transferred patients) treated with atropine, equivocating to 44% of cases. No statistically significant difference could be found when comparing patients with atropine toxicity and those without toxicity (Table III).

There was also no correlation between pseudocholinesterase levels and duration of stay, as shown in Fig 3.

Discussion

The liberal use of pesticides in the agriculturally rich region of the Western Cape has contributed significantly to the ever-increasing number of reported poisonings in this region. Pesticide poisoning in children under 14 years of age has a reported average incidence of 0.367/100 000. OPP accounts for 49.9% of all poisonings.[8] OPP is a notifiable disease in South

Table III. Comparison of atropine toxicity groups (standard deviation)

Patient data	Atropine toxicity	No atropine toxicity
Age (yrs)	5.38 (3.623)	3.5 (2.415)
Duration of hospital stay (days)	4.82 (0.99)	4.9 (1.75)
Pseudocholin-esterase level (IU)	563.1 (285.6)	425.2 (401.8)
Ingestion of poison	5	4
Inhalation and skin exposure	2	3
Unknown source of poisoning	7	7

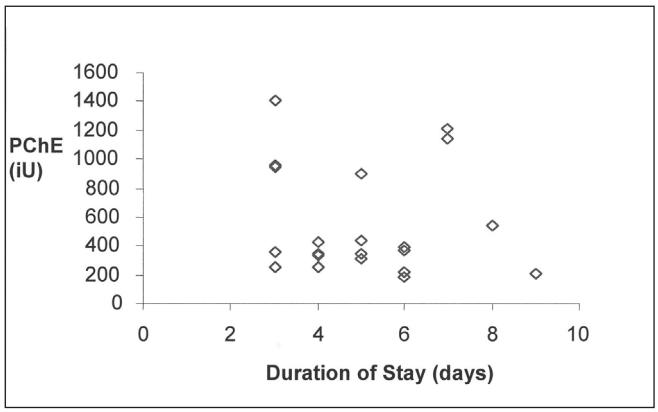

Fig. 3. Scatter plot of pseudocholinesterase level v. duration of stay.

Africa and it can be assumed that the reported numbers are a gross underestimation of the real problem.[9] Our study region is well represented in the above statistic.

The seasonal predominance between October and January is an overriding feature of these poisonings. The fact that incidence coincides with peak spraying activities (a trend also noted by other authors) could prove pivotal to the success of future preventive strategies.[10] OPP indicates a problem of increased exposure to and circulation of agricultural pesticides. More stringent enforcement of current legislation is required, along with a need for education. Education of both employees and employers cannot be overemphasised, as this remains pivotal in reducing exposure to these hazardous chemicals, especially among children. Legislation forcing farms to erect clear signage warning children and adults to keep away from recently sprayed areas may be an effective solution. School-based programmes (as attempted by the Department of Health a few years ago) and child-to-child programmes should be introduced. The high number of referrals from the De Doorns area (35%) in combination with 61% of poisonings by accidental ingestion indicates a high-risk area that would benefit from a structured education programme. Legislation, particularly in the De Doorns area, should be more strictly enforced, with seasonal air monitoring, more stringent control

of pesticide storage and regular/random blood levels done on employees.

Diversity in mode of presentation was the result of the population having access to a variety of OP-containing insecticides of varying concentration, and of delay in presentation because of the large patient drainage area. Atropine is without doubt extremely effective for rapid stabilisation of these patients, but its side-effects and high risk of toxicity should be criticised. All patients in our study group were treated according to recommended OPP treatment protocols regarding dosage, monitoring and weaning from atropine; despite these guidelines toxicity was recorded in 44% of cases. When assessing age, pseudocholinesterase levels, or mode of poisoning as risk factors for atropine toxicity, no independent risk factor could be identified.

Possible reasons for the high rate of toxicity include a poor definition of atropine toxity that resulted in an overestimation of cases, small sample size, or physicians erroneously attributing symptoms/signs to OPP, and therefore increasing atropine dosage.

EDH functions as a regional hospital, with ventilatory facilities limited to short-term (less than 48-hour) stabilisation of children before transfer to a tertiary facility. Ventilatory support was provided for 4 patients. Ingestion was sighted as the source of poisoning in both the transferred patients, possibly implying a higher dosage of OP but correlated poorly with the serum pseudocholinesterase level. The symptomatology for the 4 ventilated patients showed marked variability, accentuating the multifactorial influences governing OPP. The only overlapping trend was hypoxia and copious secretions cited as the indication for intubation in 3 of the cases. In our experience pseudocholinesterase correlated poorly with regard to severity of poisoning, based on duration of stay and clinical response to treatment. Some children with levels below 300 international units (IU) had a brief uncomplicated stay and others with levels in excess of 1 000 IU had a prolonged stay even requiring intubation. The decision to transfer to a tertiary facility should only be explored once the patient has been stabilised with atropine, as the response may be rapid and warrants regular reassessment.

One patient received glycopyrrolate. Recent advances in the field of anticholinergics have generated renewed interest in glycopyrrolate, particularly its potential for managing OPP. Drugs such as glycopyrrolate and scopolamine are used extensively in anaesthesiology as alternatives to atropine. Glycopyrrolate, a quaternary amine, penetrates biological membranes, especially the blood-brain barrier, slowly; this pharmacokinetic distinction from atropine has resulted in a number of studies comparing the use of glycopyrrolate and atropine in OPP.[4,11,12] One study performed on adults found no particular difference in outcome between the 2 drugs but found a statistically significant decrease in bronchial secretions in those treated with glycopyrrolate.[4] The study also commented on glycopyrrolate's potential to distinguish atropine toxicity from conditions that mimic it such as repoisoning with OP and septicaemia.[4] Compared to atropine its side-effect profile is also considerably better. There are fewer tachycardias; potential central nervous system effects such as headaches, insomnia, nervousness, etc. are unlikely owing to poor blood-brain barrier penetration; while xerostomia, loss of taste, decreased sweating and urticaria are similar to atropine. However glycopyrrolate enhances gastro-oesophageal reflux and has the potential to cause muscle weakness.[11]

The study has a number of shortcomings. The fact that it was a retrospective folder review with a small sample size limits the conclusions that can be drawn. For the most part the sample group is derived from a predictable population, at high risk of exposure or previous exposure, which could have affected response to standard treatment protocols. The high number of referrals from the De Doorns area may represent artefactual results due to a high index of suspicion, proximity to EDH, and other OPP cases draining to outlying hospitals. There was a small peak of cases during June because 2 siblings presented to EDH after an OP for pest control had been used inside their home. The use of obidoxime may perpetuate atropine toxicity but is unlikely with single-dose administration. Pseudocholinesterase is not specific for OPP alone but is also decreased in organocarbamate poisoning.[13] Clearly defining the terms 'atropine toxity' and 'poor prognosis' is troublesome.

OPP is a reality, with serious consequences; however the high risk of atropine toxicity during treatment may potentially be even more detrimental to the child, masking sepsis or repoisoning. Regular re-evaluation is essential.

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