UK childhood exposures to pesticides 2004–2007: a TOXBASE toxicovigilance study

R D Adams, D Lupton, A M Good, D N Bateman

ABSTRACT

Objective: There are no systematic methods for toxicovigilance of non-medicinal products in the UK. This is particularly relevant for pesticides, where there is significant public concern about potential adverse effects. This study describes a prospective toxicovigilance scheme based on follow-up of enquiries to the National Poisons Information Service (NPIS) through its online poisons information system TOXBASE. These enquiries reflect acute exposures and the patterns of acute illness that result.

Results: A total of 10 061 pesticide-related enquiries were identified. After follow-up, data were gathered on 2364 suspected exposures, of which 1162 involved children. After exclusions, 1147 exposures are reported here. No deaths were reported and only 37 children were admitted to hospital. The majority were considered to have either minimal or no features (925, 80.6%). Symptoms for 38 children were unknown. Symptoms reported in the other 184 children included nausea or vomiting (58), eye irritation, pain or conjunctivitis (29), skin irritation (28), abdominal pain (24), mouth or throat irritation (18) and diarrhoea (15). Where age was recorded, 60.5% (680) of children involved in suspected pesticide exposures were aged 2 years or less. The most common scenario for acute accidental exposure to pesticide in children was exposure after application (329, 24, because of the difficulties of identifying case exposure were combined.

Conclusions: Areas of potential concern identified included storage, access of young children to “laid” baits and pesticides, and exposures as a result of medication errors, with liquid head lice preparations being confused with other medicines. Use of NPIS systems provides a potentially useful method of toxicovigilance.

There are at present no formal toxicovigilance structures in the UK for monitoring the effects of exposures to pesticides. These continue to cause anxiety among members of the public.³⁻⁴ Management of these cases presents a challenge to health professionals, particularly in childhood, where there is relatively little information on acute outcomes from these exposures. For most pesticides, acute effects reflect the extent of exposure. This information is of relevance to licensing, improved safety in use and advice on treatment.

We therefore conducted a longitudinal study, the first of this type reported in the UK, to examine the health effects of pesticide exposures using National Poisons Information Service (NPIS) systems.²⁻⁴ Here we report findings in exposures of children (≤ 12 years old) to pesticides about which enquiries were made to TOXBASE between 1 April 2004 and 31 March 2007.

What is already known on this topic

- There is very little information on the nature and effects of acute pesticide exposures in children.
- Internationally, annual reports from the American Association of Poison Control Centers’ NPDS (National Poison Data System) and TESS (Toxic Exposure Surveillance System) have not looked specifically at this issue.
- In the UK, data on accidental pesticide exposures in children are currently limited.

What this study adds

- This first longitudinal study of its type to be performed in the UK provides information on the nature and range of exposures.
- It provides significant reassurance that pesticide products currently available do not present a generalised acute health hazard after accidental exposure.
- It also demonstrates that toxicovigilance studies such as this can gather potentially valuable exposure information.

METHODS

TOXBASE is the internet database of the NPIS.³ A list of pesticides of specific interest was agreed between the Pesticides Safety Directorate of the UK Health and Safety Executive and NPIS Edinburgh in 2004, and monographs for these pesticides were identified on TOXBASE. By March 2007, 324 TOXBASE entries for products and specific agents were being tracked. Users accessing these pesticides for a patient-related enquiry were requested to complete an online form. If they did not, a postal questionnaire based on that of Leverton and colleagues⁵ was sent, with a covering letter and prepaid return envelope. No postal questionnaires were sent to NHS Direct or NHS 24, because of the difficulties of identifying case details in their systems. Responses about the same exposure were combined.

All telephone enquiries to NPIS Edinburgh (>90% from Scotland) about pesticides received during the period were followed up. Thus the total number of questionnaires comes from three sources: electronic questionnaires, follow-up of TOXBASE users who did not complete an...
RESULTS

Between 1 April 2004 and 31 March 2007, a total of 10 061 patient-related pesticide enquiries were identified.

Data on 2364 patient exposures were subsequently gathered, of which 1162 concerned exposures of children. Nine children were excluded from the analysis because their symptoms were thought not to be related to the exposure (eg, timings of exposure and symptoms; other illness deemed responsible). Other reasons for exclusion were deliberate self-harm (1), exposures reported as chronic (3) and exposures where the nature of the putative exposure was not identified (2). Of the 529 cases where the exposure occurred after application, 119 (36.2%) involved rodenticides; 96 (29.2%), ant killers; and 83 (16.1%), slug killers. The most frequent route of exposure was ingestion (778, 69.1%). Multiple routes of exposure were found for 17.9% (201) of children.

Symptoms were absent in 925 (80.6%); for 38 the question was answered “unknown” or was not recorded; in the 184 children who had symptoms, these included nausea or vomiting (58), eye irritation (29), skin irritation (28), abdominal pain (24), mouth or throat irritation (18) and diarrhoea (15).

Of exposure to head lice treatments, therapeutic error accounted for 29 (16.5%) of 178, these products being mistaken for an oral medication (41.4% for paracetamol). Seven (24.1%) patients exposed because of therapeutic error had symptoms, similar to the prevalence of symptoms in head lice exposures overall (43, or 24.4%).

Of 259 patients exposed to rodenticides, 44 respondents recorded measuring the INR (international normalised ratio) or prothrombin time, although most (26) did not report the result. Of the 18 who did record the outcome, 16 found normal and only two prolonged prothrombin time.

Specific treatment was reported as not required in 86.5% (608) of the 708 cases. In the 29 cases where a specific treatment was recorded, it involved eye irrigation (15), oral activated charcoal (5), skin decontamination (5), topical antibiotics to the eye (4), oral fluids (2), analgesia (2), gastric lavage (1), intravenous fluid (1), oral antihistamines (1), oral antibiotics (1) or topical emollient (1), in line with the advice provided on TOXBASE. No children were admitted to intensive care, required ventilation or were reported to have significant complications or longer-term effects from the exposure. There were no deaths reported in our study group, and the national data sets on mortality are not product specific and do not assist further analysis in this regard.

DISCUSSION

In contrast to the situation for drugs, there is at present no formal system for toxicovigilance for other products in the...
The importance of post-marketing surveillance has been recently emphasised in connection with adverse effects in respect of waterproofing sprays and toys.

TOXBASE product entries were accessed more than 1,000,000 times in 2007. Since pesticide accesses are a small proportion of the total database use, intensive monitoring of the type described is possible. There was a disappointingly low response rate (7.5%) to online use of a questionnaire and this may reflect the way in which TOXBASE is used in front-line clinical situations. Follow-up rates were far higher for telephone enquiries (53.6%) and postal questionnaires (25.6%). It is not possible to say whether symptoms may positively bias the return of reports, but as the children in 80.6% of cases reported were asymptomatic, this seems unlikely.

The distribution of patient age and gender reported in this study reflects many of the patterns that have been found in previous epidemiological studies of general poisoning and suggests that the data collected reflect the overall pattern of exposure. These similarities support the concept that the surveillance approach we have used is likely to reflect overall patient exposure patterns, and while it is possible that this low response rate might bias the results, these similarities make it less likely.

It is unlikely that all patients were exposed to pesticide if exposures reflect other experience in childhood poisoning where laboratory confirmation was conducted. Confirmation of exposure to pesticides is challenging in routine practice, as exposures reflect other experience in childhood poisoning where frequency (84.0%) occurred in children under the age of 5 years, with children aged 2 the most frequently exposed (fig 1). These findings concur with those of previous studies on childhood poisoning.

Most of the exposures reported either occurred after the pesticide, usually a bait-type compound, had been applied (22.7%) or were due to unsatisfactory storage (19.9%). Exposures through ingestion were common (69.1%), with rodenticides (22.5%), ant killers (20.8%) and slug killers (12.1%) being prominent.

Despite the large number of children presenting to healthcare professionals, most exposures did not produce symptoms (80.6%) asymptomatic and were considered of “minor” severity (76.2%) by the healthcare professional involved. Most of the children exposed (96.4%) either were not admitted to hospital or were discharged on the same day. No patients were reported as being admitted for more than 2 days. The cases in which an admission of 2 days was recorded followed exposure to rodenticides.

Head lice treatments accounted for 15.5% of exposures. There is potential to reduce therapeutic error through education, repackaging or improved storage. These products were either mistaken by children themselves or by carers as an oral pharmaceutical.

**CONCLUSIONS**

The effects of potentially toxic pesticides on health can be monitored using NPIS resources. Most suspected pesticide exposures of children resulted in no clear acute adverse health outcome and were considered of minor severity. No children were reported to have died or to have been admitted to intensive care. Nevertheless, issues such as safety of storage and care after application of bait-style products were highlighted. There would appear to be potential for reducing such exposures through health education and improved packaging and labeling.

**REFERENCES**

Hyperinsulinism-hyperammonaemia syndrome

The hyperinsulinism-hyperammonaemia syndrome (HHS) was reported in a series of eight patients in 1988. Since then several series of up to 14 patients have been reported. The cause is an activating missense mutation in the GLUD1 gene at chromosome 10q23.3 that encodes glutamate dehydrogenase (GDH). The mutations occur either de novo or with dominant inheritance. The activity of GDH is enhanced by reduction of the inhibitory effect on GDH of guanosine triphosphate (GTP) and adenosine triphosphate (ATP). In HHS the biochemical disturbance affects the pancreas, the liver, and possibly the brain. The main clinical features are recurrent hypoglycaemia (it is a cause of leucine-induced hypoglycaemia) beginning in early infancy, and mild to moderate hyperammonaemia without lethargy, headaches or acute hyperammonaemic crises. Now the neurological aspects of the syndrome have been emphasised in a report of 22 patients from 17 families from centres in France, Italy and Belgium (Nadia Bahi-Buisson and colleagues. Developmental Medicine and Child Neurology 2008;50:945–9; see also Commentary, ibid: 888). The series consisted of 12 males and 10 females aged 18 months to 40 years, all with HHS proved genetically or biochemically. Learning disability was present in 17 patients and 14 had childhood-onset epilepsy, often with atypical absences. Less frequent seizure types included focal motor seizures and generalised tonic–clonic seizures. Eleven patients responded well to anticonvulsant drugs. Two patients had pyramidal tract involvement and one had generalised dystonia.

Four patients had signs of hypoglycaemia within 3 days of birth, but the median age at recognition of hypoglycaemia was 5 months. Seventeen patients had hypoglycaemic seizures. The hypoglycaemia was usually well controlled with diazoxide or a leucine-restricted diet or cornstarch, but one patient needed partial pancreatectomy. Mean ammonia concentrations varied from 117 to 128 µmol/l in different groups, but did not differ significantly between patients with or without epilepsy or learning disability. GDH overactivity affects the pancreas (hypoglycaemia), the liver (hyperammonaemia) and the brain. Whether the neurological problems seen in HHS are a consequence of hypoglycaemia or hyperammonaemia, or reflect brain GDH activity remains uncertain, but there is a suggestion from this series that mutations in the GTP binding site of GDH might predispose to epilepsy. Brain GDH activity could be important in regulating neurotransmitters such as GABA.
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