



# Adverse events associated with the use of complementary and alternative medicine in children

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## ABSTRACT

**Objective** To determine the types of adverse events associated with the use of complementary and alternative medicine (CAM) that came to the attention of Australian paediatricians.

**Design** Monthly active surveillance study of CAM-associated adverse events as reported to the Australian Paediatric Surveillance Unit between January 2001 and December 2003.

**Results** There were 39 reports of adverse events associated with CAM use, including four reported deaths. Reports highlighted several areas of concern, including the risks associated with failure to use conventional medicine, the risks related to medication changes made by CAM practitioners and the significant dangers of dietary restriction. The reported deaths were associated with a failure to use conventional medicine in favour of a CAM therapy.

**Conclusion** CAM use has the potential to cause significant morbidity and fatal adverse outcomes. The diversity of CAM therapies and their associated adverse events demonstrate the difficulty addressing this area and the importance of establishing mechanisms by which adverse effects may be reported or monitored.

## INTRODUCTION

Complementary and alternative medicine (CAM) is commonly administered to children.<sup>1-3</sup> Parents often use CAM with the idea that it is natural and therefore harmless,<sup>4</sup> however, adverse events associated with CAM use can occur.<sup>5-6</sup> There are limited data on the incidence and nature of adverse events associated with CAM use.

Despite the fact that there is inadequate safety information for many CAM treatments, there is no defined mechanism for reporting adverse outcomes. Adverse effects may be related to medicinal CAM products such as herbal treatments, non-medicinal therapies or a failure to use conventional medicine. Monitoring for adverse events associated with CAM may identify areas of concern and thus enable appropriate action to be taken.

The aim of this study was to determine the types of adverse events associated with the use of CAM that come to the attention of Australian paediatricians.

## METHODS

A surveillance study of adverse events associated with the use of CAM was conducted using the resources of the Australian Paediatric Surveillance Unit (APSU). The APSU methodology has been described in detail previously.<sup>7</sup> In summary, the APSU conducts an active surveillance system to detect selected rare disorders of childhood.<sup>8</sup>

## What is already known on this topic

- ▶ Complementary and alternative medicine (CAM) is commonly administered to children.
- ▶ As CAM is frequently regarded as natural and therefore safe, adverse events may go unreported.

## What this study adds

- ▶ Surveillance is possible for adverse events related to CAM use.
- ▶ CAM therapies, in particular in association with a failure to use conventional medicine, can lead to serious and fatal adverse events.

The APSU distributes monthly report cards to Australian paediatricians who indicate any cases seen or that they have nothing to report.

Clinicians who reported a suspected CAM-associated adverse event received a two-page questionnaire. The questionnaire collected de-identified information including details of the adverse event, the CAM therapy used and an assessment of causality and severity as judged by the reporting physician. Clinicians also indicated if the adverse event was potentially related to a failure to use conventional therapy.

The study was approved by the Ethics in Human Research Committee of the Royal Children's Hospital, Melbourne.

## RESULTS

Surveillance for adverse events via the APSU was conducted over 36 months from January 2001 to December 2003. There were 46 reports of CAM-associated adverse events. Forty questionnaires were returned to the investigators, giving a return rate of 85%. However, one was a duplicate report, so there were 39 reported events.

Reports described children from birth to 16 years of age and events ranged in severity from mild to severe, with four fatalities. In 25 cases (64%), the adverse events were rated as severe, life-threatening or fatal. In 30 cases (77%), the adverse events were considered by the reporters to be either probably or definitely related to CAM. In 17 cases (44%), the reporters stated that they believed that their patient had been harmed by a failure to use conventional medicine. All four fatalities resulted from a failure to use conventional medicine in favour of CAM therapies.

The reports described a wide variety of adverse events and CAM therapies. Reported adverse events were categorised into two groups: those associated with a CAM therapy and those associated with a failure to use conventional medicine

in favour of CAM. These results are summarised in tables 1 and 2.

All reported deaths related to a failure to use conventional therapy. One involved an 8-month-old infant admitted with

**Table 1** Adverse events associated with the use of medicinal CAM

AE	CAM
Previously reported AEs	
1. Constipation	Valerian
2. Constipation	Large volumes of chamomile tea
3. Bleeding	Gingko/ginseng
4. Carotenaemia	High dose vitamins including beta-carotene and high intake of carotene containing foods
5. Thyrotoxicosis	Thyroxine for chronic fatigue syndrome
6. Hypercalcaemia	Oral and intravenous calcium
7. Argyria	Colloidal silver
8. Leg pain and left sciatic neuropraxia	Intramuscular injection of daily vitamins
Potential AEs	
9. Poor growth	Echinacea
10. Allergic reaction	Ingestion of vitamin mixture
11. Acidosis	Crushed pearl
12. Mouth ulcers	Homeopathic drops
13. Seizure and apnoea	Homeopathic medicines
14. Acute hepatitis and liver failure requiring a transplant	Multiple herbal therapy and minerals
15. Fever, vomiting, drowsiness and respiratory symptoms	Pulsatilla 30 (with protoanemonin)
16. Vomiting and dehydration	High dose taurine and inositol added to infant formula
17. Intraoperative bleeding	Herbal medicines, including slippery elm
Pregnancy	
18. Premature closure of ductus arteriosus	Raspberry tea leaf
19. Neonatal hyponatraemic seizures	Multiple herbal and vitamin/mineral supplements
Overdose	
20. Admission for observation as no specific information on toxicity available	Gingko and brahmi
21. Tachycardia, fever, drowsiness and hypoglycaemia	Accidental ingestion of Infacalm drops
Contamination	
22. Steroid excess	Herbal centre medicine (ingredients)

AE, adverse event; CAM, complementary and alternative medicine.

**Table 2** Adverse events associated with a failure to use conventional therapy

AE	CAM
Dietary restriction	
23. Malnutrition, sepsis and death	Naturopathy and rice milk diet with life-start supplement for congestion
24. Malnutrition, sepsis and death	Homeopathy and dietary restriction for eczema
25. Malnutrition and oedema	Homeopathy and dietary restriction for eczema
26. Failure to thrive	Rice milk in toddler for constipation
27. Dehydration, encephalopathy, acidosis and subsequent refeeding syndrome	Massage and fluid restriction for cough
Failure to use conventional therapies	
28. Worsening seizures	Osteopathic treatment for epilepsy and anticonvulsant withdrawal
29. Admitted to hospital with seizures	Homeopathy and magnetic field generation for epilepsy instead of anticonvulsants
30. Further seizures and unexpected death	Infant with epilepsy and seizure with cardiorespiratory arrest; CAM used instead of anticonvulsants
31. Death following pulmonary embolus	Failure to use anticoagulants for clotting disorder and CAM used instead
32. Hyperglycaemia, polyuria and polydipsia	Naturopathy for diabetes and reduction in insulin dose
33. Haemophilus influenzae b pneumonia	Failure to immunise child
34. Infant with Down's syndrome and regret regarding prenatal testing	46-Year-old woman advised against prenatal testing by a traditional Chinese herbalist
35. Confused and complex grieving process	Opinion from chiropractor regarding aetiology of disease after perinatal asphyxia
36. Urinary tract infection not diagnosed for 6 weeks	Chiropractic treatment for irritable infant
37. Delayed management of severe cerebral palsy	Naturopathy, craniospinal therapy and hyperbaric oxygen
Unnecessary treatment recommended	
38. Routine referral of all common infant problems by maternal child health nurse	Chiropractic
39. Normal back examination	Advised expensive chiropractic treatment for kyphoscoliosis

AE, adverse event; CAM, complementary and alternative medicine.

malnutrition and septic shock following naturopathic treatment with a rice milk diet from the age of 3 months for 'congestion' (case 23). Another death involved a 10-month-old infant who presented with septic shock following treatment with homeopathic medicines and dietary restriction for chronic eczema (case 24).

Sudden unexplained death in epilepsy was reported in a child who had presented with multiple seizures, including one with cardiorespiratory arrest (case 30). In this case, a number of different CAM therapies had been used instead of anti-convulsant therapy due to concerns about potential drug side effects. The fourth reported death was of a child who was prescribed anticoagulants following pulmonary emboli (case 31). However, a complementary medicine was used for treatment instead of anticoagulants and the child died following complications relating to a pulmonary infarction.

## DISCUSSION

The reports described a wide variety of CAMs, and types and severity of adverse event. Those at highest risk were infants with restricted dietary intake and children with chronic illness in whom conventional therapies were withdrawn in favour of CAM treatment.

Some reports associated with medicinal CAM use were consistent with known side effects. In others, there was insufficient information to establish causality, highlighting the importance of spontaneous reporting of potential adverse drug reactions.

Reporting of CAM adverse effects can be complicated as information about the product may not always be available. This was clearly demonstrated in our study where product names were frequently unknown or brand names were known but ingredients were not. Additionally, many medicinal CAM products contain multiple ingredients and thus determining which, if any, of the ingredients contributed to the adverse outcome may not be possible. Products may also be contaminated or adulterated with conventional medicines, such as steroids (case 22).

Two reports were related to CAM use in pregnancy (cases 18 and 19). Problems with CAM use in pregnancy have been reported previously.<sup>9 10</sup> Data about the use of CAM (and other medicines) in pregnancy are often lacking, emphasising the importance of educating women about the risks of taking any medicines, including CAM.

As with other medications, there is a potential safety risk with overdoses of medicinal CAM. Two overdoses were reported during the study period (cases 20 and 21). When overdose occurs, there may be limited data about potential overdose effects making management difficult. In addition, as CAM products are often viewed as natural and harmless, they may not be stored appropriately within the home.

Several reports were received about marked dietary restriction in infants and associated malnutrition (cases 23–27). Two reported fatalities related to CAM use in association with marked dietary restriction leading to malnutrition and sepsis. Children with illnesses such as eczema in which allergy is frequently seen as an aetiological factor, may be at higher risk of significant dietary restriction. These cases of significant dietary restriction are also examples of families who sought healthcare options firmly outside conventional treatments and thus presented late. Regulation of CAM practices may minimise practice risks by enforcing appropriate safety standards.<sup>11</sup>

Another area highlighted in a number of reports was the situation where conventional medication was stopped or altered in favour of a CAM therapy. Discussions with families about CAM use may empower them to talk about any medication changes suggested by a CAM practitioner before altering or ceasing the medication. However, many of the adverse events associated with failure to use conventional medicine resulted from the family's belief in CAM and determination to use it despite medical advice.

The most important limitation of any spontaneous reporting system is under-reporting. Our study relied on paediatricians recognising an adverse event associated with CAM and then reporting it through the APSU. Many factors may influence reporting rates, including time pressures, uncertainty about causality and severity of outcome.<sup>12</sup>

Estimation of adverse events is further limited in this study because information was collected from paediatricians only. Therefore the number of reports received will provide an underestimate, as adverse events may be reported to another clinician or back to the treating CAM practitioner. There is some evidence to suggest that consumers are less likely to present with an adverse event relating to the use of a complementary treatment compared with an event of similar severity with a conventional drug.<sup>13</sup>

The high proportion of severe, life-threatening and fatal reports reflects referral patterns to paediatricians, as well as the higher likelihood of reporting a more serious event. The rate of reported likely causality reflects the fact that clinicians are more likely to report cases where they have reasonable suspicions of causality.

All appropriate reports from our study were forwarded to the Australian Adverse Drug Reactions Advisory Committee. Clinicians seeing any potential adverse effects associated with CAM products should complete an adverse drug reactions form.

This study describes a small case series of adverse events seen by paediatricians, the most worrying feature being the significant proportion of life-threatening and fatal reports, particularly in families using CAM to the exclusion of conventional medicine. The reports highlight a number of areas of concern and identify children with chronic illness or restricted diets as potentially the most vulnerable.

The diversity of reports received demonstrates the difficulty of monitoring this area given the range of CAM therapies and different adverse outcomes. General surveillance for CAM adverse effects as in this study and reporting adverse drug reactions for medicinal CAM may be helpful in continuing to identify specific areas of concern. The aim should be to establish regulation frameworks in which standards of practice can be established for individual CAM disciplines.

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**Competing interests** None.

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