Adverse events associated with paediatric use of complementary and alternative medicine: Results of a Canadian Paediatric Surveillance Program survey

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S Vohra, J Brulotte, C Le, T Charrois, H Laeeque. Adverse events associated with paediatric use of complementary and alternative medicine: Results of a Canadian Paediatric Surveillance Program survey. Paediatr Child Health 2009;14(6):385-387.

BACKGROUND: Despite many studies confirming that the use of complementary and alternative medicine (CAM) by children is common, few have assessed related adverse events.
OBJECTIVE: To conduct a national survey to identify the frequency and severity of adverse events associated with paediatric CAM use.
METHODS: Survey questions were developed based on a review of relevant literature and consultation with content experts. In January 2006, the Canadian Paediatric Surveillance Program distributed the survey to all paediatricians and paediatric subspecialists in active practice in Canada.
RESULTS: Of the 2489 paediatricians who received the survey, 583 (23%) responded. Respondents reported that they asked patients about CAM use 38% of the time and that patients disclosed this information before being questioned only 22% of the time. Forty-two paediatricians (7%) reported seeing adverse events, most commonly involving natural health products, in the previous year. One hundred five paediatricians (18%) reported witnessing cases of delayed diagnosis or treatment (n=488) that they attributed to the use of CAM.
CONCLUSION: While serious adverse events associated with paediatric CAM appear to be rare, delays in diagnosis or treatment seem more common. Given the lack of paediatrician-patient discussion regarding CAM use, our findings may under-represent adverse events. A lack of reported adverse events should not be interpreted as a confirmation of safety. Active surveillance is required to accurately assess the incidence, nature and severity of paediatric CAM-related adverse events. Patient safety demands that paediatricians routinely inquire about the use of CAM.

Key Words: *Adverse effects; Complementary therapies; Health survey; Manipulation; Natural products; Paediatrics; Spinal*

Les effets indésirables liés à l'utilisation des approches complémentaires et parallèles en pédiatrie : Les résultats d'un sondage du Programme canadien de surveillance pédiatrique

HISTORIQUE : Malgré les nombreuses études confirmant la fréquence d'utilisation des approches complémentaires et parallèles (ACP) par les enfants, peu d'entre elles en ont évalués les effets indésirables.
OBJECTIF : Procéder à un sondage national pour déterminer la fréquence et la gravité des effets indésirables liés à l'utilisation des ACP en pédiatrie.
MÉTHODOLOGIE : Les questions du sondage découlaient d'une analyse des publications pertinentes et de consultations auprès d'experts du contenu. En janvier 2006, le Programme canadien de surveillance pédiatrique a distribué le sondage à tous les pédiatres et pédiatres avec surspécialité en pratique active au Canada.
RÉSULTATS : Des 2 489 pédiatres qui ont reçu le sondage, 583 (23 %) y ont répondu. Ces répondants ont déclaré avoir demandé à leurs patients s'ils adoptaient des ACP dans 38 % des cas et avoir été informés d'une telle utilisation par les patients avant qu'ils leur posent la question dans seulement 22 % des cas. Quarante-deux pédiatres (7 %) ont déclaré avoir constaté des effets négatifs, portant surtout sur les produits de santé naturels, au cours de l'année antérieure. Cent cinq pédiatres (18 %) ont déclaré avoir été témoins de retards de diagnostic ou de traitement (n=488) qu'ils attribuaient à l'utilisation d'ACP.
CONCLUSION : Les effets négatifs graves liés à l'utilisation d'ACP chez les enfants semblent rares, mais les retards de diagnostic ou de traitement semblent plus courants. Étant donné l'absence de discussions entre les pédiatres et les patients au sujet de l'utilisation des ACP, nos constatations peuvent être sous-représentatives des effets indésirables. Il ne faut pas interpréter l'absence d'effets indésirables déclarés comme une confirmation d'innocuité. Il faut assurer une surveillance active pour évaluer correctement l'incidence, la nature et la gravité des effets indésirables liés aux ACP. Pour garantir la sécurité des patients, il faut que les pédiatres s'informent systématiquement de l'utilisation des ACP.

Complementary and alternative medicine (CAM), broadly defined as "a group of diverse medical and health care systems, practices and products that are not presently considered to be part of conventional medicine" (1), includes practices such as spinal manipulation, acupuncture and massage therapy, and natural health products (NHPs) such as vitamins, minerals, probiotics and supplements (2). Approximately 17% to 33% of the general paediatric population uses CAM (3-7). Recently, it was found that 49% of the population (n=1804) sampled from a large Canadian tertiary care paediatric emergency room used CAM (8). Despite an abundance of studies documenting paediatric CAM use, few studies have assessed related adverse events (AEs). AEs can be defined as unfavourable and unintended signs (including abnormal laboratory findings), symptoms or diseases associated with the use of CAM, whether confirmed to be related to the therapy (9). More than 100 paediatric CAM use studies were identified, only 19 of which describe safety data (unpublished data).

The authors collaborated with the Canadian Paediatric Surveillance Program (CPSP) to identify AEs associated with paediatric CAM. Each month, the CPSP administers ongoing and one-time surveys, gathering data from more

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Accepted for publication December 22, 2008

than 2400 paediatricians and other health care providers across Canada about the more than seven million children for whom they provide care (10). The aims of the present study were to identify the frequency of patient-clinician discussion about paediatric CAM use and the frequency and severity of CAM-related AEs, including those directly related to the therapy itself (coded as direct AEs), as well as those associated with delays in diagnosis and/or conventional treatment due to CAM use (coded as indirect AEs).

METHODS

In accordance with standard CPSP methodology for the administration of their one-time surveys, the questionnaire was limited to one page, which allowed for four multiple-part short-answer and yes/no questions. Paediatricians were specifically asked how often they inquired about patients' CAM use; how often patients mention CAM use before being questioned about it; whether they have seen an AE following CAM use in the past year; how many AEs were seen and what types of CAM (spinal manipulation, NHPs or other) were associated; what was the outcome of the most serious AE encountered; and how many, if any, indirect AEs were seen. A definition of CAM and examples, including chiropractic, massage therapy and NHPs (eg, herbals, homeopathic remedies), were provided.

In January 2006, the Canadian Paediatric Surveillance Program distributed the survey to all paediatricians and paediatric subspecialists in active practice in Canada in its monthly mailing. Respondents returned the survey to the CPSP with their monthly reporting forms. All returned surveys were forwarded to the investigators for data entry and analysis. Both partially completed surveys (ie, those with at least one but not all questions answered) and fully completed surveys were included in the data analysis. Data were descriptively analyzed using Excel (Microsoft Corporation, USA), and correlation analysis was conducted with 95% CIs where appropriate. The study was approved by the health research ethics board at the University of Alberta (Edmonton, Alberta).

RESULTS

Of 2489 mailed surveys, 583 were returned (23% response rate): 37 surveys were partially completed and 546 surveys were fully completed. Given that partially completed surveys were included in the analysis, the number of respondents varied from question to question. Paediatricians (n=574) reported asking their patients about CAM use 38% of the time. They (n=583) also reported that families spontaneously disclosed CAM use before being questioned only 22% of the time. There was a weak but statistically significant correlation between paediatricians who asked about CAM use and those who reported that parents/patients volunteered CAM use (r=0.11; P=0.01).

Forty-two (7%) respondents indicated that they had seen at least one AE following CAM use in the past year. They reported 41 AEs related to NHPs, 14 to spinal manipulation and three to other types of CAM. They also reported that 17 patients required medical treatment and an additional eight patients were hospitalized. With regard to the outcome of the most serious AEs seen in the previous year, paediatricians (n=46) reported that 26 AEs spontaneously resolved, nine led to a loss of school/work days, eight resulted in limitations to daily activities and four led to permanent disability. Respondents provided additional information regarding the cases that led to permanent disability: two patients suffered from kwashiorkor after being placed on restrictive diets (one respondent reported both cases); one had a disability requiring skin grafts after NHP use; and another had loss of vision, widespread scarring and decreased movement of the limbs, especially in the hands, after ingestion of Chinese herbal tea. Due to space limitations, additional data regarding the nature of these AEs were not gathered.

In terms of indirect AEs, 105 paediatricians reported seeing patients within the past year who had experienced delayed diagnosis or treatment because of CAM use. These paediatricians indicated that they saw 488 incidences of indirect AEs. Of note, an additional paediatrician reported 100 cases of delayed diagnosis and/or treatment due to CAM use in the past year; no details were provided and this participant's data were excluded because they were deemed outliers. No additional information regarding these indirect AEs was collected.

DISCUSSION

To our knowledge, we present the first Canadian national survey assessing AEs associated with paediatric CAM use. We found that AEs related to paediatric CAM do occur and may be most likely associated with the use of NHPs and spinal manipulation, likely reflecting the relative popularity of these therapies in children. Given Health Canada's estimate that 71% of Canadians use CAM therapies (11), the occurrence of CAM-related AEs as well as the lack of both inquiry and disclosure reported in the present study suggest a major information gap that could affect patient safety.

Poor physician-patient communication about CAM use has been documented previously and is considered a significant barrier to the discovery of CAM-related AEs (12-14). Other studies have reported that 64% to 67% of parents whose children used CAM did not disclose this use to their paediatrician (12,15-18). Previous work suggests that health care providers do not report potential AEs and that this situation may be exacerbated for some complementary therapies (19-23). This issue can be overcome by encouraging physician-patient dialogue about CAM use and reporting all AEs should they occur. The slight positive correlation between paediatrician inquiry and family disclosure in our study could mean that paediatricians who are willing to discuss CAM therapies create an environment that promotes open discussion and spontaneous disclosure on the part of patients and their families.

The present study has several limitations. First, the data obtained can only suggest a possible association between CAM use and AEs; more rigorous methodology is required to

determine causality. Second, the nature of the present survey did not allow for denominator data to be collected, which precludes the determination of the incidence of AEs. Third, the survey had a poor response rate, which limits the generalizability of the data. However, the response rate is comparable to the majority of other CPSP one-time surveys (personal communication) as well as other physician surveys that did not offer incentives or reminders (24-26). It may be speculated that paediatricians who have encountered AEs related to CAM use were more likely to respond to our survey. Fourth, respondents may have been more likely to indicate that AEs were associated with NHPs or spinal manipulation, versus other types of CAM, because these two types of CAM were specifically listed as options. Finally, the survey only captured AEs encountered by paediatricians. Children and youth are cared for by a variety of health care professionals including, but not limited to, family physicians and nurse practitioners.

It has been well recognized that reliance on spontaneous reporting often results in under-reporting as well as poor quality reports (20), and that a lack of reported AEs should not be interpreted as confirmation of safety. We intend to follow up this one-time survey by collaborating with CPSP and the American Academy of Pediatrics' Pediatric Research in Office Settings to conduct active surveillance of serious AEs associated with paediatric CAM.

CONCLUSION

The present national survey found that Canadian paediatricians routinely inquired about CAM use less than one-half of the time, and that families of CAM users disclosed paediatric CAM use less than one-quarter of the time. Reported AEs were most often associated with paediatric use of NHPs and spinal manipulation. The underlying question, "Is CAM safe for children?", remains largely unanswered. Given the sheer number of children exposed to CAM and the relatively few AEs that have been documented, the answer may well be yes. However, it would be preferable to document, rather than to assume, safety. Patient-centred care demands that paediatric health care providers routinely inquire about paediatric CAM use. Active surveillance of CAM-related AEs is necessary to ensure patient safety, because it would increase the detection and reporting of CAM-related AEs, allowing for greater understanding of which CAM therapies should be avoided and which appear to be safe in children.

ACKNOWLEDGEMENTS: The authors thank Dr Danielle Grenier as well as members of the CPSP steering committee and Sarah Srikanthan, all of whom provided input into the direction of the study. Sunita Vohra receives salary support from the Alberta Heritage Foundation for Medical Research and the Canadian Institutes of Health Research.

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