Nutraceuticals for the prevention of migraine in children: Do we know what the benefits and the risks are?

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Children with headache have limited evidence-based preventive options. When pharmacological measures are considered, it is not surprising that children are using agents considered to be complementary and alternative in dealing with their headaches. Unfortunately, the use of many of these (and other) headache preventives has outpaced the research which may show clear evidence for their use, or, equally possibly, for their inefficacy. Recognition of the current situation should serve both as a call for more research using well-designed, double-blind, randomized control trials in pediatric headache prophylaxis, as well as for caution until such evidence accumulates.

In their review paper in this edition of Cephalalgia, ‘Nutraceuticals in the prophylaxis of pediatric migraine’, (1) Orr and Venkateswaran summarize and critically appraise observational studies and randomized controlled trials in children and adults of six different treatments for migraine prophylaxis: butterbur, riboflavin, ginkgolide B, magnesium, coenzyme Q10 and polyunsaturated fatty acids. Their review is timely and important, given the prevalence of headache in children, widespread interest in nutraceuticals, and their frequent use for a variety of pediatric and adult medical conditions.

Nutraceutical use by patients is likely to be driven by several factors: incomplete efficacy of (prescription) drugs, a reluctance to use (prescription) drugs, perceived safety versus prescription drugs, perceived additional health benefits, availability and, perhaps, advertising. Disadvantages of nutraceutical use include expense if not covered by drug plans, fewer randomized control trials of these agents and so less evidence of efficacy, and increased headache burden when effective therapies are overlooked. Additionally, when individual nutraceuticals are untested or used in an unregulated setting, there is potential increased risk of harm. On the other hand, the use of nutraceuticals in the absence of good studies may cause them to be marginalized by physicians seeking such evidence before recommending them, when, if properly supported and launched, good trials might otherwise have shown those nutraceuticals to be effective.

Data from the past decade from the US National Health and Nutrition Examination Survey reveal that 34% of children and adolescents routinely use vitamin and mineral supplements (2), despite the American Academy of Pediatrics not recommending supplemental vitamin use in healthy children older than 1 year who consume a varied diet. Multivitamin preparations for older children and adolescents are not regulated by the Food and Drug Administration, leading to concerns about safety and potential adverse effects.

A recent analysis of linked data from the 2007 National Health Interview Survey and the 2008 Medical Expenditures Panel Survey evaluated the prevalence of complementary and alternative medicine (CAM) use among all youth in the USA, as well as youth with recurrent headaches (3). As stated by Orr and Venkateswaran, nutraceuticals are a form of CAM, making this analysis relevant. Of all youth between the ages of 10 and 17, 18.7% used at least one CAM modality (and 10.3% of all youth used specific vitamins/minerals). The estimate of youth experiencing headache was 10.6%; of these, 29.6% had used one or more types of CAM in the previous 12 months, compared with 17.4% of youth with the same diagnoses but without headache. Compared with youth with headache who did not use CAM, CAM users were more likely to be older, white, to live in homes with higher incomes, to have private health insurance and higher maternal education (3).

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The evidence to support the use of CAM for pediatric health conditions is poor. A recent overview of Cochrane reviews in pediatrics assessed the efficacy, clinical implications and limitations of CAM use in children (4). The main outcome variables assessed were the percentage of Cochrane reviews that concluded that a CAM intervention provides a benefit, the percentage of reviews that concluded that a CAM intervention should not be performed and the percentage of studies that concluded that the current level of evidence is inconclusive. Of the total 135 reviews included in this overview, only five gave a recommendation in favor of a CAM intervention; 26 gave a conditional positive recommendation and nine concluded that certain CAM interventions should not be performed. Ninety-five reviews were inconclusive. The most common criticisms of the quality of studies were the small number of study participants, low methodological quality or that more research was needed.

Orr and Venkateswaran’s review has made similar conclusions. For the prophylaxis of pediatric migraine, only a few studies of nutraceuticals have been performed. These studies include small numbers of patients and are of overall poor quality, making it difficult to make recommendations for their use. As Meyer and colleagues concluded in their overview, “unless the study of CAM is performed to the same science-based standards as conventional therapies, CAM therapies risk being perpetually marginalized by mainstream medicine” (4). A priori there is no reason to dismiss the potential efficacy of nutraceuticals which have not been tested, but there is also no reason to accept their efficacy. Many, if not most, prescription medications originate or are derived from similar sources.

This review paper used the GRADE system to make formal recommendations for and against the use of six nutraceuticals for the prophylaxis of migraine in children: butterbur (Petadolex formulation only) recommended; riboflavin not recommended; ginkgolide not recommended (in isolation); (some formulations of) magnesium recommended; coenzyme Q10 recommended; polyunsaturated fatty acids (not recommended). Reasons leading to not recommending agents varied: low-quality evidence and paucity of pediatric literature (riboflavin), open label and combination with other nutraceuticals (ginkgolide), and lack of efficacy (polyunsaturated fatty acids). The authors thoughtfully presented postulated mechanisms of action and summaries of the literature in adult populations for each of these agents as well.

Although the authors correctly applied the theory of the GRADE system to make recommendations, it is important for readers to be aware that the authors did not follow traditional guideline development processes. The GRADE system is an integral part of guideline development, which begins with the prioritization of a health problem, and the assembly of a guideline panel that includes multiple stakeholders. The GRADE system is then used to define the questions to be addressed, prepare a systematic review, assess the relative importance of outcomes, prepare evidence profiles, assess the overall quality of evidence, and finally, decide on the direction and strength of recommendations (5). Although the authors have done a thorough literature review, have made excellent observations on this topic, and have applied the principles of GRADE correctly to downgrade or upgrade evidence, this manuscript was not based on a systematic review of the evidence and did not involve a guideline panel of multiple stakeholders. Readers may find that the recommendations are at variance from their own practice, and it must be said that as a review rather than a guideline, this paper has not been able to incorporate expert consensus or experience of practice, where physicians so often turn when faced with a dearth of data.

This is not a guideline, but a literature review that provides recommendations for and against the use of nutraceuticals using the principles of GRADE. The limits of the review reflect the limits of our current knowledge of the efficacy of these and other pharmacological headache preventives. As the review stands, three of six agents for headache prevention in children have recommendations for use, and each of these with caveats. The opportunity to expand our knowledge is great, and the collective need of young headache sufferers is pressing.

References