INVITED COMMENTARY

Nutraceuticals in Pediatric Headache: Food for Thought

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oth parents and health care practitioners worldwide seek safe, effective and tolerable treatments for migraine in children. While many evidence-based pharmacologic options exist [1], families often turn to complementary and alternative medicine with a hope that effective and safe therapies can be offered to their children with a more tolerable side effect profile and equivalent efficacy. To that end, nutraceuticals represent "food, or parts of a food, that provide medical or health benefit, including the prevention and treatment of disease" [2]. In varying international markets they represent a variety of agents including functional foods, nutritional supplements, vitamins and herbal remedies, some of which have been used for thousands of years.

In India, the regulatory aspects of herbal medicine falls under the Drug and Cosmetic Act (D and C) of 1940 enforced by the Department of AYUSH (Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy) which requires manufacturers to acquire a license to manufacture and market herbal medicines. Within this, information regarding the manufacture, registration, sale, license and GMP (good manufacturing practice) certificate from manufacturers are required by various sections of the D and C act, with the recent mandate of product labelling with manufacturing and expiry dates on product labels as of 2017 [3].

In Canada, all natural health products must have a product license before sale in Canada under the provisions of the Natural Health Products Regulations in effect since January, 2004. The license is obtained following submission of information to Health Canada including medicinal ingredients, source, dose, potency, non-medicinal ingredients and recommended use(s). Once Health Canada has assessed a product as safe, effective and of high quality it issues a product license with an eight-digit Natural Product Number (NPN) or Homeopathic Medicine Number (DIN-HM) which must by law appear on the label. Good manufacturing practices (GMPs) are also enforced in Canada to ensure safe and high quality

products with specific labelling and packaging requirements [4].

Options studied in children [5] for the treatment of migraine include vitamins such as vitamin D and B2 (riboflavin), antioxidants such as coenzyme Q10, minerals including magnesium, phytomedicines such as butterbur and dietary sources of polyunsaturated fatty acids (PUFAs) such as omega-3 fatty acids. A recent review [5] concluded that due to low quality evidence and limited studies, no definite conclusions could be drawn upon the efficacy of nutraceuticals for the treatment of pediatric migraine. However further study was encouraged due to preliminary efficacy signals, favorable safety profiles and plausible mechanism of action in migraine for both coenzyme Q10 and magnesium. A particular recommendation of the review was to consider stratifying patients based on pre-treatment level if the nutraceutical under investigation is measurable.

The study by Bhurat, et al. [6] in Indian Pediatrics highlights this important gap in the literature in the case of the mineral magnesium. In particular, magne-sium plays an important role in in nerve transmission and a protective role against excessive excitation. The study by Bhurat, et al. [6] adds further evidence to the body of knowledge that adolescents with migraine are deficient in magnesium [7,8] and therefore a role for magnesium supplementation may contribute to the management of migraine in children. This particular cross sectional study of age and sex matched children found that in an adolescent (10-18 year old) subgroup serum magnesium levels were signifi-cantly lower in children with migraine compared to those without a headache disorder. While the sample sizes were small, the study adds important evidence to the consi-deration that magnesium replacement may be a useful migraine therapy in magnesium deficient adolescents with migraine. This requires further study, with previous evidence suggesting potential efficacy of magnesium in the prevention of pediatric migraine [9].

In regions where access to prescription medication for migraine may be limited due to access or finances,

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nutraceuticals may represent an alternative source of therapy for migraine in children. However, great care must be taken with children as regulatory bodies internationally differ with respect product testing and safety regulations and practitioners should be well aware of local licensing policies and products prior to recommen-dation for their use of children. With further rigorous study ideally through randomized controlled trials, if produced safely and dosed appropriately for weight and age, nutraceuticals may represent a path of accessible and effective migraine therapy for children worldwide.

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REFERENCES

- Oskoui M, Pringsheim T, Billinghurst L, et al. Practice Guideline Update Summary: Pharmacologic Treatment for Pediatric Migraine Prevention: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2019;93:500-9.
- DeFelice SL. The nutraceutical revolution: its impact on food industry R&D. Trends Food Sci Tech. 1995;6:59-61.

- Swathi J, Venkatesh DN. A review of herbal regulations in India and Worldwide. Research J Pharmacy Technol. 2022;15:1348-52.
- 4. About Natural Health Product Regulation in Canada. Accessed on August 8, 2022. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription/regulation.html
- Orr SL. The evidence for the role of nutraceuticals in the management of pediatric migraine: a review. Curr Pain Headache Rep. 2018;22:1-8.
- Bhurat R, Premkeenar S, Manokaran RK. Serum magnesium levels in children with and without migraine: A crosssectional study. Indian Pediatr. 2022;59:623-25.
- Soriani S, Arnaldi C, De Carlo L, et al. Serum and red blood cell magnesium levels in juvenile migraine patients. Headache. 1995:35:14-6.
- Gallai V, Sarchielli P, Coata G, Firenze C, Morucci P, Abbritti G. Serum and salivary magnesium levels in migraine. Results in a group of juvenile patients. Headache. 1992; 32:132-5.
- Wang F, Van Den Eeden SK, Ackerson LM, Salk SE, Reince RH, Elin RJ. Oral magnesium oxide prophylaxis of frequent migrainous headache in children: a randomized, double blind, placebo controlled trial. Headache. 2003;43:601-10.