

Complementary and alternative medicine: a world to be explored

Damião AOMC. Complementary and alternative medicine: a world to be explored. *Arq Gastroenterol.* 2017;54(3):175-6.

Complementary and alternative medicine (CAM) or nonallopathic therapies have been defined as healthcare systems, practices, and products that are not considered part of conventional medicine^(3,13). Western medicine, which is usually referred to as conventional (allopathic) or “mainstream” medicine (as opposed to “non-mainstream” in the case of nonallopathic therapy), involves medical care provided by practitioners and allied health professionals with accredited qualifications (e.g., physicians, psychologists, physical therapists, nurses)^(3,13). Complementary medicine refers to the use of CAM as an adjunct to conventional therapy and alternative medicine when it replaces conventional treatment. CAMs are diverse and range from a myriad of herbs, mainly used in the Eastern world and as a part of the traditional Chinese or Japanese medicine (e.g., curcumin, aloe vera, *Terminalia coriacea*, *Andrographis paniculata*, *Tripterygium wilfordii*, Padma Lax, STW5, Boswellia, daikenchuto, etc) to cannabis/marijuana, pre- and probiotics, helminths (e.g., *Trichuris suis*), peppermint oil, fish oil, hypnosis, acupuncture, meditation, reflexology, and so forth (the list is huge!)^(3,8,13). Many Western physicians are rather skeptical regarding CAMs. They claim the science behind CAM is weak compared to pharmaceutical drugs. Also, most of the CAMs are approved as food supplements, which usually are subject to lower-standard regulatory policies as compared to pharmaceutical drugs. This has potentially serious implications. Although food supplements are monitored strictly for heavy metals and other potential contaminants, the purity and concentration of their active ingredients often is neither controlled nor adequately regulated. For instance, pharmacy and nutritional food store shelves are filled with a large number of products claimed to contain curcumin, but they also have numerous additives. Thus, many curcumin-containing compounds commercially available are very impure. In fact, in one research, marketed curcumin food supplements differ in the concentration of active curcumin from 5% to 95%⁽¹¹⁾. The skepticism is further increased by the limited knowledge of CAMs by physicians, who reflect a lack of formal training on the topic, either in medical schools or in residency programs⁽³⁾. Despite this, CAM practices are generally perceived to be safe, “natural” treatment modalities with holistic appeal and individualized approach^(3,13). However, we do know that safety is an issue in some instances. For example, “wheat grass” disclosed promising effects in patients with active ulcerative colitis (UC), but one in every three patients developed nausea⁽³⁾. This corroborates the need of robust, randomized, blinded, well-controlled studies with safety reports with CAMs. In fact, a systematic review on the efficacy of herbal therapy in inflammatory bowel disease (IBD)⁽¹⁰⁾ concluded that “larger controlled studies with stricter endpoints and better-defined patient groups are required to obtain more conclusive results on the use of CAM therapies in IBD”.

CAMs are widely used by gastroenterological patients. It is estimated that the expenditure on CAM practices may be comparable to expenditure on conventional medical services⁽¹³⁾. Up to 50% of adult patients with functional disorders refer use of CAMs, in particular irritable bowel syndrome (IBS)^(8,13). Female patients who experienced milder bowel symptoms and less interference with work and activities were most likely to use CAMs⁽¹³⁾. In the pediatric setting, approximately 40% of children with GI complaints use CAMs each year including herbal medicines, massage therapy, megavitamin therapy, dietary supplements, and acupuncture^(3,12). In one study, 41% of children with IBD used CAMs⁽⁵⁾. The most important reasons for using CAMs were side effects from prescribed medicines, prescribed medicines not working as well as they had hoped, and “hoping for a cure.” Parenteral CAM use and number of adverse effects from conventional therapies were predictors of CAM use. Interestingly, 60% of the patients not taking CAMs were interested in learning more about it⁽⁵⁾. In a recent review on the use of CAMs in IBD, the main predictors of CAM use were side effects of or dissatisfaction with conventional therapies, female sex, higher education, use by friends or relatives, long-term progression of disease, and prolonged use of steroids⁽³⁾. The most commonly used CAMs among adult and pediatric patients were probiotics, herbs, vitamins, fish oil and mind-body techniques such as acupuncture. In some studies, CAM use reduced adherence to conventional therapy. Another study showed that 35.5% of patients with liver and biliary disorders used herbal remedies⁽⁹⁾.

It is relevant to point out that patients are frequently using CAMs without a physician’s knowledge. They are often reluctant to mention CAMs with their treating physician and most of them do not divulge their use to their provider. Patients are usually afraid that their physician will have a negative response in case they mention use of CAMs, and often are more comfortable discussing their use with a nurse or nonphysician⁽³⁾.

In the present issue of *Archives of Gastroenterology*, two elegant studies on CAMs are presented^(1,6). Both groups have the merit of getting some insights on the mechanisms behind the benefits of CAMs. In one of them, Ali Khan et al.⁽¹⁾, from India, in experimental models (Wistar rats) of gastric ulcers (aspirin and ethanol induced ulcers) demonstrated that *Terminalia coriacea*, a traditional herb used in India for the treatment of ulcers, had a marked dose-dependent gastroprotective effect, which was attributed to the presence of flavonoids in the herb. At least five flavonoids were identified (Kaempferol, Lutolina, Myricetin, Quercetin and Rutin). These flavonoids exert their anti-ulcer activity by means of anti-secretory, anti-oxidant, prevention of lipid peroxidation and induction of mucous secretion. It seems that in India, traditionally, many patients with peptic ulcer are treated with *Terminalia*

coriacea. It remains to be elucidated whether this CAM strategy would be effective regardless of the *Helicobacter pylori* status, or whether it should be used as a complement to conventional therapy (antibiotics) in *H. pylori* positive ulcer patients. Controlled trials are needed to clarify those options. In this context, it is important to mention that one of the flavonoids described – quercetin – has inhibitory effects on the *H. pylori* growth. It turns out to be interesting to include CAMs in the discussion of treatment of *H. pylori*, in a time when lots of antibiotics have been tested and the danger of bacterial resistance is undoubtedly an issue. In the other work, Judaki et al.⁽⁶⁾, from Iran, in a randomized clinical trial with *H. pylori* positive chronic gastritis patients, showed that the addition of curcumin (700 mg, oral, three times a day, for 4 weeks) to the usual triple therapy (omeprazole 20 mg, amoxicillin 0.1 g and metronidazole 800 mg, each given orally twice a day, for 1 week), significantly decreased histopathologic and endoscopic inflammatory scores and increased the eradication rate of *H. pylori* infection (86.4% versus 74.5%, $P < 0.05$). Additionally, they demonstrated that the combination with curcumin ameliorated the oxidative stress, and increased total antioxidant capacity of the gastric mucosa. It remains to be proven whether curcumin will be effective in conjunction with other antibiotics, since metronidazole is not commonly used in some countries due to *H. pylori* metronidazole-resistance (e.g., in Brazil, clarithromycin is used instead of metronidazole). Furthermore, the blindness in this kind of study is difficult since curcumin can turn stool to a yellow color.

Curcumin is a phytochemical derived from the Indian herb turmeric (*Curcuma longa*), which is a very popular food ingredient in Eastern cuisine. This plant has been used extensively in both Indian and Chinese herbal medicine for a wide variety of inflammatory situations, including gastrointestinal inflammation. Besides

its antioxidant properties, curcumin has been shown to inhibit nuclear factor-kappa B, tumor necrosis factor-alpha secretion, signal transducer and activator of transcription 3 (STAT-3), p38 mitogen-activated protein kinase, and T helper-1 cytokines⁽²⁾. It is also pro-apoptotic. Due to its anti-inflammatory, immunomodulating, proapoptotic, and antiangiogenic actions, and effects on housekeeping genes, it is potentially useful in inflammatory and oncologic conditions like colorectal cancer, and some have considered curcumin to be the most promising CAM to be used as an adjuvant in colorectal cancer management⁽²⁾. In refractory UC patients (full doses of mesalamine, oral plus topic), addition of oral curcumin (3 g/day) for 1 month was superior to placebo in inducing clinical (53.8% x 0, $P = 0.01$) and endoscopic remission (38% x 0, $P = 0.04$)⁽⁷⁾. Moreover, in quiescent UC patients, the addition of oral curcumin (2 g/day) to aminosalicylates for 6 months was better than placebo in the maintenance of remission⁽⁴⁾. Enemas of NCB-02, a curcuminoid preparation with 70% curcumin, trended toward a benefit on response, remission and endoscopic healing in distal resistant UC⁽³⁾.

In conclusion, physicians should be aware of the frequent use of CAMs by patients with gastrointestinal complaints. Unfortunately, few studies have adequately evaluated these therapies and the mechanisms that justify their salutary effects in health. These barriers have limited the acceptance of CAMs by the medical community who value evidence-based medicine. Yet, one should explore the CAM universe and recognize the evidence behind certain CAMs in order to offer rational advice to patients and take advantage of them in selected cases. Curcumin, in this sense, seems to be a good way to start.

Adérson Omar Mourão Cintra DAMIÃO *

Damião AOMC. Medicina alternativa e complementar: um mundo a ser explorado. Arq Gastroenterol. 2017;54(3):175-6.

REFERENCES

1. Ali Khan MS, Nazan S, Mat Jais AM. Flavonoids and anti-oxidant activity mediated gastroprotective action of *Leathery Murdah*, *Terminalia coriacea* (Roxb.) Wigh & Arn. Leaf methanolic extract in rats. Arq Gastroenterol. 2017;54(3):183-91.
2. Bernstein CN. Spicing up the treatment of mild to moderate colitis. Clin Gastroenterol Hepatol. 2015;13:1450-2.
3. Cheifetz AS, Gianotti R, Luber R, Gibson PR. Complementary and alternative medicines used by patients with inflammatory bowel diseases. Gastroenterology. 2017;152:415-29.
4. Hanai H, Iida T, Takeuchi K, Watanabe F, Maruyama Y, Andoh A, Tsujikawa T, Fujiyama Y, Mitsuyama K, Sata M, Yamada M, Iwaoka Y, Kanke K, Hiraishi H, Hirayama K, Arai H, Yoshii S, Uchijima M, Nagata T, Koide Y. Curcumin maintenance therapy for ulcerative colitis: randomized, multicenter, double-blind, placebo-controlled trial. Clin Gastroenterol Hepatol. 2006;4:1502-6.
5. Heuschkel R, Afzal N, Wuerth A, Zurakowski D, Leichtner A, Kemper K, Tolia V, Bousvaros A. Complementary medicine use in children and young adults with inflammatory bowel disease. Am J Gastroenterol. 2002;97:382-8.
6. Judaki A, Rahmani A, Feizi J, Asadollahi K, Hafezi Ahmadi MR. Curcumin in combination with triple therapy regimes ameliorates oxidative stress and histopathologic changes in chronic gastritis-associated *Helicobacter pylori* infection. Arq Gastroenterol. 2017;54(3):177-82.
7. Lang A, Salomon N, Wu JCY, Kopylov U, Lahat A, Har-Noy O, Ching JYL, Cheong PK, Avidan B, Gamus D, Kaimakliotis I, Eliakim R, Ben-Horin S. Curcumin in combination with mesalamine induces remission in patients with mild-to-moderate ulcerative colitis in a randomized controlled trial. Clin Gastroenterol Hepatol. 2015;13:1444-9.
8. Magge S, Lembo A. Complementary and alternative medicine for the irritable bowel syndrome. Gastroenterol Clin N Am. 2011;40:245-53.
9. Marignani M, Gallina S, Di Fonzo M, Deli I, Begini P, Gigante E, Epifani M, Angeletti S, Delle Fave G. Use and safety perception of herbal remedies in patients with liver/biliary tract disorders. An Italian study. J Clin Gastroenterol. 2010;44:S54-S57.
10. Ng SC, Lam YT Tsoi KKF, Chan FKL, Sung JYJ, Wu JCY. Aliment Pharmacol Ther. 2013;38:854-63.
11. Salomon N, Lang A, Ben-Horin S. Curcumin for inflammatory bowel disease: a caution. Clin Gastroenterol Hepatol. 2016;14:168.
12. Whitfield KL, Shulman RJ. Treatment options for functional gastrointestinal disorders: from empiric to complementary approaches. Pediatr Ann 2009;38:288-94.
13. Wu JCY. Complementary and alternative medicine modalities for the treatment of irritable bowel syndrome: facts or myths? Gastroenterol Hepatol 2010;6:705-11.

* Professor at the Department of Gastroenterology, University of São Paulo Medical School.