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LETTER TO THE EDITOR

Regression of an esophageal ulcer using a dietary supplement containing melatonin

To the Editor

Gastroesophageal reflux disease (GERD) is the reflux of gastric contents into the esophagus. The most prominent symptom is 'heartburn', with or without regurgitation of gastric contents into the mouth [1]. The usual drugs used for GERD are proton pump inhibitors (PPI), which are associated with several complications [2, 3].

A formula developed in our laboratory, for GERD [melatonin (2.5 mg), vitamin B12 (50 μg), vitamin B6 (200 mg), tryptophan (25 mg), methionine (100 mg), betaine (100 mg) and folic acid (10 mg) encapsulated in gelatin capsules)], was prescribed for a patient (with chronic GERD) in an attempt to interrupt the reflux and heal an ulceration of 6 cm in the esophagus. This formulation is based on information existing in scientific literature that melatonin has an inhibitory action on gastric acid secretion [4] and inhibitory activity on biosynthesis of nitric oxide [4]. As the constituents of the formula are natural compounds found in foods, it may present fewer side effects than medications currently used in clinical medicine.

A 35-year-old white male patient with chronic GERD had, initially, regurgitation and heartburn. He had these symptoms for more than 2 years and thereafter he treated himself with baking soda and antacids. Then, a gastroenterologist prescribed omeprazole. Neither treatment produced even partial relief of his symptoms. Subsequently, he started to lose weight because he could no longer eat properly because of the acute pain impaired swallowing and massive hematemesis. Even when he tried to drink an apple blended with water, he vomitted blood. Endoscopic examinations showed that he had an ulcer of 6 cm in the esophagus (Fig. 1A). As a consequence, he lost 40 kg in 6 months. After he consulted five gastroenterologists, he brought to me his endoscopy record and medical report. I immediately prescribed the following formulation: melatonin (2.5 mg), vitamin B12 (50 μg), vitamin B6 (200 mg), tryptophan (25 mg), methionine (100 mg), betaine (100 mg) and folic acid (10 mg) encapsulated in gelatin capsules. Two hours after he took the first gelatin capsule, his pain disappeared. He told me that he was hungry and he bought a roast chicken which he ate in its entirety, without feeling pain. After 32 days of treatment, he had recovered 30 kg. In photographs taken in October and November 2003, the color of his hair was yellow. The patient reported that his hair had changed color from black to yellow after the ulcer appeared (he did not dye his hair). This is consistent with the observations in rats where malnutrition changed hair color to yellow [5]. After treatment, the patient recovered the natural color of hair.

The patient stopped taking omeprazole to avoid malabsorption of vitamin B12 (present in the formula), as it has previously been reported that omeprazole (and other PPIs) and histamine (2)-receptor antagonists are associated with vitamin B12 deficiency; the concentration of this vitamin may be decreased when gastric acid is markedly suppressed for prolonged periods [6].

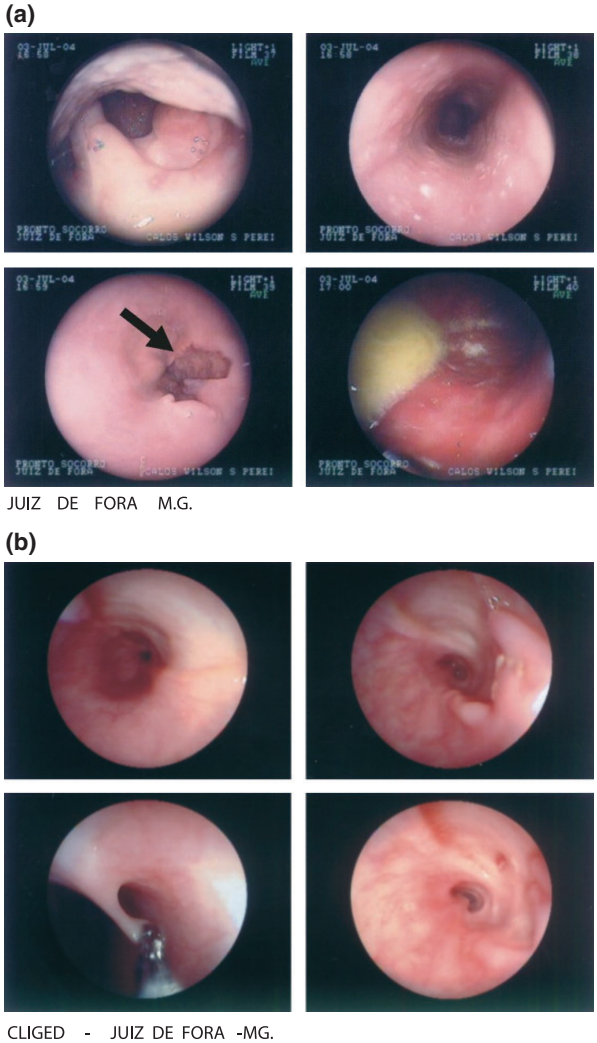

Fig. 1. Endoscopy records performed on a patient in: (A) July 2003, showing the ulcer (indicated by an arrow); (B) July 2004, showing that the ulcer has practically disappeared after 9 months of treatment.

At the end of treatment, the patient had taken 280 capsules over 9 months. The patient underwent endoscopy and biopsy again so as to evaluate the healing of active ulcer.

Fig. 1A,B shows endoscopic records of the patient's esophagus. According to the Savary–Miller classification [7], the esophagitis was grade 4 (Fig. 1A) and regressed to a grade 1 after 9 months of treatment using this formulation (Fig. 1B).

The regression of GERD symptoms and the relief of the pain may be related to the following: experiments indicate that melatonin has an inhibitory action on gastric acid secretion [4], and influences ulcer healing [4], which involves hyperemia at the ulcer margin [8]. Ulcer healing and the gastroprotective effects of melatonin are specifically mediated by the interaction of this indole with melatonin MT2 receptors [4]. Bubenik et al. (1998) demonstrated that a 4-week administration of melatonin in the diet significantly reduced the incidence of spontaneous gastric ulcers in young pigs. The ulcers in this case may have been due to a local deficiency of the melatonin synthesis [9].

Transient lower esophageal sphincter relaxation (TLESR) is a major mechanism of reflux in patients with GERD. Several agents have been shown to reduce the rate of TLESR, including morphine, somatostatin, nitric oxide synthase inhibitors, among others [10]. Melatonin inhibits nitric oxide biosynthesis [4] which may explain the regression of GERD symptoms.

Vitamin B12 (cobalamine), vitamin B6 and tryptophan, in high doses, can alleviate acute pain [11]. The analgesic effect is attributed to an increased availability and/or effectiveness of noradrenaline and serotonin acting as inhibitory transmitters in the nociceptive system [11]. Folic acid protects against gastroenterological cancers [12]. Probably, these agents and other components of the formula (betaine and methionine) induce the synthesis of S-adenosyl-L-methionine (SAMe) [13], a methyl donor, which has anti-inflammatory as well as analgesic activity without damaging the gastrointestinal mucosa of experimental animals [14]. Economically, these biochemicals are less expensive than SAMe and the capsules could be accessible to poorer populations.

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