

# Use of a preparation based on zinc, carnosine and *Macrocystis pyrifera* in the treatment of gastric disorders due to *Helicobacter pylori*: a case series

## Abstract

The term 'gastritis' refers to an inflammatory process of the gastric mucosa characterized by heartburn, retrosternal pain, dysphagia and cough, and is one of the most widespread causes of discomfort in the world population. The identification of *Helicobacter pylori* (*H. pylori*) has significantly contributed to elucidation of the aetiopathogenesis and treatment of some diseases of the upper digestive tract, for which this Gram-negative and acid-tolerant flagellated bacterium is now recognized as the main aetiological agent. Traditional medications against chronic gastritis can produce adverse effects, so nutritional strategies are desirable to prevent the aggravation of gastric mucosal damage.

Five patients with a long history of gastrointestinal disorders were diagnosed with reflux oesophagitis and were positive for *H. pylori* as confirmed by the urea breath test and antigen detection in stools.

All carried out first-line medical therapy for eradication, with the exception of a pregnant woman: standard triple therapy, with pump inhibitor and antibiotics (amoxicillin and clarithromycin) or sequential therapy, first with a pump inhibitor associated with antibiotics, then a pump inhibitor and metronidazole. All patients reported serious side effects related to the use of drugs, which is why they refused second-line therapy, but agreed to undergo treatment with esomeprazole pump inhibitor (40 mg) combined with a preparation based on zinc, carnosine and *Macrocystis pyrifera* (ZCM) (three capsules per day, 20 minutes after meals) for one month. The patients varied by sex and age: two females of 36 and 54 years and three males of 19, 39 and 60 years. In the observed cases, the combination of pump inhibitors with a preparation based on ZCM led to the reduction of symptoms in patients who did not respond to drug treatment alone, and in two subjects to the eradication of *H. pylori*. Despite the small size of the sample, the findings are of considerable interest and studies should be conducted on a larger scale to confirm them.

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## Introduction

Gastritis is an inflammation of the gastric mucosa that can be caused by numerous aetiological factors, including infections (*Helicobacter pylori*), use of drugs and substances (nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol), stress and autoimmune phenomena. Many cases are asymptomatic, but sometimes dyspepsia and gastrointestinal bleeding may occur <sup>[1]</sup>. The chronicization of gastritis is a multistep progressive process characterized by persistent inflammation. Inflammation can be present from childhood, as a simple 'superficial' chronic inflammation, and then evolve through various stages until it reaches that of atrophic gastritis. Gastritis progresses gradually, over years and decades, leading to a situation of atrophy characterized by a loss of normal mucosal glands in the antrum or in the body (and fundus), or both <sup>[2]</sup>. The diagnosis is made by endoscopy. Therapy is aimed at removing the cause, and antibiotics are used for *H. pylori* infection, although acid suppression is often included <sup>[1]</sup>. *H. pylori*, one of the most globally prevalent pathogens, colonizes about 50% of the world's population. It is transmitted from human to human and causes chronic gastritis in all colonized subjects. It can lead to peptic ulcer, atrophic gastritis, gastric adenocarcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma. *H. pylori* eradication cures gastritis and can alter the development of long-term complications <sup>[3]</sup>. The chronic inflammation is associated with a neutrophilic inflammation, the intensity of this acute and 'active' component of gastritis most likely being dependent on the cytotoxicity of the *H. pylori* strain <sup>[2]</sup>.

## Case presentation

The cases were observed in a general medical practitioner (GMP) outpatient facility

in Altamura (BA) under the supervision of a medical doctor and in accordance with the Declaration of Helsinki.

### Case 1

A 19-year-old boy with persistent gastric symptoms, negative for lactose and gluten intolerance and positive for the urea breath test, underwent triple therapy for eradication of *H. pylori*, with amoxicillin (1 g b.i.d.), clarithromycin (500 mg b.i.d.) and esomeprazole (20 mg b.i.d.). Halfway through the treatment, the patient complained of gastric and intestinal symptoms such as abdominal pain and gastric heartburn, but he managed to complete the therapeutic cycle. After about two months, with negative control tests for *H. pylori* but persistent gastric symptoms, the patient was treated with esomeprazole (20 mg b.i.d.) and ZCM (three capsules per day, each after a main meal) for two weeks, with an evident relief of symptoms within the first week and resolution of the symptoms at the end of the suggested therapy.

### Case 2

A 60-year-old man positive for the urea breath test for *H. pylori* underwent antibiotic therapy associated with pantoprazole (40 mg daily). The patient completed the therapy, despite problems and inconsistencies in adhering to it, with a negative outcome of the control examination for *H. pylori* but persistent symptoms. The patient continued therapy with pantoprazole and a product with antireflux activity (three times per day), without resolving the symptoms. Again under my observation, the therapeutic plan was modified, replacing pantoprazole with esomeprazole (20 mg b.i.d.) and the antireflux product with ZCM (three capsules per day, each after a main meal) for one month. With this treatment there was an improvement of the painful symptoms after the first 10 days, and complete remission of the symptoms after 15 days. Ten days after the suspension of therapy,

the gastric symptoms recurred: by the patient's autonomous decision, therapy with ZCM was resumed and maintained for three months, reaching complete remission of symptoms.

### Case 3

A 54-year-old woman treated with triple therapy for positivity to *H. pylori* obtained the remission of painful gastro-oesophageal symptoms for about 15 days from the completion of the therapy. When the symptoms reappeared, the gastroenterologist prescribed a therapy with a pump inhibitor, which produced a slight improvement in symptoms. Although the urea breath test confirmed that the *H. pylori* infection had been negativized, the painful symptoms persisted. The same gastroenterologist prescribed ZCM (three capsules per day, each after a main meal) in association with the pump inhibitor; this led to a reduction in symptoms, and their complete disappearance after 15 days.

### Case 4

A 39-year-old man with a positive urea breath test for *H. pylori* and gastric symptoms was treated by his GMP with triple therapy (esomeprazole 20 mg b.i.d., amoxicillin 1 g b.i.d. and clarithromycin 500 mg b.i.d.), with no effect on the symptoms. After two months he underwent a urea breath test to verify the eradication of *H. pylori* and was still positive, so he was offered a second-level therapy, which he refused. Instead, he agreed to treatment with a pump inhibitor (esomeprazole, 20 mg b.i.d.) and ZCM (three capsules per day, each after a main meal). The gastric symptoms regressed after about 20 days and the patient, finally finding relief, decided to continue the treatment without informing his GMP for a further three months without interruption. At the end of this period he spontaneously underwent the urea breath test; this unexpectedly proved negative for *H. pylori*.

### Case 5

A 36-year-old woman with a positive urea breath test for *H. pylori* and gastro-oesophageal reflux symptoms, with retrosternal burning and cough for about a year, underwent no therapy because she was pregnant. The first month after birth, she stopped breastfeeding due to lack of milk and began therapy with a pump inhibitor (pantoprazole, 40 mg per day) and ZCM (3 capsules per day, each after a main meal). After about three months of treatment, the patient underwent the urea breath test again, in preparation for the eradication therapy. Unexpectedly, she tested negative for *H. pylori*.

## Discussion

The survey considered five patients with gastric symptoms and positivity to *H. pylori* (via the urea breath test), some of whom did not consent to medical treatment for eradication due to side effects. These patients gladly accepted pump inhibitor therapy and supplementation with the preparation based on ZCM. This association was effective in resolving painful symptoms quickly and without unwanted side effects, which induced two patients to continue treatment with the nutritional preparation independently.

Zinc and carnosine (ZnC) are known in the literature to be the components of a chelated compound, used in Japan since 1994 for gastritis, gastric ulcers and dyspepsia symptoms. Zinc-carnosine is an artificially produced derivative of carnosine in which a zinc ion and carnosine are bound in a 1-to-1 ratio to create a chelate compound. ZnC is said to have superior health benefits compared to zinc or carnosine alone, as carnosine enhances the absorption of zinc because of its solubility and perhaps because it delivers zinc to the tissues in a delayed/extended-release manner.

The beneficial effects on gastric symptoms may depend on the antioxidant and anti-inflammatory properties of the two components, together with the stimulation of mucus production, a stabilizing action of the membrane and the induction of thermal shock protein [4, 5]. In an animal model of ethanol-induced damage to the gastric mucosa, inflammatory cytokines such as interleukin-1 $\beta$ , interleukin-8, interleukin-6 and tumour necrosis factor decreased in a dose-dependent manner in the group receiving ZnC when compared to the control group [6]. Another animal model evaluated the ability of ZnC to induce expression of 72 kDa heat shock protein (HSP72, stress-inducible HSP70), which is known as an endogenous cytoprotectant in a wide variety of cells, including rat gastric mucosa *in vitro* and *in vivo*. Zinc derivatives, especially ZnC, could be strong HSP72 (chaperon) inducers, which have been known to enhance mucosal protective ability [7]. Ishihara *et al.* demonstrated that the chelated compound ZnC significantly attenuated the development of polymorphonuclear neutrophil activity, mononuclear infiltration and surface epithelial erosion in both pyloric and fundic mucosae compared with those of the control group in an animal model [8]. The efficacy and safety of the use of the chelate combined with triple therapy have recently been evaluated in humans, compared with triple therapy alone, in the eradication of *H. pylori*: the study shows that the mucosal protective agent ZnC when combined with clarithromycin-based triple therapy can significantly improve the rate of *H. pylori* eradication compared to standard clarithromycin-based triple therapy, without significant side effects [3].

*Macrocystis pyrifera* (*M. pyrifera*), commonly known as giant kelp or giant bladder kelp, is one of four species of large brown algae in the genus *Macrocystis*. The primary commercial product obtained from giant kelp is alginate, useful in

hindering gastro-oesophageal reflux and protecting the stomach lining. *M. pyrifera* is also a source of fucoidans (polysaccharides containing substantial contents of L-fucose and sulfate ester groups), which are constituents of brown seaweed. Zhang *et al.* provided evidence that the fucoidan produced by *M. pyrifera* is a powerful immune modulator, which can enhance natural killer (NK) cell activation, dendritic cell maturation, Th1 immune responses, antigen-specific antibody production and memory T cell generation [9].

The data on the eradication of *H. pylori* are more difficult to interpret. Activation of the immune system by the components, with consequent control of bacterial infection, as well as the high content of algae polysaccharides that could reduce the adhesion of bacteria to the mucosa, could be cited.

## Conclusions

This personal experience of using a dietary supplement, even if limited to five patients with gastro-oesophageal reflux symptoms, highlights the effects of the combined supplementation of zinc, carnosine and *Macrocystis pyrifera* algae on symptom control and, surprisingly, on the eradication of *H. pylori*. These efficacy results, together with the high profile of safety of use and tolerability, represent an interesting opportunity for large-scale studies.

## Availability of data and material

The datasets in, or analyzed in, the current study available from the author on reasonable request.

## Conflict of interest

The author declares no conflict of interest.

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