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Mini-Review

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Ginger as a Possible Alternative Treatment for Gastroparesis

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Abstract

Gastroparesis is frequently a difficult gastrointestinal disease to adequately treat with currently available conventional medications producing a variable response at the cost of a potentially significant side effect burden. The medicinal herb ginger has been found effective in the management of nausea and vomiting related to pregnancy and chemotherapy, post-operative nausea and vomiting, and functional dyspepsia. These data, supported by animal model data and human studies demonstrating an augmentation of gastric motility, indicate that ginger may be a potential alternative or adjunct treatment for gastroparesis.

Keywords

Ginger : Gastroparesis

Nausea : Vomiting

Introduction

Ginger has been used for thousands of years for both dietary and medicinal purposes. The first recorded medical application was from the fourth century B.C. in China, at which time the proposed uses included stomach upset, diarrhea, nausea, cholera, bleeding, rheumatic disease, and toothache [1]. For centuries derived from the perennial herb *Zingiber officinale* from southern Asia, it is now grown throughout the tropics. The root or rhizome is the part consumed in varying preparations: dried, fresh, pickled, crystallized, candied, ground, and powdered. Medicinal formulations are available in capsules, tablets, tinctures, and extracts. It can be broken down into volatile oils (zingiberol) and nonvolatile phenol compounds (gingerols, shogaols, paradols, and zingerone), with the gingerols and shogaols demonstrating the most medicinal effect. These compounds appear to have both anticholinergic and antiserotonergic effects which may contribute to a pharmacologic effect [2].

Research into the medicinal use of ginger has increased significantly, with investigators exploring the benefits in a variety of clinical situations. The largest number of studies have looked at nausea and vomiting, functional dyspepsia, and gastric motility, but there have also been studies that have shown a benefit of ginger in conditions such as ulcerative colitis [3,4], peptic ulcer disease [5], gastrointestinal cancer [6], drug induced liver toxicity [7], and non-alcoholic fatty liver disease [8].

Disordered gastric motility clinically manifests as a gastroparesis [9]. Among gastroparesis patients seen at large referral centers the predominant underlying etiologies include diabetes mellitus (29%), postsurgical (13%), typically following procedures to the stomach and/or distal esophagus, and idiopathic (36%) in which no primary etiology is apparent [10]. Patients with this upper gastrointestinal motility disorder display symptoms related to both impaired gastric peristalsis and delayed emptying, but also the loss of accommodation (reflex relaxation of the gastric fundus to accommodate a volume of ingested food). Symptoms range from bloating and pressure after meals, early satiety, persistent abdominal fullness, epigastric pain, and nausea and vomiting which may be intractable. Available treatment options including behavioral modification (eating behavior and dietary

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changes), pharmacotherapy, the implantation of a gastric electrical stimulator or even surgery [9]. Unfortunately many patients experience significant debility despite best medical efforts. Available reports suggest a possible role for ginger in the management of gastrointestinal motility disorders, notably gastroparesis.

Nausea and vomiting

A variety of studies have investigated the use of ginger to treat nausea and vomiting, particularly that associated with pregnancy, chemotherapy, and the post-operative state. Animal models have suggested that the mechanism of action is related to gingerol and shogaol inhibition of cholinergic M3 receptors and serotonergic 5-HT3 receptors in the gastrointestinal tract [11].

For pregnancy-associated nausea and vomiting, ginger has shown benefit in two separate randomized controlled trials. The first trial showed decreased self-reported nausea and episodes of vomiting versus placebo [12] and the second showed treatment equivalence with pyridoxine hydrochloride (a commonly recommended therapy for pregnancy-associated nausea) [13].

Nausea and vomiting is a very common side effect of cancer chemotherapy with up to 60% of patients reporting nausea despite prescription antiemetics [14]. Four separate randomized controlled trials, with a total of over 700 patients studied, have shown benefit of ginger for patients undergoing chemotherapy in both adults and children [15-18]. The largest of the studies included greater than 500 adult patients from 23 private oncology groups in New York in their final analysis. Three dosages of ginger (0.5g, 1.0 g, and 1.5 g orally) were compared to placebo. A significant reduction in the self-reported severity of nausea was demonstrated with all doses of ginger, with the greatest benefit in the 0.5 g and 1.0 g groups [16].

Ginger has also shown benefit in regards to nausea and vomiting in surgical patients. A meta-analysis of 10 randomized controlled trials totaling 918 patients concluded that overall post-operative nausea and vomiting (PONV) was decreased with use of ginger [19]. The need for postoperative antiemetics was greatly reduced. A study of 120 laparoscopic gynecologic surgery patients showed equivalence between ginger and metoclopramide versus placebo in terms of PONV and antiemetic requirements [20]. A randomized controlled study of laparoscopic cholecystectomy patients showed superiority of pre-operative ginger (500mg administered 1 hour prior to surgery) versus intravenous Zofran for PONV [21].

Functional Dyspepsia

Functional dyspepsia is defined as chronic or recurrent epigastric or upper abdominal pain without identified underlying organic gastrointestinal pathology. Although overlapping, there appear to be two syndromes of dyspepsia: postprandial distress syndrome and epigastric pain syndrome [22]. Associated symptoms may include bloating, early satiety, fullness, belching, and nausea with or without vomiting, and may be associated with

eating. Proposed causes for these symptoms include impaired proximal stomach relaxation in response to meals, increased visceral sensitivity to distension, gastric motility disorders, and alterations in central nervous system function. Given these varying mechanisms, treatment for this condition can be difficult. Trials with H2-blockers and proton-pump inhibitors have only shown slight benefit relative to placebo [23]. That said, separating functional dyspepsia and gastroesophageal reflux or a gastroparesis may be a challenge [22].

One multi-center randomized controlled trial in Italy randomized 126 adults with functional dyspepsia to receive either a combination of ginger and artichoke leaf or placebo twice daily (before lunch and dinner) over 4 weeks [23]. Patients in the treatment group showed significant self-reported symptom reduction after 14 days of treatment, and this benefit was continued for the duration of the study. Specific benefit was noted for nausea, epigastric fullness, epigastric pain, and bloating. The reported treatment benefit for ginger and artichoke extract (measured as a percentage difference between the treatment group and placebo group) was higher than reported in studies of artichoke extract alone, antisecretory medications (such as proton-pump inhibitors and H2-blockers), and prokinetic medications [23]. These patients had a high prevalence of motility disorders and motility-related symptoms, including early satiety, bloating, and fullness [23].

Gastric Motility

Disorders of gastric motility such as gastroparesis are relatively common. The medications most often prescribed for these conditions, erythromycin (a motilin agonist), domperidone (a dopamine D2 receptor antagonist) and metoclopramide (a dopamine D2 receptor agonist), display variable clinical response and may be associated with significant side effects, making many patients unable to tolerate them [9]. An alternative treatment for this patient population, especially one with minimal side effects and improved tolerance, would be of significant clinical benefit. Studies of ginger have provided evidence that it may be a good alternative for patients that are either unable to tolerate or unwilling to risk the side effects of prescription prokinetic medicines.

Animal models have demonstrated a positive effect of ginger extract on gastric motility. Electromyography demonstrated increased contractions of the reticulum and rumen of sheep after administration of ginger extract [24]. A separate study looked at the effects of ginger extract on rabbit, rat, and guinea-pig small bowel motility. The largest stimulatory effect was noted in rabbit and rat small bowel, with a lesser but still significant effect in guinea-pigs [25]. Interestingly, the mechanism of action was found to be somewhat different between the animal models, with rabbits and rats demonstrating muscarinic receptor involvement and guinea-pigs showing a separate and unknown mechanism. Ex vivo animal preparations used as bioassays were exposed to gingerols and shogaol, active ingredients from ginger, with results suggesting mild antagonistic effects on the M3 and 5-HT3 receptors (possibly involved in alleviating nausea) but no effect on 5-HT4 receptors involved in gastroduodenal motility [26].

Hu et al. [27] evaluated the physiological effect of ginger versus placebo on gastric motility in patients with functional dyspepsia. After fasting for 8 hours, patients were given either capsules of ginger (1.2g) or placebo, followed 1 hour later by 500mL of soup. Ultrasound was used to measure antral area, fundal area/diameter, and antral contraction frequency; gastric half-emptying time was calculated using the change in antral area seen on ultrasound. The patients in the ginger group demonstrated faster gastric emptying, with median half-emptying time of 12.3 minutes versus 16.1 minutes in the placebo group, as well as demonstrating an increase in antral contractions. Ginger administration did not result in significant changes in GLP-1, motilin or ghrelin [27]. A larger study in 24 healthy volunteers, performed in the same method, showed a similar effect on gastric motility. In this study, the median gastric half-emptying time in the test group was 13.1 minutes versus 26.7 minutes in the placebo group [28]. Emptying of liquids clinically is considered a passive process, and no authors have yet evaluated changes in solid phase gastric emptying.

A double-blind, randomized controlled trial of 12 healthy men showed stimulation of gastroduodenal motility based on stationary manometry [29]. A total of 200mg of ginger extract was administered, and the fasting and post-prandial motility was then assessed. Motility was found to be increased by ginger extract in both the fasting state and after the test meal in the test group.

The stimulatory effect of ginger on gastric motility was applied in a clinical setting in a separate study on adult patients admitted to an intensive care unit with respiratory distress [30]. This study randomized 32 ventilator-dependent patients with nasogastric feedings to either receive 120mg of ginger extract or 1g of coconut oil as placebo. Patients were evaluated for 21 days for end-points including the amount of feeding tolerated within 48 hours, total amount of feeding tolerated, nosocomial pneumonia (attributed primarily to aspiration), number of ICU-free days, number of ventilator-free days, and overall mortality. Patients in the test group were found to tolerate an increased amount of feeding during the first 48 hours and developed fewer nosocomial pneumonias. The remaining end-points were not significantly altered. The authors suggested a utility for ginger extract in stimulating gastric motility in patients not known to have gastroparesis who were at risk for decreased gastric motility and associated aspiration pneumonia.

Summary

Ginger, an ancient medicinal herb, clearly appears to have a role in contemporary medicine. A clear benefit in the management of nausea and vomiting, both during pregnancy and associated with the administration of cancer chemotherapy, has been demonstrated. Interesting data in humans and animal models suggest a possible role in the management of patients with functional dyspepsia or gastroparesis. The availability of a readily available, inexpensive product with little reported toxicity would be welcome as clinicians try to manage these complicated and challenging patients. It is our hope that this review will result in a

more in depth investigation of the use of ginger in the management of patients with a gastroparesis.

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