Pancreatic enzyme supplementation

Agents which reduce gastric acidity in cystic fibrosis

Code: 032 **Updated:** June 18, 2019

Background

In CF inadequate buffering from bicarbonate-poor pancreatic secretions, as a part of the effect in the CFTR protein defect, may predispose to gastric acidity contributing to a lower duodenal pH and leading to inactivate pancreatic enzymes replacement in case of pancreatic insufficiency, which in turn may induce increased gastric acidity. Heartburn, epigastric pain and gastric or duodenal ulcers may result from increased gastric acidity.

Exocrine pancreatic insufficiency associated to fat malabsorption in patients with CF is classically treated with pancreatic enzyme replacement therapy (PERT). Despite PERT, intestinal fat absorption remains insufficient in most CF patients. A significant delay in the small intestinal transit and a deficient buffering capacity required to neutralize gastric acid in the proximal small bowel of patients with CF may have impact on timely release of PERT (Gelfond D et al, 2013). Based on this background previous data indicate that acid suppressive drugs could be helpful in individual CF patients to optimize fat absorption and/or nutritional status.

As derived from registry data and epidemiological reports gastroesophageal reflux (GER) is common in patients with CF, with a reported prevalence ranging from 35 to 81%. Despite more than 50% of U.S. patients with CF were being treated with proton pump inhibitors it is not still clear whether GER may lead to more severe lung disease including lower pulmonary function and increased numbers of respiratory exacerbations. Data regarding safety and efficacy of acid and non-acid agents in CF are lacking (Robinson NB et al, 2014). Recently (DiMango E et al, 2014) a randomized controlled study in 17 adults with CF showed a trend to earlier exacerbation and more frequent exacerbations in subjects randomized to esomeprazole (40mg twice daily for 36 weeks) compared with placebo. More recently (Ayoub F et al, 2017) it has been shown that exposure to proton pump inhibitors (PPI)is independently associated with a higher number of hospitalizations for pulmonary exacerbation in a cohort of CF adult patients. These data have been confirmed through a retrospective study i (McCrory Be et al, 2018) that enrolled 126 patients in the PPI group (34.9% had an indication for both gastroesophageal reflux and enzyme enhancement) compared to 49 patients in the control group.

Issues

To assess the effect of major agents that reduce gastric acidity, such as proton pump inhibitors, including omeprazole and H2 receptor antagonists as ranitidine, cimetidine and famotidine, as well as further drugs such as prostaglandin E2 analogues and sodium bicarbonate, on:

1. reducing symptoms related to increased gastric acidity such as epigastric pain, heartburn;
2. improving nutritional status as assessed by weight, height and other indices of growth;
3. reducing complications of increased gastric acidity such as gastric or duodenal ulcers;
4. improving fat absorption, fecal nitrogen excretion and other measures of fat malabsorption;
5. improving lung function, quality of life and survival;
6. improving any adverse effects, reported as secondary outcomes.

What is known

One CDSR (Ng Sze May, 2016) evaluated 17 RCTs enrolling 273 patients with CF on 39 examined (22 failed to be suitable for inclusion).

All the trials were carried out as single-centre (14 cross-over trials) and the duration of treatment was variable, ranging from five days to six months. Proton pump inhibitors and H2 receptor antagonists were assessed compared to placebo or other treatments for evaluating the effects on fat absorption in addition to different doses of pancreatic enzymes.

Seven trials reported significant improvement in measures of fat malabsorption.

Two trials reported no significant improvement in nutritional status.

One trial found that drugs reducing gastric acidity improved gastro-intestinal symptoms such as abdominal pain. Only one trial reported also data on the potential efficacy of antacid-agents on respiratory function.

One trial reported adverse effect with prostaglandin E_2 analogue misoprostol.

No trials were identified to assess the effectiveness of these agents in improving quality of life, complications of increased gastric acidity, or survival.

Unresolved questions

Currently, there is insufficient evidence to indicate whether there is improvement in nutritional status, lung function, quality of life or

survival when antiacids are used.

Adequately-powered, multicentered randomized controlled trials should be carried out in CF over a longer duration to provide further information of long-term effects on lung function and quality of life, as well as for comparing different agents for reducing gastric acidity.

Keywords

Nutrition Disorders; Antacids;