The effects of oral, gastric and jejunal feeding on symptoms, gastrointestinal (GI) function and neuroendocrine response in diabetic gastroenteropathy

Summary / Zusammenfassung

Diabetic ‘Gastroparesis’ or ‘Gastroenteropathy’ is a condition that causes episodes of nausea, vomiting, abdominal bloating and pain after eating. These symptoms occur in the absence of any structural abnormality of the stomach, rather abnormal gastric function underlies the condition. Up to one in five patients with type I diabetes experience symptoms consistent with this diagnosis. Many have delayed gastric emptying however the link between this and the severity of symptoms is not strong. Moreover the presence of delayed gastric emptying does not necessarily impact on clinical management or prognosis. For these reasons the term ‘gastroenteropathy’ is preferred.

If symptoms of gastroenteropathy cannot be managed by dietary modification and medications, repeated hospital admissions with intractable nausea and vomiting are the result. The effects on diabetic control, physical health and emotional quality of life are severe. The management of severe gastroenteropathy is difficult. Patients do not respond reliably to general supportive management or conventional prokinetics and antiemetics. Surgical options have disappointing results on symptoms. Health and social costs are high. The need for more effective treatment is acknowledged universally.

The primary reason for the lack of effective treatment in gastroenteropathy is that the cause has not been established. High blood glucose slows gastric emptying; however patients do not necessarily respond to tight insulin and glucose control and it is clear that other pathophysiological processes are present. Diabetic gastroenteropathy is associated with impaired accommodation (relaxation) of the stomach after a meal, reduced gastric contractility and pyloric spasm. This dysfunction may be related to vagal neuropathy; however a general disturbance of the GI response to feeding is likely.

Feeding into the small bowel beyond the stomach (jejunal feeding) is established management in diabetic patients with gastroenteropathy not able to meet their nutritional requirements. The benefits of jejunal feeding have been assumed secondary to improved general health and diabetic control; however this assertion has never been studied. Recently we observed that patients with severe gastroenteropathy recovered promptly and could eat normally during and for a few hours after jejunal feeding. These observations suggest that jejunal feeding has ‘quasi-pharmacological’ rather than merely ‘supportive’ effects in patients with gastroenteropathy. One attractive explanation for these observations is that gastroenteropathy represents a failure of oral intake to ‘switch’ the stomach from the fasted to the fed state. According to this hypothesis, jejunal feeding ‘restores’ the normal fed state on the gastrointestinal tract by bypassing the dysfunctional stomach.

This project will assess the effects of feeding on gastrointestinal sensory and motor function in diabetic gastroenteropathy. Healthy volunteers and disease controls with type I DM free of symptoms will also be investigated. Studies will assess:

1. Effects on GI symptoms and function to gastric distension in fasted and fed states
2. Effects on GI symptoms and function to oral vs. nasogastric delivery of a test meal
3. A randomised controlled trial of gastric test meal with and without prior jejunal feeding on GI symptoms and function

These studies will provide important, new information regarding the cranial, gastric and post-gastric response to feeding in health and disease. This response is complex and conventional measurements are limited to measurements of a single aspect of GI function (e.g. emptying) that cannot adequately address this complexity. With long-term SNF support and in collaboration with the Institute for Biomedical Engineering, University and ETH Zurich, our group has developed
magnetic resonance imaging (MRI) techniques to provide simultaneous assessment of tonic and peristaltic motor GI function, intragastric distribution of macronutrients and gastric secretion. Having validated these methods in normal subjects, we are now in a position to apply this comprehensive, quantitative assessment of GI function in the study of clinical disease. Effects of feeding on symptoms and gastric function will be related to alterations in neuroendocrine hormones (eg CCK, GLP1) and autonomic activity (eg cardiovagal tone) to assess how the integrated response of the GI tract to feeding fails in patients with diabetic gastroenteropathy. The primary aim of this project is to assess the effectiveness of jejunal feeding in the management of diabetic gastroenteropathy. However, by defining the processes that ‘switch’ gastric function between the fasted and the fed states and control the rate of gastric emptying, we hope also to identify candidate targets for more effective pharmacologic treatment of this severe disease.

Publications / Publikationen

Keywords / Suchbegriffe
Diabetes Mellitus, Gastroenteropathy, Magnetic Resonance Imaging (MRI), Gastrointestinal symptoms, Gastric function, Intragastric pressure, Gastrointestinal hormones, Autonomic nervous system

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Funding Source(s) / Unterstützt durch
SNF Reference Number: 118273

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Duration of Project / Projektdauer
May 2008 to May 2013