Diagnosis & dietary intervention in patients with diabetic gastroparesis

Akademisk avhandling
som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademin vid Göteborgs Universitet kommer att offentligen försvaras i Sahlgrens Aula, Sahlgrenska Universitetssjukhuset/S, Göteborg, fredagen den 20 september 2013 kl 9.00.

Av

Eva A Olausson
Leg dietist

Fakultetsopponent

Professor Inga Thorsdottir

Unit for Nutrition Research, Faculty of Food Science and Nutrition,

University of Iceland, Reykjavik, Iceland

Avhandlingen baseras på följande arbeten:

1. Olausson EA, Brock C, Drewes AM, Grundin H, Isaksson M, Stotzer P, Abrahamsson H, Attvall S, Simrén M. Measurement of gastric emptying by radiopaque markers in patients with diabetes: correlation with scintigraphy and upper gastrointestinal symptoms. Neurogastroenterol Motil . 2013 Mar;25(3):e224-32.

2. Olausson EA, Grundin H, Isaksson M, Brock C, Drewes A.M, Attvall S, Simrén, M. Plasma glucose response after a test meal, and gastrointestinal symptom severity in patients with diabetic gastroparesis. Submitted.

3. Olausson EA, Alpsten M, Larsson A, Mattsson H, Andersson H, Attvall S. Small particle size of a solid meal increases gastric emptying and late postprandial glycaemic response in diabetic subjects with gastroparesis. Diabetes Res Clin Pract. 2008 May;80:231-7.

4. Olausson EA, Störsrud S, Attvall S, Simrén M. A small particle size diet reduces upper gastrointestinal symptoms in patients with diabetic gastroparesis: A randomized controlled trial. Submitted.

University of Gothenburg

Abstract

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Eva A Olausson
Department of Internal Medicine and Clinical Nutrition, Sahlgrenska University Hospital, Univeristy of Gothenburg, Gothenburg, Sweden.

Background: Gastroparesis is a diabetic complication, which is often under-recognised. Existing treatment options are limited and diagnostic methods not easily accessible. **Aims of the thesis**: To compare two alternative diagnostic methods for gastroparesis in patients with insulin-treated diabetes (DM) and to compare gastrointestinal (GI) symptoms and metabolic control after intake of diet with a large (LP) and small particle size (SP) in patients with insulin-treated DM with gastroparesis.
Methods: In Paper I, gastric emptying of radiopaque markers (ROMs) from the stomach using fluoroscopy was compared to gastric scintigraphy (current gold standard for diagnosing gastroparesis)) and the link to GI symptom severity was determined. In Paper II, the plasma glucose response after a test meal with a LP was compared to gastric scintigraphy in diabetic subjects with and without gastroparesis and the association with GI symptom severity was evaluated. In Papers III and IV, the effects of meals with a LP or SP were compared in randomised controlled trials (RCT). In Paper III, the effect of SP and LP diets on gastric emptying measured using scintigraphy and on the postprandial glucose response were studied in subjects with DM type 1 and gastroparesis and in healthy controls. In Paper IV, subjects with insulin-treated DM and gastroparesis were treated with a SP or LP diet for 20 weeks and the effects on GI symptoms and metabolic control were compared between the groups.
Results: *Paper I:* 115 patients with insulin-treated DM were included and 83 subjects had gastroparesis determined using scintigraphy. A moderately strong correlation was demonstrated between scintigraphic (% retained radioactivity at 120 min, T120) and ROM emptying (markers retained at 6 h) ($r = 0.47$; $p < 0.0001$).The sensitivity and specificity of the ROM test was 34% and 97% respectively. Only scintigraphic gastric emptying correlated significantly with GI symptom severity with the strongest associations for fullness/early satiety ($r = 0.34$; $p < 0.001$) and nausea/vomiting ($r = 0.30$; $p < 0.001$). *Paper II:* We included 83 patients with insulin-treated DM – 53 with gastroparesis and 30 with normal gastric emptying determined by gastric scintigraphy. The patients with gastroparesis had a blunted postprandial glucose response and demonstrated a lower maximum postprandial plasma glucose increase ($p < 0.05$) and a lower incremental area under the plasma glucose curve ($p < 0.05$). GI symptom severity had the best discriminative value to positively identify gastroparesis (sensitivity 87%, specificity 80%). By adding the plasma glucose response to GI symptom severity to identify patients with gastroparesis, the specificity increased (100%), but the sensitivity decreased (37%). *Paper III:* We studied seven patients with DM type 1 and gastroparesis and seven healthy controls. The lag phase in the stomach and the T120 was significantly shorter and the postprandial blood glucose dip in diabetic subjects was less and of shorter duration after a SP meal compared to a LP meal. Gastric emptying did not differ significantly between groups after an SP meal. *Paper IV:* We randomised 56 subjects with insulin-treated DM and gastroparesis to eating diet with a SP ('intervention diet'), compared to the recommended diet for DM ('control diet') for 20 weeks. A significantly greater reduction in the severity of the key gastroparetic symptoms – nausea/vomiting, postprandial fullness and bloating - were seen in patients on the intervention diet compared to the control diet.
Conclusions: The alternative diagnostic methods for gastroparesis tested in this thesis – gastric emptying of ROM, plasma glucose response after a standardized test meal and GI symptoms assessment – can add information in the clinical setting, but cannot replace the current gold standard, gastric scintigraphy. A meal with a small particle size increases the gastric emptying rate and reduces the postprandial blood glucose dip in DM Type 1 subjects with gastroparesis. Dietary treatment with a SP significantly improves the key symptoms of gastroparesis in patients with DM.

Key words: diabetic gastroparesis, gastrointestinal symptoms, scintigraphy, radiopaque markers, postprandial glucose, hypoglycemia, gastric emptying, quality of life.

ISBN 978-91-628-8743-8