Early clinical experience of duodenal mucosal resurfacing (DMR), a new endoscopic approach to treating type 2 diabetes

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Abstract

INTRODUCTION: Bariatric surgery improves glycaemia in type 2 diabetes (T2D). Exclusion of nutrient contact with an abnormal duodenal surface may be a key mechanistic contributor, involving potential weight-independent changes in insulin sensitivity. DMR, a minimally invasive, upper endoscopic procedure involving thermal ablation of the duodenal mucosa, also appears to elicit glycemic improvements in T2D. We report the first-in-human clinical trial of DMR; Assess procedural safety and glycemic measures for 6 months after a single DMR procedure in patients with T2D and HbA1c ≥ 7.5% on at least 1 oral anti-diabetic agent. METHODS: Using novel balloon catheters, DMR was conducted on varying lengths of duodenum in anatomized patients at a single center (Santiago, Chile). RESULTS: A total of 39 patients were treated (baseline HbA1c: 9.5%): 28 had ablation of a long-duodenal segment (LS-DMR: -9.3 cm treated) and 11 had short-segment ablation (SS-DMR: -3.4 cm treated). Baseline HbA1c was reduced by 1.2% at 6 months in the full cohort. More potent glycemic effects were observed among the LS-DMR cohort, who experienced a 2.5% reduction in baseline mean HbA1c at 3 months post-procedure vs 1.2% with SS-DMR (p=0.05). Excluding patients who had concomitant anti-diabetic medication post-procedure, LS-DMR among patients with a baseline HbA1c of 7.5% to 10% (n=8) lowered HbA1c from a mean of 8.8% to 7.1% at 6 months (p=0.05), accompanied by a modest weight reduction of 2.3 kg. Overall, DMR was well tolerated with minimal gastrointestinal symptoms post-procedure. Three patients experienced duodenal stenosis treated successfully by balloon dilation. CONCLUSIONS: To date, single procedure DMR elicits a robust improvement in glycaemia in T2D with acceptable safety and tolerability. Further examination of safety, efficacy, durability and possible mechanisms is needed.

Introduction

• Interventions that prevent nutrient contact with the duodenum (i.e. bariatric surgery, intra-luminal sleeve) improve glycaemic control in T2D
• Exclusion of nutrient contact with an abnormal duodenal surface may be a key mechanistic contributor, involving potential weight-independent changes in insulin sensitivity
• Duodenal mucosal resurfacing (DMR) is a minimally invasive, endoscopic procedure that potentially offers similar metabolic benefit through ablation of the duodenal mucosa surface
• This was a first-in-man, proof-of-concept study to assess procedural safety and glycemic control after endoscopic DMR

Methods

• Adults with poorly controlled T2D (HbA1c > 7.5% on at least 1 oral anti-diabetic agent) underwent ablation of a short segment (SS-DMR: <6 cm ablated) or long segment of duodenum (LS-DMR: >9 cm ablated) using novel balloon catheters (Revita™ DMR System, Fractyl Laboratories, Waltham, MA, USA)
• Procedural steps: duodenal sizing→ saline expansion of sub-mucosa→ hydrothermal ablation of superficial mucosa
• All procedures were performed at a single center in Santiago, Chile by trained endoscopists
• 2-week, low calorie, graduated diet for all patients post-procedure (liquids→soft→purees)
• No specific recommendation on management of anti-diabetic medication post-procedure

Results

• 44 consecutive patients were enrolled, 39 treated
  o 28 LS-DMR (mean length ablated: 9.3 cm)
  o 11 SS-DMR (mean length ablated: 3.4 cm)
• Baseline (mean) prandial y weight=84.5 kg; HbA1c=9.5%; fasting plasma glucose (FPG)=184 mg/dL
• 5 excluded patients: 4 did not receive DMR (2 failed screening endoscopy, 1 tortuous anatomy, 1 procedure duration), 1 excluded for anti-GAD +

Safety & Tolerability

• Procedure well tolerated with minimal GI symptoms
• 3 patients experienced duodenal stenosis that required endoscopic balloon dilation, with good resolution
• No GI bleeds, perforation, pancreatitis, evidence of malabsorption or hypoglycaemia
• Follow up endoscopies indicate full mucosal healing by 1 month post-procedure (Fig. 1)

Fig. 1. Full mucosal healing is evident 1 month after DMR

Conclusions

• In this first-in-man study, single procedure DMR substantially improved glycemic control in patients with T2D, with acceptable safety and tolerability to date
• Upper GI procedural intervention may be a novel way to improve glycaemia in T2D

Fig. 2. Mixed-meal tolerance test (long segment; n=28)

Fig. 3. Fasting plasma glucose by ablation cohort


Fig. 4. Effect of changes in concomitant anti-diabetic medication use on DMR outcome (n=18)

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