Duodenal mucosal resurfacing (DMR) as a new endoscopic treatment for type 2 diabetes (T2D): Safety and proof-of-principle cohort study

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Introduction

- Interventions that prevent nutrient contact with the duodenum (i.e., bariatric surgery, intra-luminal sleeve) improve glycemic control in type 2 diabetes (T2D)
- Duodenal mucosal resurfacing (DMR) is a non-invasive, endoscopic procedure that potentially offers similar metabolic benefit through ablation of the duodenal mucosa surface

Objectives

- First-in-man, proof-of-concept study to assess procedural safety and glycemic control after DMR

Methods

- A minimally invasive, upper endoscopic procedure employing novel balloon catheters (Revita™ DMR System, Fractyl Laboratories, USA) was used to ablate either a short segment (SS-DMR; <6 cm ablated) or long segment of duodenum (LS-DMR; >9 cm ablated) in adult patients with poorly controlled T2D
- HbA1c >7.5% on at least 1 oral anti-diabetic agent
- Procedural steps: duodenal sizing → saline expansion of submucosa → 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 → puree)
- No specific recommendation on management of anti-diabetic medication post-procedure

Results

- 44 consecutive patients enrolled, 39 treated
  - 28 received LS-DMR (mean length ablated: 9.3 cm)
  - 11 received SS-DMR (mean length ablated: 3.4 cm)
- Baseline (mean): age=53.3 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 dilatation, with good resolution
- No GI bleeds, perforation, pancreatitis evidence of malabsorption or hypoglycemia
- Follow up endoscopies indicate full mucosal healing by 1 month post-procedure (Fig. 1)

Efficacy

- HbA1c reduction of 1.2% at 6 months in full cohort (Fig. 2)
- LS-DMR had more potent glycemic effects
  - 2.5% reduction in baseline mean HbA1c with LS-DMR at 3 months post-procedure vs 1.2% with SS-DMR (p<0.05)
  - Early and sustained improvement in FPG (Fig. 3)
- Greater DMR effects in patients on stable medications (Fig. 4)
- Modest weight reduction (2-4%), but no apparent correlation between degree of weight loss and glycemic improvement

Conclusions

- In this first-in-man study, single procedure DMR substantially improves glycemic control in patients with T2D, with acceptable safety and tolerability
- Upper GI intervention may represent a novel way to improve glycemia in T2D

Fig. 1. Full mucosal healing is evident 1 month after duodenal mucosal resurfacing.

Fig. 2. Reduction in HbA1c after DMR procedure

Fig. 3. Fasting plasma glucose by ablation cohort

Fig. 4. Changes in concomitant anti-diabetic medication use and DMR outcome (long segment)