Duodenal Mucosal Resurfacing Elicits Improvement in Glycemic and Hepatic Parameters in Type 2 Diabetes: 1 Year Multicenter Study Results

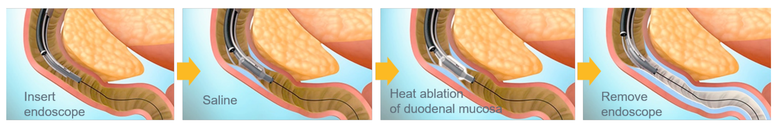
A.C.G. van Baar[1]*, M. Nieuwdorp[2], F. Holleman[3], J. Deviere[4], L. Crenier[5], R. Haidry[6], R. Batterham[7], D. Hopkins[8], L. Rodriguez Grunert[9], M. Galvao Neto[10,11], P. Vignolo[9], G. Costamagna[12], J.J.G.H.M. Bergman[1]

[1]Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, the Netherlands; [2]Internal and Vascular Medicine, Academic Medical Center, Amsterdam, Netherlands; [3]Internal Medicine, Academic Medical Center, Amsterdam, Netherlands; [4]Gastroenterology, Erasme University Hospital, Brussels, Belgium; [5]Endocrinology, Erasme University Hospital, Brussels, Belgium; [6]Gastroenterology, University College Hospital, London, UK; [7]Centre for Obesity Research, Department of Medicine, University College Hospital, London, UK; [8]Institute of Diabetes, Endocrinology and Obesity, King's Health Partners, London, UK; [9]CCO Clinical Center for Diabetes, Obesity and Reflux, Santiago, Chile; [10]Bariatric Endoscopy Service, Gastro Obeso Center, Sao Paulo, Brazil; [11]Florida International University, Miami, FL, USA; [12]Digestive Endoscopy, Policlinico Gemelli, Catholic University of Rome, Rome, Italy

Introduction

- Duodenal exclusion via bariatric surgery is associated with early improvement of glycemic regulation which cannot be explained by induced malabsorptive processes alone. It is suggested that bypassing, excluding or altering nutrient presentation to the duodenum induces this phenomenon.[1,2] Duodenal Mucosal Resurfacing (DMR; see Figure 1 below) is a novel endoscopic procedure which has been shown to improve glycemic control at 6 months in type 2 diabetes (T2D). It is thought to exert insulin-sensitizing effects.[3] DMR entails catheter based circumferential mucosal lifting followed by hydrothermal ablation.

Figure 1. Duodenal Mucosal Resurfacing



- Upper endoscopic procedure employs a novel hydrothermal balloon catheter to resurface a section of the duodenal mucosa.
- Follow up endoscopies and duodenal biopsies at 1 month and 3 months document complete mucosal healing.

Aim

- To extend DMR experience in terms of safety and feasibility and to determine efficacy of a single DMR procedure over 12 months in T2D patients on stable oral glucose lowering medication..

Methods

Study

- We conducted a single arm, open label, international multicenter study.

Patient Population

- Age 25-75 years, HbA1c 7.5-10.0%, and using oral glucose lowering medication with a preserved insulin secretion defined as fasting C Peptide serum >1 ng/mL (333pmol/l). A complete DMR procedure was defined as a duodenal ablation zone of 9-10 centimeters in length (per-protocol population).

Medication

- Sulfonylureas and meglitinides were discontinued 4 weeks before DMR to mitigate the risk of hypoglycemia. Other glucose lowering medication was kept stable for at least 6 months post DMR and adjusted according to local guidelines thereafter.

Follow-up

- At baseline and 1, 3, 6, 9, and 12 months after DMR, Adverse Events (AEs) were assessed and impact on glycemic control (HbA1c and fasting plasma glucose), insulin resistance (HOMA-IR) and liver enzymes (AST and ALT) were determined in the per-protocol population. A follow-up endoscopy was performed at 6 months.

Data analysis

- ANOVA for repeated measurements with Bonferroni correction.

Results

- Forty-six patients with T2D received a single DMR procedure. Baseline characteristics are shown in Table 1.

Table 1. Clinical characteristics at screening and baseline. Data are mean (standard deviation). Intention-to-treat population (n=46)

Patient Characteristics	Baseline (n=46)
Age, years (range)	55 (31 – 69)
Sex, n (%)	
Female	17 (37%)
Male	29 (63%)
Duration of type 2 diabetes, years (range)	6 (0.1 – 12)
Weight (kg)	90.3 (13.1)
BMI (kg/m²)	31.6 (4.3)
HbA1c	
mmol/mol	70 (9)
mg/dL	8.6 (0.8)
FPG	
mmol/mol	10.7 (2.7)
mg/dL	193 (49)
Fasting plasma insulin	15.1 (9.5)
C-peptide	2.9 (1.2)
HOMA-IR	8.0 (5.7)

Safety

- No unanticipated adverse device events were reported. One serious adverse event (SAE) was reported and considered to be procedure related (mild fever (38 C) and increased c-reactive protein level the first day after DMR that resolved quickly without sequelae. Seven additional SAEs were reported that were not procedure/device related.
- Of all AEs, 12% (n=24) was reported to be probably or definitely related to the DMR procedure. Of these, 71% (n=17) were gastrointestinal disorders (e.g. mild abdominal pain, nausea, diarrhea), classified as mild (n=14) or moderate (n=3).

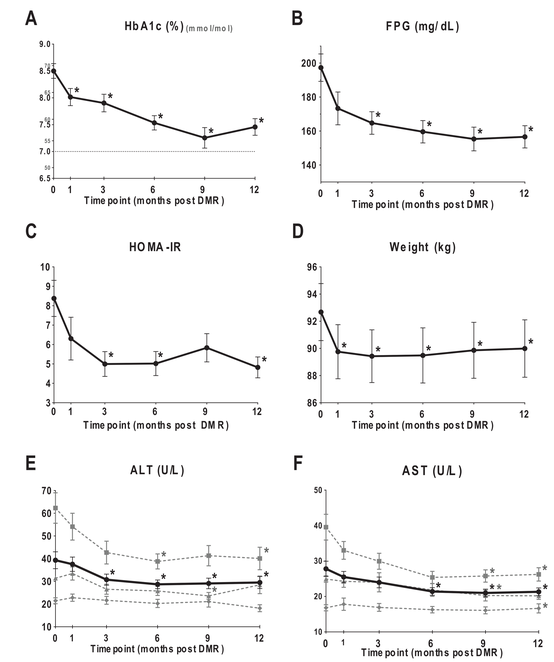
Efficacy

- The DMR procedure was complete (length of 9-10 centimeters) in 37[4] out of 46 patients (80%), defining the per-protocol population.
- At 12 months post DMR, the mean changes as compared to baseline in the per-protocol population (n=37) are shown in Table 2 (below) and displayed in Figure 2.

Table 2. 12 months post DMR, the mean changes as compared to baseline in the per-protocol population (n=37)

Indices	12 months	P value
HbA1c	-1.0±0.2%	≤ 0.001
FPG	-41±8 mg/dL	≤ 0.001
HOMA-IR	-3.6±0.9	= 0.005
Weight	2.7±0.6 kg	= 0.003
ALT	-10±2 U/L	= 0.005
AST	-6±2 U/L	= 0.002

Figure 2. Post DMR change (mean ± standard error) in (A) HbA1c, (B) FPG, (C) HOMA-IR, (D) weight, (E) ALT, and (F) AST. E-F dotted grey lines represent ALT and AST levels divided into tertiles based on baseline levels (squares: high, triangles: middle, diamonds: low baseline). Per-protocol population (n=37). *p<0.05, compared to baseline, repeated measures ANOVA with Bonferroni correction



Conclusion

Single DMR treatment elicited significant and clinically relevant reductions in glycemic and hepatic parameters that were sustained at 12 months, suggesting considerable potential of DMR for the treatment of T2D. A randomized, sham-controlled study is underway.

REFERENCES

1. Rubino, F., *et al. Ann Surg*, 2006.
2. Rubino, F., *et al. Diabetes Care*, 2016.
3. Rajagopalan, H., *et al. Diabetes Care*, 2016.
4. Reasons for an incomplete procedure were catheter malfunctioning (n=4), difficulties in positioning the catheter (n=3), a short duodenum (n=1) or insufficient mucosal lifting (n=1). Mean procedure time was 82 ± 28 minutes

DISCLOSURES

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