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Enhanced β-cell function and improved insulin sensitivity after Revita® Duodenal Mucosal Resurfacing in patients with T2D

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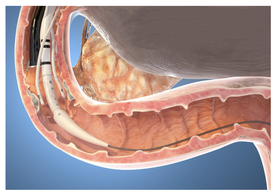
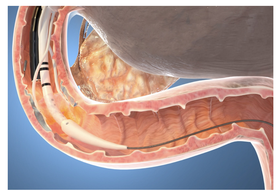
Introduction

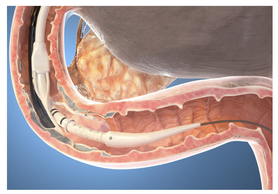
Intestinal mucosa changes due to obesogenic diets are associated with insulin resistance. Revita® Duodenal Mucosal Resurfacing (DMR), an endoscopic procedure using hydrothermal energy to ablate and regenerate the duodenal mucosa, has been shown to improve glycemic control and metabolic health in patients with type 2 diabetes (T2D). Post-DMR changes in glucoregulatory hormones, β-cell function, and insulin sensitivity are reported here.



Submucosal saline injections



Hydrothermal Ablation



Duodenal treatment to Treitz flexure

Methods

Subjects Patients (n=28):

- Glycated hemoglobin (HbA1c) 7.6 - 10.4%
- On ≥2 oral glucose lowering medications
- BMI 24 - 40 kg/m^2
- Underwent a mixed meal test (MMT)

Studies Revita-1 (n=13) and Revita-2 (open label phase; n=15)

Intervention Endoscopic Revita® DMR procedure

Change at 3 months post-DMR for the following variables:

- Fasting plasma glucose (FPG), glucoregulatory hormones and weight.
- MMT for glucose, glucagon, insulin, C-peptide, glucose-dependent insulinotropic polypeptide (GIP), and glucagon-like peptide-1 (GLP-1).
- Insulin resistance (HOMA-IR), Matsuda index (MI) of insulin sensitivity, insulin secretion rate (ISR), and disposition index (DI).

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Results

HbA1c, FPG, C-peptide, glucagon, and body weight decreased significantly post-DMR (Table 1). MMT post-DMR showed a significant increase in MI, ISR, and DI (Table 1). Improvement in insulin sensitivity was more pronounced in patients with high baseline FPG (data not shown). Both glucose and glucagon decreased significantly post-DMR (Fig. 1, A & B). Although no significant change in GIP or GLP-1 was found (Fig. C & D), improved MI correlated with decreased postprandial GIP levels (Fig E), as did HbA1c with GIP iAUC (R = 0.475, p= 0.022) (graph not shown).

	Baseline	3 Months	*p*-value
Body weight, kg	91.7	87.4	0.001
BMI, kg/m2	31.4	29.5	<0.001
HbA1c, %	8.2	7.4	0.002
Fasting glucose, mg/dl	198	162	<0.001
Fasting insulin, pmol/l	11.9	8.8	0.004
Fasting C-peptide, nmol/l	3.07	2.43	0.001
Fasting glucagon, pmol/l	27.6	24.7	0.024
HOMA-IR	5.4	3.6	0.005
Matsuda Index	2.64	3.49	0.005
Insulin Secretion Rate	4x10^5	5x10^5	0.002
Disposition Index	4.71	6.46	0.001
Fasting GLP-1, pmol/l*	9.27	8.02	0.201
Fasting GIP, pmol/l*	26.91	23.46	0.107

Table 1.
Clinical Characteristics of Study Population compared at Baseline and 3 months. *Available for 23/28 subjects

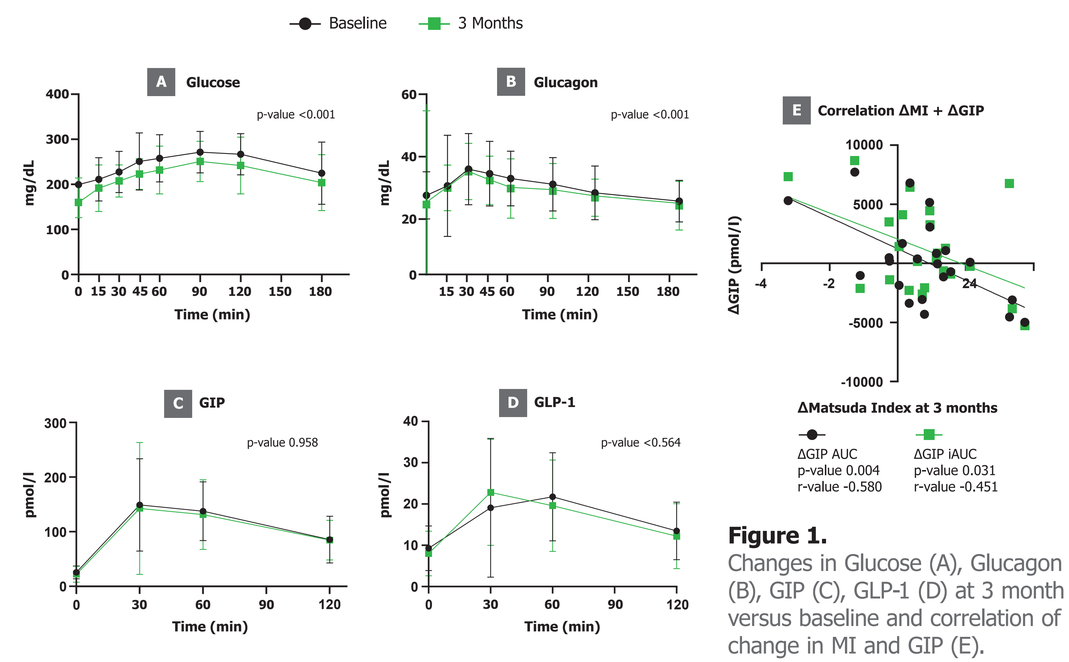

Figure 1.
Changes in Glucose (A), Glucagon (B), GIP (C), GLP-1 (D) at 3 month versus baseline and correlation of change in MI and GIP (E).

Safety

AEs included abdominal pain, nausea and diarrhea, were mild and transient, similar to those reported previously, across the Revita® DMR program of >300 patients. No pancreatitis or liver related AEs have been observed.

Conclusion

- Revita® DMR significantly improved HbA1c as well as fasting and post-meal glucose in T2D patients.
- Improvement of HOMA-IR and MI indicate an increase in whole-body insulin sensitivity, while improvements in ISR and DI indicate enhanced β-cell function.
- This data adds to the growing evidence validating the duodenum as a therapeutic target for T2D.