Elevated Systemic Fasting and Post-Prandial Glucagon-Like Peptide 1 in Patients With Symptoms of Nausea and Vomiting Following Surgical Weight Loss

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BACKGROUND

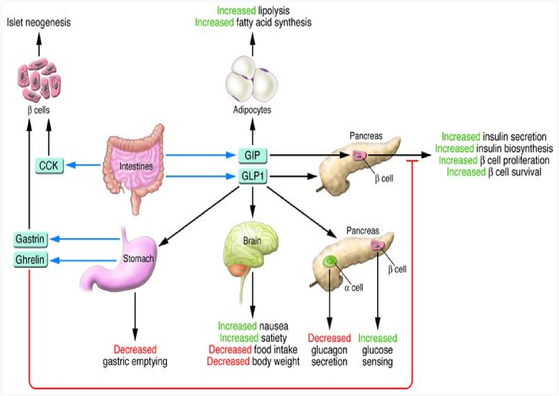
• Glucagon-like peptide-1 (GLP-1) is a gut peptide secreted by L cells which are located in small intestine. *Baggio L & Drucker DJ 2007* (Fig 1).

•It has important actions in mediating satiety and promoting insulin sensitivity and improved glucose metabolism. *Poumaras D & Le Roux C 2009*

•Postprandial GLP-1 following Roux en Y Gastric Bypass (RYGB), and gastric banding (GB), have been shown to be significantly higher compared to pre-operative levels, sustained over at least a year and associated with enhanced satiety and maintaining of insulin sensitivity. *Falken Y ea al 2011*

•. The causes of high GLP-1 levels after RYGB or GB is not fully understood but may be, at least partly, due to most L cells being located in distal part of the small intestine (ileum) and bypassing the foregut, as with RYGB, makes the ingested nutrients reach the proximal part of intestine more readily.

Figure 1. Physiological functions of GLP-1



Drucker DJ,2007. The Role of Gut Hormones in Glucose Homeostasis. J Clin. Invest. 117:24-32.

•However, an adverse effect of the surgery is that some patient develop severe, sustained and debilitating nausea and vomiting symptoms that persist well beyond the 3 months following surgey.

•As these symptoms are similar to those reported by patients on GLP-1 mimetics it may be postulated that this phenomena is associated with increased sensitivity or abnormally elevated systemic GLP-1.

AIMS

•To determine systemic levels of GLP-1 in a cohort of subjects with reported symptoms of persistent nausea compared to those free of symptoms following weight loss surgery, in the post-absorptive and post-prandial states.

METHODS

• **Study population:** Female patients following surgery for weight reduction with (n=10) or without (control group, n=10) persistent symptoms of nausea.

•**Study day: Patients attended following an overnight fast.** Anthropometric data were recorded (age, height and weight, body mass index, blood pressure)and blood obtained prior to and following a meal (180kcal) at 45, 120, and 180 minutes.

•**Sample collection:** Blood was collected from the antecubital vein.

•**Analysis:** The serum/plasma were analyzed for GLP-1 (commercial ELISA, R&D Systems, UK), glucose, and insulin (commercial ELISA; Mercodia, Sweden) at basal and postprandial stages (45m, 120m and 180m), and total-cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides in the fasting samples only.

Table 1. Ethnic mix of the study population.

	Patients with n&v	Patients without n&v
Age (years)	28-65 42	24-52 38.6
Ethnicity: Caucasian	5	7
African-caribean	3	3
South Asian	2	0

RESULTS

Figure 2. Changes in body weight following surgery

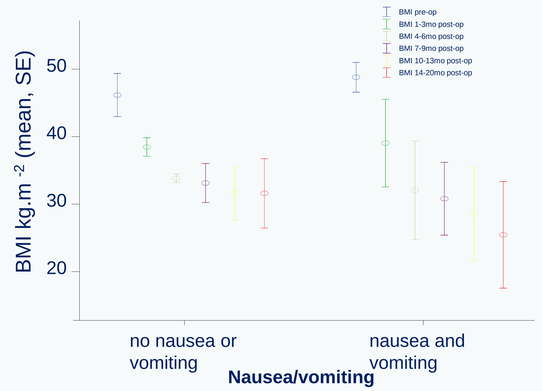
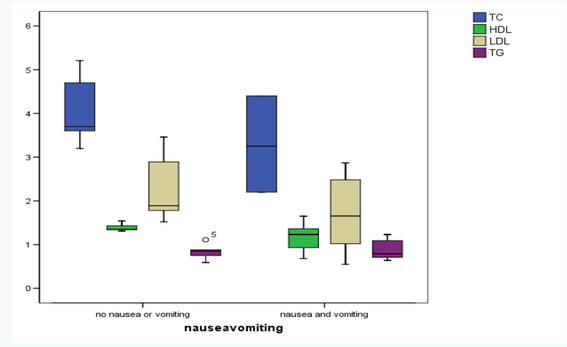


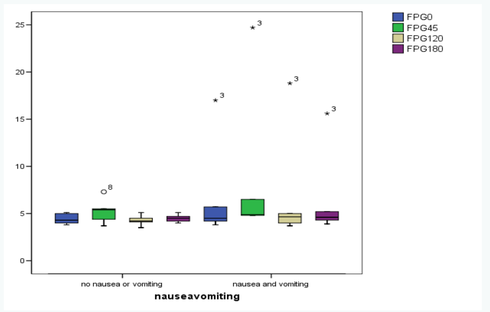
Figure 3. Serum lipids in patients without/with symptoms



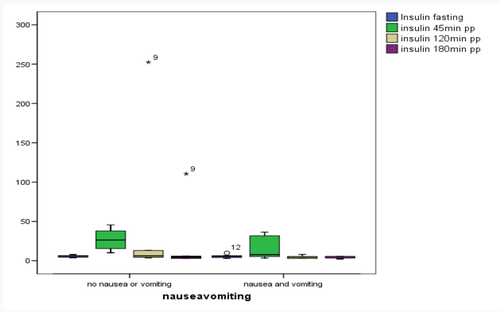
All data in mmol/L and expressed median (interquartile ranges)

Figure 4. Post-prandial concentrations of glucose (A), insulin (B) and GLP-1 (C)

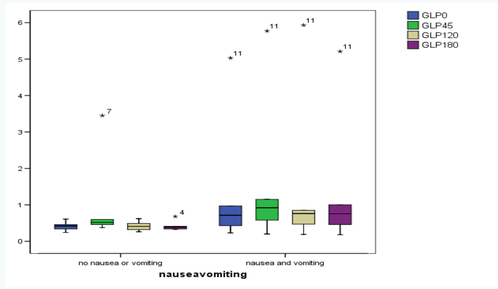
A.



B.



C.



DISCUSSION OF RESULTS

•Both groups showed significant and comparable weight loss following surgery (Fig 2).

•Change in plasma total cholesterol, LDL, HDL, triglyceride (Fig 3), as well as glucose (Fig 4A) were not significantly different between the groups.

•While basal insulin levels are similar, the first phase response (45 minutes) was lower in the symptomatic group (Fig 4B) .

•However, basal and postprandial GLP-1 levels were higher in the symptomatic group, compared to asymptomatic group, as ascertained by area under the curve (Fig 4C).

CONCLUSIONS

•Exaggerated GLP-1 responses are associated with excessive nausea and vomiting symptoms in a subset of patients post GB.

•Symptomatic patients may benefit from GLP-1 antagonist therapy, such as Exendin (9-39), to alleviate their symptoms.

Acknowledgements

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