GLP-1 analogs as treatment of postprandial hypo-glycemia after gastric bypass for morbid obesity

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Introduction

In a fraction of morbidly obese subjects undergoing gastric bypass (GBP), episodes with late postprandial hypoglycemia (PPHG) develop 1-4 years after surgery. The pathogenesis of this phenomenon is not fully understood; meal-induced rapid and exaggerated increases of circulating incretins and insulin appear to be partially responsible.(1)

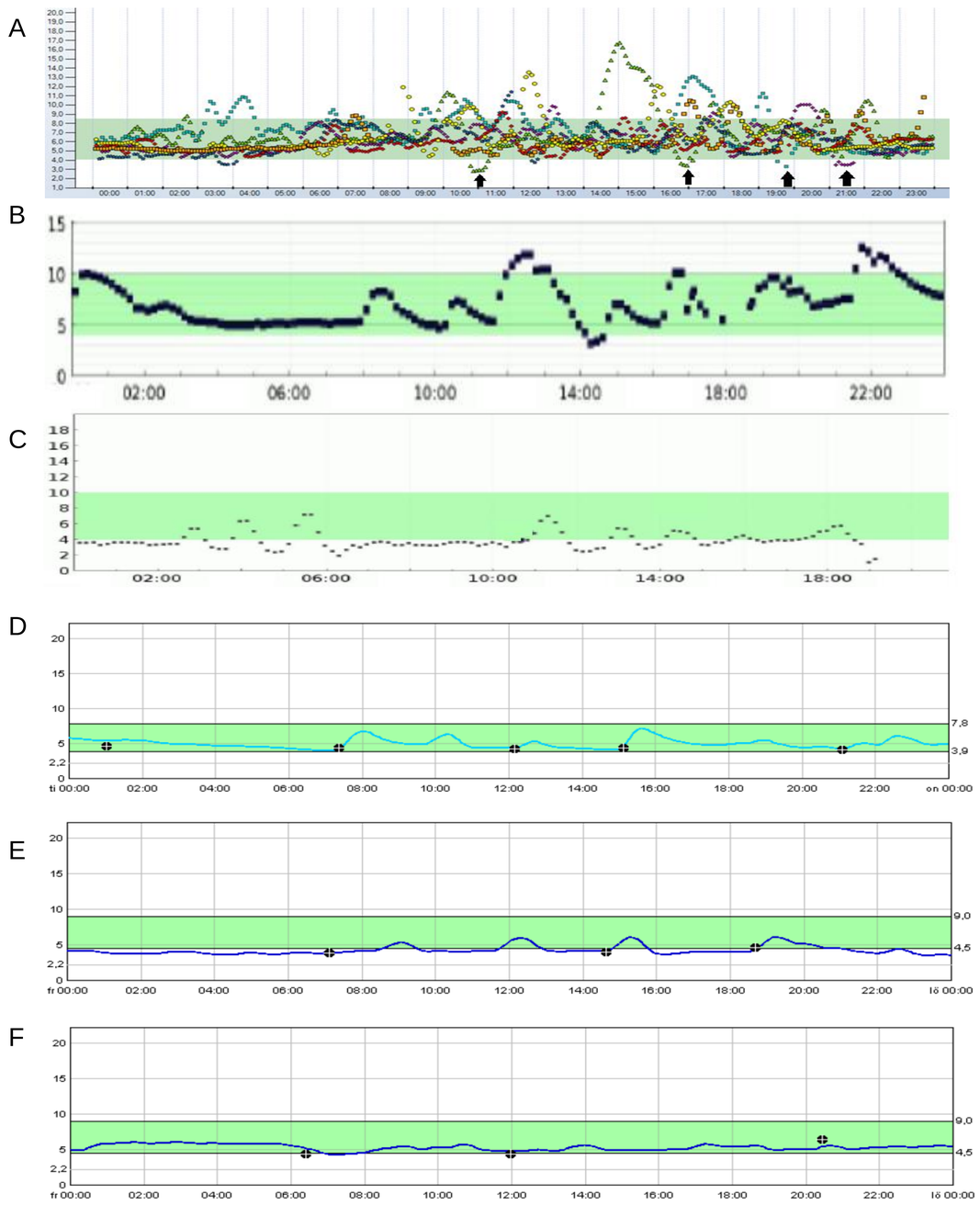
Current suggested treatments include low-carbohydrate diets, inhibition of glucose intestinal uptake, calcium channel blockers, somatostatin analogs, or diazoxide. Even partial pancreatectomy has been advocated.

In type 2 diabetes, GLP1 analogs have a well-documented effect of stabilizing glucose levels without causing hypoglycemia.(2) Here, we explored GLP1 analogs (exenatide/liraglutide) as open treatment in 10 consecutive GBP cases seeking medical attention because of late postprandial hypoglycemic symptoms.

Case Reports

Patients were admitted because of hypoglycemia 1-4 years post-GBP surgery. They were thoroughly and negatively investigated for causes of hypoglycemia other than post-GBP hypoglycemia. All patients had had frequent meetings with the clinic's specialist dieticians to optimize their eating regimen prior to medication. No glucose modifying drugs were used, and none had diabetes. Eight of the cases were examined with meal tolerance tests and CGMS for 3-5 days.

All ten patients consistently described that the analogs eliminated their symptoms. Furthermore, the symptoms relapsed when, in four of the patients, treatment was reduced/discontinued. In two cases, the drug effect was also documented by repeated 24-h continuous glucose measurements.



24-h continuous glucose measurements (CGMS) on four cases.
Y-axes represent glucose (mmol/l), X-axes represent hour of day.
A: Case 3, pretreatment. **B:** Case 4, pretreatment. **C:** Case 5, pretreatment.
D: Case 5 on treatment. **E:** Case 9, pretreatment. **F:** Case 9 on treatment.

Patient	Age	Admitted years after GBP	BMI kg/m^2 preop/admittance	Baseline fasting Glucose (mmol/L)	Baseline fasting Insulin (mU/L)	Baseline HbA1c % (mmol/mol)	Lowest P-Glucose mmol/L measured with symptoms	Freq of PPHG	Relapse of symptoms when lowered dose or off drug
1	44	3	42/29	5.2	nd	5.5 (37)	nd	weekly	yes
2	33	1	46/27	5.1	nd	5.1 (32)	2.7	eod	yes
3	36	2	47/35	5.4	nd	5.4 (36)	2.5	daily	nd
4	64	1	51/32	4.6	1.26	6.2 (44)	1.8	daily	yes
5	45	3	38/27	4.8	1.86	5.3 (34)	1.6	weekly	yes
6	26	4	55/30	4.1	nd	5.1(32)	nd	weekly	nd
7	40	1	38/30	3.6	7.6	5.9(41)	3.5	daily	nd
8	34	4	40/22	5.2	6.4	nd	1.5	daily	nd
9	45	2	36/24	5.4	6.8	nd	2.9	eod	nd
10	29	1	44/24	4.9	nd	4.8(29)	2.2	daily	nd

Basic characteristics. Eod = every other day, nd = not determined.

Conclusion

GLP1 analogs might provide a new effective treatment option in patients with problems of late PPHG. The analogs have a more benign side-effect profile than other drugs used against postprandial hypoglycemia.

Nauck et al showed in 1993 that, in type 2 diabetes patients on GLP1 treatment, glucagon levels in the normo/hypoglycemic state were elevated compared with controls.(3) Ahren et al further showed that by increasing levels of GLP1, with the DPPIV-inhibitor vildagliptin, the glucagon response to acute hypoglycemia was significantly increased.(4)

We speculate that the GLP-1 analog's beneficial effect on postprandial hypoglycemias post GBP might be by strengthening the counter-regulatory response to hypoglycemia. A randomized study examining this hypothesized effect is warranted.

References

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