Is Semaglutide superior that Liraglutide in patients with type2 diabetes on insulin therapy – case presentation Ivana Mickovski, Daniela Buklioska Ilievska, Radmila Milosheska 8th September, City General Hospital, Skopje, N.Macedonia

#### Introduction

Type 2 diabetes (T2DM) is a chronic and progressive disease associated with microvascular and macrovascular complications leading to increased morbidity and mortality. Insulin remains the cornerstone therapy for longer-duration T2DM and b-cell failure. T2DM is a complex disorder that requires individualized treatment strategies. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are a class of multifactorial T2DM medications that have been shown to improve numerous risk factors for diabetes-related complications, including glycemic control, reduction in body weight and a low risk of hypoglycaemia.

## **Case Presentation**

A 65-year old obese male presented to the outpatient clinic of Endocrinology, 8<sup>th</sup> September City General Hospital, Skopje for a regular checkup. He has T2DM for a long time and the last 10-15 years was switch on insulin therapy – at the moment was on premix insulin – Insulin Aspart and OAD. He was complaining of variation of glycaemia (5.0-16.5 mmol/l), felling a little bit thirsty, hungry and without energy. He has arterial hypertension and dyslipidemia (medications was prescribe from cardiologist) but could not tolerated any statins. He is a nonsmoker, with two children and retired.

Initial investigation showed HgA1c 55.2 mmol/mol, FPG 9.1 mmol/l, elevated cholesterol (cho -6.8 mmol/l), low density (LDL – 2.8 mmol/l) triglyceride (Tg - 2.7 mmol/l). His renal and liver functional test were within normal limits. The tests for thyroid functional were also normal. He was 180centimetar tall, 149kg weight and his body mass index (BMI) was 46.0. Echotomography showed steatotic liver, echocardiography and ophthalmic tests were in normal range for his age

### Treatment

Investigations

The patient was overweight, hasn't achieved the optimal glycemic control even though he was on insulin therapy and one of his biggest concerns was his weight, so the medical team decided to add Liraglutide on his diabetes therapy with gradual titration of the dose (Liraglutide - was started at 0.6mg daily subcutaneously for 1 week and then increased from 1.2 mg to 1.8mg daily). Also he was educated about titration of the dose of the insulin therapy together with additional lifestyle modifications Because of the positive effect from the therapy with once daily GLP-1 RA, and because we wanted to continue with weight loss, but at the same time reduce the everyday subcutaneous therapy we decide to change Sol Liraglutide 1.8mg per day with Sol Semaglutide starting with 0.25mg once a week for 1 month and then titrating the doses till 1mg per week, together with reducing the insulin therapy, metformin 2000mg daily, balance food and physical activity (Table 1).

	Table1, Patient's Diabetes Therapy Changes over Time				
	Reference date	Medical therapy for diabetes	HgA1c (mmol/mol)	Weight loss	
	Date Liraglutide was added	Liraglutide 1.2mg +Metformin 2000mg daily + Insulin Aspart (64+64i.e s.c)	55.2 mmol/mol	149kg	
	1 month after starting Liraglutide	Liraglutide 1.8mg +Metformin 2000mg daily +Insulin Aspart (58+58 i.e s.c)	53.0 mmol/mol	147kg	
	3 months after starting Liraglutide	Liraglutide 1.8mg +Metformin 2000mg daily+ Insulin Aspart (52+52i.e s.c)	51.0 mmol/mol	143kg	
;	7-8 months after starting Liraglutide	Liraglutide 1.8mg +Metformin 2000mg daily + Insulin Aspart (44+44i.e s.c)	50.0 mmol/mol	141kg	
	1 month after changing Liraglutide with Semaglutide	Semaglutide 0.25mg + Metformin 2000mg daily +Insulin Aspart (42+42i.e s.c)	48.0 mmol/mol	138kg	
	3 months after starting Semaglutide	Semaglutide 1mg + Metformin 2000mg daily +Insulin Aspart (36+36i.e s.c)	45.0 mmol/mol	132kg	
;	7-8 months after starting Semaglutide	Semaglutide 1mg + Metformin 2000mg daily +Insulin Aspart (32+30i.e s.c)	42.0 mmol/mol	127kg	
	1.5 year after starting Semaglutide	Semaglutide 1mg + Metformin 2000mg daily +Insulin Aspart (22+20i.e s.c)	39.0 mmol/mol	116kg	

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### Discussion

The objective of this case report was to demonstrate the efficacy and safety of onceweekly semaglutide vs once daily GLP-1 RAs in patient with T2DM inadequately controlled on insulin therapy (± OADs). In our case report, we observed that once-weekly semaglutide 1 mg was dominant compared with once-daily liraglutide 1.8 mg. In this case report, once-weekly semaglutide 1.0 mg was the most clinically effective GLP-1 RA for achieving glycemic targets and reducing HbA1c, FPG, and body weight in patient who is receiving insulin therapy. In patients with T2DM inadequately controlled with insulin therapy, semaglutide provided superior improvements in mean HbA1c, FPG, and superior weight loss compared with liraglutide.

# Conclusion

Semaglutide, administered subcutaneously once weekly, provided superior glycemic control and body weight reductions compared with other GLP-1 RA in patient with T2DM receiving insulin therapy. Therefore, it is likely that once-weekly semaglutide will not increase the risk of hypoglycemia when added to insulin therapy. The reasons for switching to semaglutide from liraglutide included a need to reduce HbA1c or weight further, decreased frequency of administration and cardiovascular protection. In addition, significant weight loss was observed with both doses of semaglutide vs liraglutide.



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