

GLP-1 ANALOGUES: THE EMERGING MEDICATION AS AN ADJUNCT TO BARIATRIC SURGERY FOR WEIGHT AND METABOLIC MANAGEMENT – A SYSTEMATIC REVIEW

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Introduction

Glucagon-Like Peptide-1 (GLP-1) receptor agonists have emerged as a promising treatment for obesity and obesity related comorbidity. It has been used in the management of diabetes mellitus and obesity and also used to decrease the progression to chronic kidney in diabetic patients as well as improving cardiovascular risk profile. Bariatric surgery is the most effective treatment of obesity. However, some patients have inadequate weight loss or have weight regain following bariatric surgery with recurrence of obesity related comorbidities. GLP-1 analogues have been used as an adjunct to bariatric surgery either prior to surgery or in the post operative period. The aim of this systematic review is to study the efficacy of GLP-1 receptor analogues used as an adjunct to bariatric surgery in patients with inadequate weight loss or weight regain.

Methodology

- A systematic review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines.
- A detailed search of databases including Pubmed, Medline Embase(Ovid SP) and Cochrane(CENTRAL).
- Studies from 2014- 2024 were screened
- Inclusion criteria were adult patients (age over 18 years) who received GLP-1 agonists either preoperatively or post bariatric surgery.
- Primary outcomes were total weight loss, excess weight loss or BMI change.
- Secondary outcomes were metabolic and comorbidities improvement such as hypertension, glycaemic control or lipidemia. GLP- 1 agonist related adverse reactions

Results:

- 17 studies included – with at least 1 type of GLP-1 agonist prior or after bariatric surgery with duration of intervention between 3 weeks to 21 months

Primary outcomes:

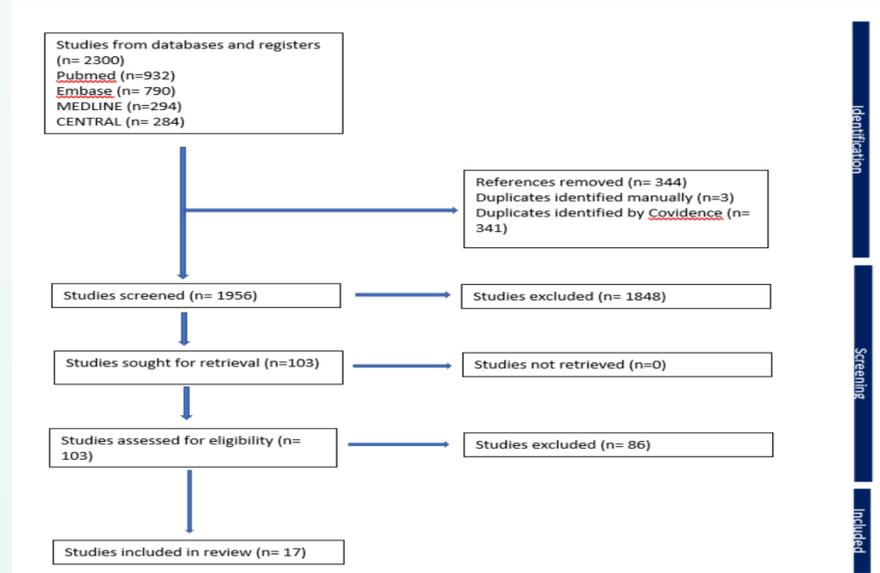
- Murvelashvili et al (1): weight loss of Semaglutide group 12.92%(14.09% to 11.75) $p < 0.001$ is more than liraglutide group (8.77% (0.01% to 7.54%), $p < 0.001$.
- Jensen et al (2): Greater weight reduction for patients on Semaglutide [9.8% (8.2,13.0), $p < 0.05$] as compared to liraglutide [7.3% (3.1,10.3), $p < 0.05$]
- Miras Et al (9): weight reduction of -4.23 kg (95% CI -6.81 to -1.64 , $p = 0.001$) for liraglutide vs placebo at week 26, and weight reduction was found to be continuous in the liraglutide group with no plateauing effect in relation to time

Secondary outcomes:

- Lautenbach et al (6): HbA1c reduction (from 5.4% +/- 0.4 to 5.1 +/- 0.4 , $p < 0.001$) and resolution of pre-diabetes in all patients ($p < 0.5$) with Semaglutide post bariatric surgery. Triglyceride levels were also noted to have significant reduction ($p = 0.016$) along with total cholesterol and LDL albeit the latter two were not clinically significant ($p < 0.52$, $p = 0.727$)
- Study done by Vinciguerra et al (11) showed improvement in both systolic and diastolic pressure ($p < 0.0001$) , as well as triglyceride levels ($p = 0.0001$) with s/c liraglutide 0.6mg daily titrated up by 0.6mg to minimum effective dosage for 24 weeks.

Discussion:

- GLP-1 agonists are emerging as a substitute for revisional surgery for patients with insufficient weight loss (IWL) or weight regain (WR) due to its good weight loss effect as demonstrated in multiple studies (refer to supplement tables by QR code)
- Semaglutide were found to have superior weight loss compared to liraglutide.
- Tirzepatide as the latest GLP-1 agonist (approved in November 2023) has the highest weight loss achievement as compared to Semaglutide.
- However, there is still lack of randomized controlled study done on both Semaglutide and Tirzepatide
- GLP-1 agonist has proven metabolic and cardiovascular effect through its incretin effect in glycemic control and was found to have significant risk reduction of 3-point major cardiovascular events (cardiovascular death, nonfatal myocardial infarction or nonfatal stroke) by 20% in SELECT trial ($n = 17604$) (13)
- Reported adverse effect from GLP-1 agonists mainly involve gastrointestinal effects during first month of initiation or at period of dose adjustment. However, no severe adverse effect were reported. (14)



Author	Baseline weight (kg)	BMI (kg/m ²)	Weight regain post bariatric surgery (%)	Agent based Weight loss (%)			P value	Agent based BMI change (kg/m ²)		
				semaglutide	liraglutide	tirzepatide		semaglutide	liraglutide	P value
Murvelashvili et al, 2023 (1)	135.3	49.3	42.43 (53.9)	12.92 (14.09 to 11.75)	8.77 (0.01 to 7.54)		0.775			
Jensen et al, 2023 (2)	112.4 (104.3, 125.3)	41.8 (39.5, 46.8)	15.10	-9.80	-7.30		0.05	-3.9 (2.9, 4.8)	-2.5 (1.1, 3.3)	0.001
Jamal et al, 2024 (3)	116.2 (25.5)	42.6 ± 6.3	22 (18.4)	10.3 (5.9)	15.5 (6.3)		0.05			

Table 1 : weight loss and BMI changes observed in post bariatric surgery patients on different GLP-1 agonists

Author	Intervention	Baseline					HbA1c control	FBG control	HbA1C control
		HbA1c control	FBG control	HbA1C control	HbA1c control	FBG control			
Amusin et al, 2022 (4)	liraglutide, exenatide, dulaglutide and semaglutide	8.3 +/- 1.4				6.7 +/- 1.11			$p = 0.92$
Jensen et al, 2023 (5)	s/c liraglutide 3.0mg OD or s/c semaglutide 1.0mg or T. semaglutide 14.0mg OD	7.1 (6.9, 7.4)				6.4 (6.3, 6.6)			
Lautenbach et al, 2023 (6)	semaglutide 0.25mg/week x 4/52 then 0.5mg/week then 1.0mg/week at 6th month	5.4 +/- 0.4				5.1 +/- 0.4			$p < 0.001$
Lautenbach et al, 2022 (7)	s/c semaglutide 0.25mg/week for first 4/52 then increase to 0.5mg/week as tolerated	5.3 (0.4)				5.2 (0.2)			$p = 0.446$
Thakur et al, 2021 (8)	S/C liraglutide 0.6mg OD titrated up to 3.0 mg OD vs placebo	6.0 +/- 1.5	6.5 +/- 1.4	106.5 +/- 38.4	127.1 +/- 69.2	7.6 (1.65)	7.4 (0.75)		$p = 0.516$, $p = 0.516$
Miras et al, 2019 (9)	S/C liraglutide 0.6mg OD up to 1.8mg OD vs placebo	7.9 (1.39)	7.4 (0.75)	8.2 (3.2)	7.5 (2.9)				Treatment effect from baseline to 26 weeks (liraglutide vs placebo): -1.22 (-1.80 to -0.64, $p = 0.0001$)
Mok et al, 2023 (10)	s/c liraglutide 3.0mg vs placebo	5.8 (0.7)	6.0 (0.9)	5.0 (1.3)	5.3 (1.5)	-0.27 (0.37)	-0.03 (0.22)		
Vinciguerra et al, 2023 (11)	S/C liraglutide 0.6mg OD titrated up by 0.6mg weekly up minimum effective dose (mean dosage: 2.4mg)			99.3 +/- 12.4					
Elhag et al, 2022 (12)	liraglutide 0.6mg, titrated to maximum dosage of 3mg	5.95 +/- 1.00		5.63 +/- 1.66		5.95 +/- 1.62			$p = 0.98$

Table 2: Glycemic effect of post-bariatric patients on GLP-1 agonists



Scan for more information on results and references