Obesity Pillars 2 (2022) 100016

Contents lists available at ScienceDirect

Obesity Pillars

journal homepage: www.journals.elsevier.com/obesity-pillars

Effect of GLP-1 agonists on weight loss in patients with polycystic ovary syndrome and obesity: A single-center study

Dushyanth Srinivasan [a,b,*], Holly F. Lofton [b,c]

[a] Division of Hospitalist Medicine, Department of Medicine, NYU Grossman School of Medicine, New York, NY, USA
[b] General Internal Medicine, Department of Medicine, NYU Grossman School of Medicine, New York, NY, USA
[c] Division of Bariatric Surgery, Department of Surgery, NYU Grossman School of Medicine, New York, NY, USA

A B S T R A C T

Background: Weight loss of >5% in patients with polycystic ovary syndrome and obesity (PCOS–O) is believed to improve underlying drivers of the syndrome. Weight loss facilitated by GLP-1 agonists in patients with PCOS–O is not well characterized. In this single-center retrospective study, we determined weight loss in patients with PCOS–O with GLP-1 monotherapy versus metformin.

Methods: In this brief report, electronic records of 183 adult patients with PCOS–O were reviewed between January 2020 and April 2021. We identified 12 and 19 patients that were treated with metformin and GLP-1 monotherapy respectively. One patient in each cohort had diabetes mellitus. Weights were reviewed at baseline (prior to therapy initiation) and at six-month follow-up. We analyzed change in weight from baseline and proportion with >5% and 10% weight loss using Fisher exact *t*-test and chi-square test. Univariate linear regression was used to identify correlations between treatment and weight loss.

Results: Baseline characteristics were similar between metformin (n = 12) and GLP-1 (n = 19) cohorts with the exception of mean days on medication. Following six months of treatment, mean weight loss was 4.9 kg (4.8%) and 9.1 kg (9.8%) in the metformin and GLP-1 cohorts (p = 0.13) respectively. Similar trends were seen in BMI with reductions of 1.8 kg/m^2 (4.7%) and 3.5 kg/m^2 (9.7%). A significantly greater proportion of patients achieved 5% and 10% weight loss with GLP-1 treatment (84.2% and 57.8%, p = 0.01 and p = 0.02) compared to metformin. Univariate linear regression analysis demonstrated a trend towards greater weight loss in patients treated with GLP-1 monotherapy (Coeff: 4.15, 95% CI: 1.3-9.7, p = 0.13) versus metformin.

Conclusion: Our study shows improvements in weight with GLP-1 monotherapy versus metformin as demonstrated by overall weight loss and proportion of patients achieving >5% weight loss. Further prospective randomized controlled studies are needed to establish GLP-1 weight loss efficacy in patients with PCOS–O and clinically related outcomes.

1. Introduction

Polycystic Ovary Syndrome (PCOS) is characterized by hyperandrogenism, ovulatory dysfunction and polycystic features. The syndrome affects nearly 6–15% of women of reproductive age depending on the diagnostic criteria used [1–5]. PCOS is thought to be associated with excess luteinizing hormone (LH) and a relative insufficiency of follicle stimulating hormone (FSH) that drive excess androgen production and ovulatory dysfunction [5]. Obesity is seen in nearly 50–80% of patients with PCOS and related insulin resistance may decrease sex-hormone binding globulin production that leads to worsening hyperandrogenism [5,6]. Obesity in this patient population is also known to be an independent risk factor for infertility. Weight loss of 5–10% is thought to reduce androgen levels, and improve metabolic markers and fertility [4,7,8]. With the additional benefits of weight loss, metformin has long been a part of the PCOS treatment paradigm. It is typically recommended in patients with PCOS with impaired glucose tolerance or diabetes mellitus type 2 that is not responsive to lifestyle modification, and is known to induce modest weight loss ranging up to nearly 4 kg in this population [9–12].

More recently, glucagon-like peptide-1 (GLP-1) agonists such as liraglutide and semaglutide have been approved for chronic weight management. GLP-1 is an incretin that delays gastric emptying, improves glucose-stimulated insulin secretion, and reduces appetite. Both liraglutide and semaglutide have demonstrated meaningful weight loss in patients with obesity and without diabetes, ranging up to 8% and 15% of baseline body weight [13,14]. The effects of GLP-1 agonists to facilitate weight loss in patients with PCOS and obesity (PCOS–O) is relatively unknown however. To our knowledge, there is only one study that has investigated the effects of GLP-1 monotherapy, specifically liraglutide, versus metformin [15]. In this single-center retrospective study, we examined weight loss effects of GLP-1 monotherapy versus metformin in patients with PCOS–O over a six-month interval.

* Corresponding author. Division of Hospital Medicine, Department of Medicine, NYU Grossman School of Medicine, 550 1st Avenue, Suite 1803 New York, NY, 10016, USA.
E-mail address: dushyanth.srinivasan@nyulangone.org (D. Srinivasan).

https://doi.org/10.1016/j.obpill.2022.100016
Received 24 February 2022; Received in revised form 30 March 2022; Accepted 30 March 2022

2. Methods

2.1. Trial design

Following approval from the New York University (NYU) Institutional Review Board, we conducted a single center retrospective cohort study. In this analysis among patients with PCOS–O, we sought to determine associations and absolute differences in weight loss in patients treated with metformin versus GLP-1 monotherapy over a six-month period.

2.2. Patients

We queried the electronic health record of the NYU Weight Management Clinic and identified 183 adult patients (18 years of age or older) with reported diagnosis of PCOS and obesity with last clinic visit between January 2020 and April 2021. We did not verify diagnosis via any criteria other than the diagnosis found in the electronic health record. Patient charts were further reviewed to identify those treated with metformin or GLP-1 monotherapy (liraglutide or semaglutide) for weight loss. Recorded weights at the start of therapy and six-month follow-up were required for inclusion. One patient in each cohort had diabetes mellitus. Patients treated with metformin included 500 mg and 1000 mg daily dosing. Patients treated with liraglutide included doses of 1.8 mg and 3.0 mg with up-titration over 3 and 5 weeks respectively. Semaglutide dosing included were up to 1 mg with titration over an 8-week period. Patients treated with metformin for less than 180 days, semaglutide less than 30 days, or liraglutide less than 21 days were excluded from analysis. Dietary and behavioral counseling was provided at the discretion of the treating provider.

2.3. Primary and secondary outcomes

Our primary outcome of interest was change in patient weight from baseline at six-month follow-up. Secondary outcomes included proportion of patients achieving >5% and >10% weight loss from baseline.

2.4. Diagnostic laboratory and imaging assessment

Patient charts were reviewed to determine baseline metabolic markers prior to initiating therapy. Metabolic markers assessed included total triglycerides, total cholesterol, high-density lipoprotein, low-density lipoprotein, and hemoglobin A1c.

2.5. Statistics

Statistical analysis was performed using STATA software (StataCorp, College Station, TX). Baseline characteristics were compared between metformin monotherapy and GLP-1 monotherapy cohorts using contingency table chi-2 analysis for categorical variables and Fisher exact *t*-test for continuous variables. Univariate linear regression was performed to determine associations between treatment cohort and weight loss at six months. A p-value <0.05 was considered statistically significant.

3. Results

183 adult patients with PCOS–O were identified in the NYU Weight Management Clinic between January 2020 and April 2021.17 and 36 patients with PCOS–O were treated with metformin and GLP-1 monotherapy respectively during this time period. Five metformin and 17 GLP-1 monotherapy patients were excluded from analysis due to lack of six-month follow up data. 12 (6.5%) and 19 (10.3%) metformin and GLP-1 monotherapy treated patients were included for analysis. Of the GLP-1 patients included, 3 (15.7%) and 16 (84.2) were on semaglutide and liraglutide respectively.

Baseline characteristics are described in Table 1 and were similar between metformin and GLP-1 cohorts with the exception of mean days on medication. Mean days on medication was 855.3 and 499.9 in the metformin and GLP-1 monotherapy groups. Baseline weight among metformin and GLP-1 patients was similar at 101.8 kg and 93.4 kg ($p = 0.26$) respectively. Following six months of treatment, mean weight loss was 4.9 kg (4.8%) and 9.1 kg (9.8%) in the metformin and GLP-1 cohorts ($p = 0.13$, Table 2). Similar trends were seen in BMI with reductions of 1.8 kg/m^2 (4.7%) and 3.5 kg/m^2 (9.7%). 25% and 16.6% of patients treated with metformin achieved >5% and 10% weight loss respectively at six-month follow-up. A significantly greater proportion of patients achieved 5% and 10% weight loss with GLP-1 treatment, with 84.2% and 57.8% meeting these thresholds respectively at six months ($p = 0.01$ and $p = 0.02$). Univariate linear regression analysis demonstrated a trend towards greater weight loss in patients treated with GLP-1 monotherapy (Coeff: 4.15, 95% CI: 1.3-9.7, $p = 0.13$) versus metformin.

4. Discussion

In this study of adult patients with PCOS–O, treatment with GLP-1 monotherapy resulted in a trend towards greater weight loss of 9.1 kg versus 4.9 kg in those treated with metformin. To our knowledge, only one previous study by *Jensterle* et al. has sought to evaluate the effect of GLP-1, specifically liraglutide, versus metformin monotherapy on weight loss [15]. In this 12-week randomized study of 32 patients with PCOS–O, weight loss of 3 kg and 2.3 kg in those treated with liraglutide and metformin was seen. There was no statistically significant difference seen between treatment groups. The study, however, utilized liraglutide 1.2 mg and likely did not see the full effect of GLP-1 given weight loss dosing of 3 mg. A separate observational analysis by *Rasmussen* et al. demonstrated weight loss of 9 kg (9.1%) in patients with PCOS treated with combination therapy of liraglutide and metformin, with titration up to 1.8 mg of liraglutide [5]. Mean duration of treatment was 27.8 weeks and overall improvement in weight loss was similar to that seen with monotherapy in our cohort. We suspect differences likely lay within differences in max dose liraglutide utilized and variation in lifestyle modifications implemented.

Table 1
Baseline characteristics of GLP-1 and metformin treated patients.

	Metformin (N = 12)	GLP-1 (N = 19)	p-value
Mean Age (SD)	34.5 (8.5)	40.5 (11.3)	0.12
Mean days on medication (SD)	855.3 (413.7)	499.9 (207.9)	0.003
Ethnicity (%)			
Caucasian	7 (58.3)	10 (52.6)	0.94
African American	2 (16.6)	3 (15.8)	
Hispanic	2 (16.6)	3 (15.8)	
Asian	1 (8.3)	2 (10.5)	
Other	0	1 (5.3)	
Metabolic markers			
Baseline Total Cholesterol	170.1 (20.2)	176.8 (35.1)	0.68
Baseline Triglyceride	190.5 (177.6)	178.9 (82.6)	0.86
Baseline HDL	58.3 (11.7)	50.1 (13.4)	0.24
Baseline LDL	136.8 (120.1)	96.0 (18.6)	0.33
Baseline A1C	5.7 (0.94)	5.4 (0.49)	0.43
Comorbidities (%)			
Hyperlipidemia	5 (41.6)	7 (36.8)	0.79
Hypertension	2 (16.6)	4 (21.1)	0.76
Diabetes Mellitus Type 2	1 (8.3)	1 (5.3)	0.73
Osteoarthritis	1 (8.3)	0	0.20
Obstructive Sleep Apnea	1 (8.3)	2 (10.5)	0.84
GERD	7 (58.3)	10 (52.6)	0.76
Hypothyroidism	1 (8.3)	3 (15.8)	0.55
Asthma/COPD	3 (25.0)	3 (15.8)	0.53
NAFLD	2 (16.6)	0	0.06
CAD	0	0	0.00
Gastric Surgery			
Sleeve	0	1 (5.3)	0.32
Bypass	2 (16.6)	2	
Band	0	0	

Table 2
Weight loss achieved by cohort.

	Metformin (N = 12)	GLP-1 (N = 19)	p-value
Starting Body Weight kg (SD)	101.8 (30.1)	93.4 (10.8)	0.26
Starting BMI (SD)	38.1 (10.2)	35.0 (2.8)	0.22
6 month Change in Weight kg (SD)	−4.9 (8.6)	−9.1 (6.4)	0.13
6 month Change in BMI (SD)	−1.8 (3.2)	−3.5 (2.4)	0.11
>5% weight loss (%)	3 (25.0)	16 (84.2)	0.01
>10% weight loss (%)	2 (16.6)	11 (57.8)	0.02

A significantly greater proportion of patients treated with GLP-1 monotherapy achieved a higher degree of weight loss in our study. 84.2% and 57.8% achieved greater than 5% and 10% weight loss with GLP-1 monotherapy, respectively, versus metformin (25% and 16.6%). The 5% weight loss threshold has been shown to improve overall health and metabolic parameters in patients with obesity, but also provides benefit in patients with PCOS by improving androgen levels and menstrual irregularities [8]. Our data suggests that GLP-1 agonists are likely better agents to facilitate meeting this weight loss threshold in patients with PCOS–O and can translate into long-term benefit. As a result, we propose that GLP-1 agonists could be used in a complementary fashion to first line metformin.

The primary limitation of our study is that it was a retrospective single-center analysis with a small sample size, and is thus underpowered. Our sample size was limited given many patients with PCOS had been on multiple weight loss medications within a six-month period that would have confounded results. Secondly, given our small sample size, the GLP-1 cohort was coupled to include both semaglutide and liraglutide usage and weight loss seen may not be accurately reflective of the efficacy of each medication. However, we note only three patients in the GLP-1 cohort were on semaglutide. Finally, due to the retrospective nature of our study, lifestyle modifications and dietary changes may not have been standardized across patients and could be considered a confounding variable in our analysis.

5. Conclusion

Our study shows meaningful improvements in weight with GLP-1 monotherapy versus metformin monotherapy as demonstrated by overall weight loss and proportion of patients achieving >5% weight loss. We think use of GLP-1 in patients with PCOS–O should be considered to facilitate greater weight loss and lead to improvements in underlying drivers of the syndrome. Further prospective randomized control studies, however, are needed to establish GLP-1 weight loss efficacy in this patient population and correlation with PCOS related clinical outcomes.

Disclosures

Dr. Lofton receives research funding from EliLilly Pharmaceuticals. She also receives research funding, speaker honoraria, and consulting fees from Novo Nordisk, Inc. Dr. Srinivasan has no relevant financial disclosures.

Author contribution

Dushyanth Srinivasan and Holly Lofton were involved in data collection, analysis, manuscript writing and editing.

Ethical review

This submission represents original works. All data collection and analysis was performed following approval from the respective institutional review board.

Source of funding

None.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Holly Lofton reports a relationship with Eli Lilly and Company that includes: funding grants. Holly Lofton reports a relationship with Novo Nordisk Inc that includes: consulting or advisory and funding grants.

Acknowledgment

none.

References

[1] Broekmans FJ, et al. PCOS according to the Rotterdam consensus criteria: change in prevalence among WHO-II anovulation and association with metabolic factors. BJOG 2006;113(10):1210–7.
[2] Fauser BC, et al. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Fertil Steril 2012;97(1):28–38 e25.
[3] March WA, et al. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod 2010;25(2):544–51.
[4] McCartney Ch R, Marshall JC. Polycystic ovary syndrome. N Engl J Med 2016;375(14):1398–9.
[5] Rasmussen CB, Lindenberg S. The effect of liraglutide on weight loss in women with polycystic ovary syndrome: an observational study. Front Endocrinol (Lausanne) 2014;5:140.
[6] Dumesic DA, et al. Scientific statement on the diagnostic criteria, epidemiology, pathophysiology, and molecular genetics of polycystic ovary syndrome. Endocr Rev 2015;36(5):487–525.
[7] Moran LJ, et al. Treatment of obesity in polycystic ovary syndrome: a position statement of the androgen excess and polycystic ovary syndrome society. Fertil Steril 2009;92(6):1966–82.
[8] Nandi A, et al. Polycystic ovary syndrome. Endocrinol Metab Clin North Am 2014;43(1):123–47.
[9] Conway G, et al. The polycystic ovary syndrome: a position statement from the European Society of Endocrinology. Eur J Endocrinol 2014;171(4):P1–29.
[10] Harborne LR, et al. Metformin and weight loss in obese women with polycystic ovary syndrome: comparison of doses. J Clin Endocrinol Metab 2005;90(8):4593–8.
[11] Legro RS, et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2013;98(12):4565–92.
[12] Naderpoor N, et al. Metformin and lifestyle modification in polycystic ovary syndrome: systematic review and meta-analysis. Hum Reprod Update 2015;21(5):560–74.
[13] Pi-Sunyer X, et al. A randomized, controlled trial of 3.0 mg of liraglutide in weight management. N Engl J Med 2015;373(1):11–22.
[14] Wilding JPH, et al. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med 2021;384(11):989.
[15] Jensterle M, et al. A 12-week treatment with the long-acting glucagon-like peptide 1 receptor agonist liraglutide leads to significant weight loss in a subset of obese women with newly diagnosed polycystic ovary syndrome. Hormones (Athens) 2015;14(1):81–90.