Liraglutide 3.0 (Saxenda) in bariatric patients: a retrospective real-world clinical evaluation of effectiveness

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Abstract

Background: Glucagon-like peptide-1 analogues such as liraglutide 3.0 mg (Saxenda) have yielded significant weight loss in clinical trials when combined with lifestyle interventions. Despite the recent approval of liraglutide 3.0 mg, its success among patients attending specialist bariatric units remains uncertain.

Objective: This study investigated the effectiveness of liraglutide 3.0 mg on weight, body mass index (BMI), treatment tolerability and its effects on glycated haemoglobin (HbA_{1c}).

Methods: Clinical data were retrospectively obtained from medical records within Tier 3-4 bariatric weight management clinics. Wilcoxon signed rank tests were employed to establish the statistical significance ($p<0.05$) of changes in weight and HbA_{1c}.

Results: 33 patients were identified (72.7% female with mean baseline age, weight and BMI of 44.8 years, 156.6 kg and 55.0 kg/m^2, respectively). Eighteen patients had completed 26 weeks of treatment. Of the 18 patients, the discontinuation rate due to side effects was 15.2%, indicating substantial treatment tolerance. After 26 weeks of treatment, BMI (±standard deviation) was significantly reduced by 7.9±6.3% ($p<0.05$) and 72.2% of patients achieved at least 5% weight loss. Additionally, a significant decrease in median HbA_{1c} (4.5±4.5 mmol/mol) was observed ($p<0.05$), concurrent with increased remission from prediabetes.

Conclusion: This retrospective study revealed that liraglutide 3.0 mg, together with lifestyle management, reduced weight and improved glycaemic control. These results support liraglutide's application in certain high-risk populations, including patients waiting for bariatric surgical intervention.

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Introduction

The obesity pandemic presents a major global challenge to public healthcare and chronic disease prevention, with 28.0% of English adults estimated to be obese and a further 36.2% considered overweight.[1] Obesity is correlated with several chronic non-communicable diseases including insulin resistance and type 2 diabetes mellitus (T2DM).[2] Given that the overriding modifiable risk factor for diabetes is weight, accounting for approximately 44% of diabetes, there is a significant treatment opportunity to prevent the development of T2DM with appropriate interventions.[3]

Randomised controlled trials have discovered that a fall in weight of 5-10% is associated with metabolic benefits.[4] Furthermore, approximately £44.7 billion is spent annually by the NHS on obesity and its related costs.[5] Preventing and treating obesity presents a significant opportunity to alleviate substantial financial pressure and vastly reduce societal health complications.[6]

In December 2020, the UK National Institute for Health and Care Excellence (NICE) recommended liraglutide 3.0 mg as a cost-effective obesity treatment for adults with a BMI ≥ 35 kg/m^2 who meet a hyperglycaemic prediabetic threshold, exhibiting clinical signs of hypertension and/or dyslipidaemia. Liraglutide (proprietary name Saxenda) has recently become accessible through specialist bariatric services. The treatment costs approximately £196.20 monthly in the NHS but a discount was applied since all our patients were prescribed the treatment from the hospital Tier 3 weight management service.[7]

This glucagon-like peptide-1 (GLP-1) analogue expresses 97% similarity in amino acid sequence homology to the endogenous GLP-1 molecule. It acts by raising glucose-dependent postprandial insulin and decelerating gastric emptying.[8] Weight loss is significantly induced through a reduced appetite, thus decreasing food consumption.[9]

The primary aim of this retrospective observational study was to investigate the percentage weight change at 26 weeks, with a weight reduction of ≥5% considered clinically significant given its association with a reduction in cardiovascular and metabolic risks.[4] The secondary aims focused on observing HbA_{1c} changes and the tolerability profile of 3.0 mg liraglutide.

Methods

Setting

This was a service evaluation report, as requested by our hospital formulary and medicine management following approval of Saxenda prescription from Tier 3 service.

Patients included were Tier 3 patients (n=26) diagnosed with prediabetes (HbA_{1c} = 42-47 mmol/mol) and Tier 4 patients (n=7) on the waiting list for bariatric surgery since 2019. Treatment was based at the East Midlands Bariatric Metabolic Institute (EMBMI) at the Royal Derby Hospital, NHS Foundation Trust. The evaluation was carried out using a Standard Evaluation Framework for Weight Management Interventions,[10] and compared alongside the necessities outlined in the Clinical Commissioning Policy: Complex and Specialised Obesity Surgery.[11] Treatment was given in accordance with NICE guidelines, with preliminary treatment initiation and lifestyle interventions advice provided by the Oviva patients support programme commissioned by Novo Nordisk. Patients received follow-ups from a Tier 3 clinician (physician, nurse or dietician) depending on their compliance and engagement within the service.

Data collection

Clinical data were retrospectively obtained at six, 12 and 26 weeks after commencing liraglutide. The short-term weight outcomes included the median weight change and the proportion of patients achieving a ≥5% and ≥10% weight loss.

Statistical analysis

Patients who received liraglutide treatment between 9th January 2021 and 25th November 2021 were examined. Data were collected from medical records dated between 9th December 2020 and 27th November 2021. The baseline weight and HbA_{1c} did not follow a normal distribution on visual inspection of the histograms and the Shapiro-Wilk test. Therefore, Wilcoxon ranked signed tests were used to determine whether there was a statistically significant change in the treatment indicators from baseline to 26 weeks. The criteria for statistical significance were set at 5% and all statistical tests were two-tailed. Statistical analysis was undertaken using IMB SPSS Statistics for Macintosh version 27.0.1.0.[12] Patients with missing data were excluded.

Results

Patient flow

A 33-patient cohort was identified. A total of 26 patients had 6-week data, 22 had data at 12 weeks and 16 at 26 weeks (Figure 1). Since their treatment period was incomplete at the time of analysis, seven (21.2%) patients were excluded from analysis in the study.

Descriptive baseline characteristics and co-morbidities

Table 1 summarises the cohort baseline characteristics and Table 2 the data available for each follow-up period. The mean±SD age, weight, BMI and HbA_{1c} were 44.8±9.7 years, 156.6±31.7 kg, 55.0±10.4 kg/m^2 and 42.2±5.0 mmol/mol, respectively. The entire cohort was classified as class III obese (BMI ≥40 kg/m^2). Commonly occurring co-morbidities included prediabetes (75.7%), depression (57.6%), gastro-oesophageal reflux disease (45.5%) and asthma (36.4%).

Figure 1. A flowchart displaying the follow-up data available after initiating liraglutide 3.0mg treatment

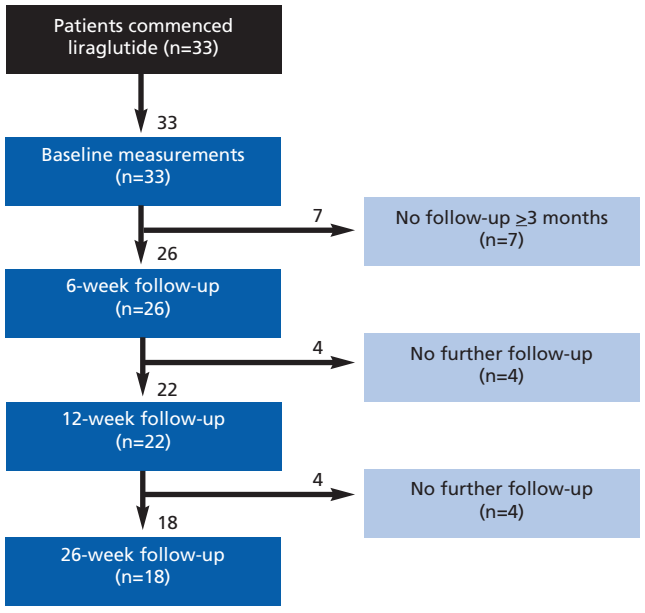


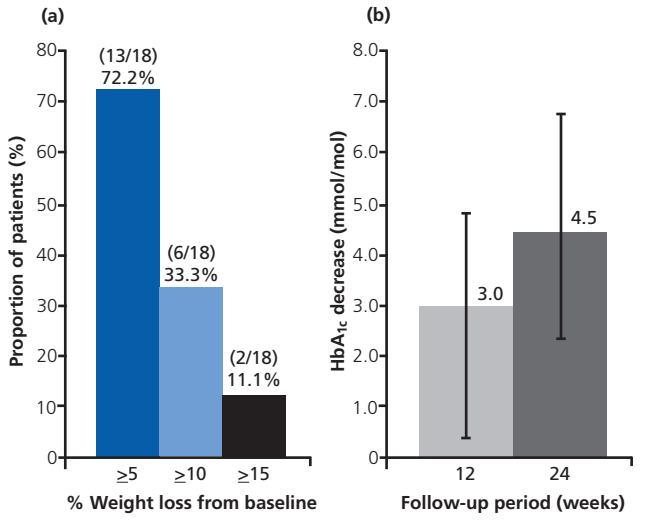
Table 1 Baseline characteristics of the cohort

Characteristic	N	Mean (%)	SD	Range
Age (yrs)	33	44.8	9.7	39
Male	9	27.3		
Female	24	72.7		
Class III obese	33	100.0		
Characteristic	**N**	**Median**	**IQR**	
Baseline weight (kg)	33	151.0	29.5	
Body mass index (kg/m^2)	33	53.2	12.1	
HbA_{1c} (mmol/mol)	33	42.0	2.0	

Table 2 The available follow-up data

	Number of patients with follow-up data		
	6-weeks	12-weeks	26-weeks
Weight (kg)	26	22	18
Body mass index (kg/m^2)	26	22	18
HbA_{1c} (mmol/mol)	13	13	9

Figure 2. (a) Proportion of patients achieving ≥5%, ≥10% and ≥15% weight reduction at 26-weeks; (b) Absolute HbA_{1c} decrease observed at 12 and 26-weeks following liraglutide 3.0mg treatment. Error bars indicate 1st and 3rd quartile



Dose tolerated, discontinuation rate and adverse events

The mean±SD maximum tolerated dose of liraglutide was 2.6±0.8 mg. Five patients (15.2%) discontinued treatment: three due to intolerable gastrointestinal side effects, one for a novel T2DM diagnosis and one with no documented motive. Adverse events were experienced by 66.7% of the cohort. Nausea was the most frequently observed symptom, with 24.2% of patients experiencing at least one episode over the follow-up period. Abdominal discomfort was almost as prevalent, reported in 21.2% of the cohort.

Study outcomes

A statistically significant weight decrease was observed at six, 12 and 26 weeks after commencing 3.0 mg liraglutide. A median loss of 5.0±7.5 kg (3.3±4.4 %) was observed at six weeks, which increased to 6.6±8.0 kg (4.0±4.7%) at 12 weeks, reaching a 12.0±10.0 kg (7.9±6.3%) decrease at 26 weeks.

Among those who completed the treatment period (n=18), clinically significant weight loss was achieved by 72.2% of the cohort at 26 weeks, with greater changes of 10% and 15% weight loss observed in 33.3% and 11.1%, respectively (highlighted in Figure 2A). The entire cohort experienced an absolute weight loss after 26 weeks. Additionally, a median 3.0± 4.5 mmol/mol (p=0.049) decrease in HbA_{1c} was experienced at 12 weeks, and this increased to a 4.5±4.5 mmol/mol (p=0.005) reduction at 26 weeks (see Figure 2B).

Discussion

Liraglutide treatment, as an adjunct to lifestyle management, was associated with a 12.0 kg (7.9%) weight reduction and 4.5 mmol/mol (10.3%) HbA_{1c} decrease at 26 weeks. This subsequently led to a greatly decreased prevalence of prediabetes among those who had prediabetes at baseline, from 100% to 9.1%. Interestingly, these differences occurred even though 10.1% of patients were taking sub-optimal liraglutide doses, which likely restricted their weight loss. Liraglutide 3.0 mg was well tolerated, with a discontinuation rate of only 15.2%, mostly due to intolerable gastrointestinal side effects.

A total of 40.9% of this cohort achieved a 5% weight loss at 12 weeks, and 72.2% at 26 weeks. These figures are much higher than the 39% of patients who achieved 5% weight loss at 26 weeks in our previous systematic review of clinical outcomes of a Tier 3 service in England.[15] Crucially, 100% of this cohort experienced an absolute weight loss after 26 weeks of treatment. It can be inferred that a lengthier treatment duration promotes weight loss which is beneficial across multiple domains. Incorporating a suitably long treatment duration is recommended.

The 90.9% incidence reversal from prediabetes to normoglycaemia indicates liraglutide had the capacity to reverse prediabetes in this highly selective cohort. This reversal is likely to have substantial clinical relevance.

The study has produced observations comparable with or superior to previous studies. This is further reassurance that liraglutide's effectiveness can be translated into a real-world setting within this specific population group, with the potential to achieve superior results.

Although this study provides promising short-term outcomes, it is essential to examine liraglutide's long-term impact in weight management. Future real-world investigations must determine whether there is a plateau, or even a reversal to baseline, once treatment is stopped. To form a more accurate long-term evaluation, it is advisable to revisit the data at 12- and 24-month assessment points. Similarly, there is scope for future work to decipher the liraglutide dose which optimises weight reduction and costs. This could help determine whether a lower dosage could achieve equal benefits at a reduced direct cost.

Several intrinsic limitations must be considered. Given its retrospective nature, the absence of a control group hindered the study's ability to differentiate between the impact of liraglutide plus lifestyle management and the impact of lifestyle management in isolation. Additionally, measuring weight loss during an active intervention would likely produce results when the impact is at its greatest. Consequently, an artificially inflated view of effectiveness relative to the true long-term impact is possible. This is underpinned by evidence suggesting that many patients regain weight after an intervention that is deemed 'successful'. The representative nature may be weakened by missing data, leading to a reduced ability to rule out type-two errors.

Crucially, numbers were small and those who did not tolerate Saxenda or who did not find it to be effective will not have adequate data at follow-up. This limits the generalizability of our findings. The efficacy of liraglutide may, therefore, be overstated here. Nonetheless, this single-centre study demonstrated promising results describing liraglutide's effectiveness within routine practice. Combined with lifestyle interventions, liraglutide 3.0mg treatment resulted in a statistically significant reduction in weight

Key messages

- Use of Saxenda in our Tier 3 service is associated with significant reduction in weight
- Use of Saxenda in our Tier service conferred a reduction in HbA_{1c} levels and reversal from pre-diabetes to normoglycaemia state
- Overall, the effectiveness of Saxenda in the obese bariatric population is comparable to evidence reported from clinical trials

and improvement in glycaemic control for this high-risk cohort. It is reassuring that the adverse events experienced during treatment were mild and largely transient.

The investigation corroborates the findings of previously published RCTs and observational studies in different patient population groups with different comorbid conditions.[13-20] This provides confirmatory evidence of liraglutide's ability to benefit weight management and to enhance the reduction of metabolic and cardiovascular risk factors. The results will inform and aid clinicians in conducting evidence-based treatment decisions across the clinical spectrum of obesity. Although the investigation is not free from limitations, it is reasonable to conclude that the results exemplify the use of pharmacotherapy as an effective approach to weight management. However, further assessment is required to evaluate its cost-effectiveness.

Conflict of interest None.
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