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BRIEF REPORT

Routine clinical use of liraglutide 3 mg for the treatment of obesity: Outcomes in non-surgical and bariatric surgery patients

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In this study we prospectively collected data on the use of liraglutide 3 mg in obese Arab patients. As part of routine care, 2092 patients were dispensed liraglutide 3 mg. Median age was 38 years and 77% were women. Median baseline weight was 95 kg and body mass index was 36.6 kg/m^2. Of the patients, 188 (9%) had previous bariatric surgery. Seven hundred and eighty-seven patients were treated for ≥16 weeks and their median (interquartile range) weight loss was 6.0 (2.4-9.4) kg, equivalent to 6.4% (2.6%-9.7%) of baseline weight (P < 0.0001, n = 787). Of those treated for ≥16 weeks, 474 (60%) achieved a weight loss of >5% of baseline weight while 182 (23%) achieved >10% weight loss. There was no difference in percentage weight loss between postbariatric surgery (n = 76) and non-surgical patients (n = 711). As a result of adverse events, mainly gastrointestinal symptoms, 140 (6.7%) of the patients stopped treatment. One patient developed acute pancreatitis in the context of gallstone disease but made an uneventful recovery. Liraglutide 3 mg was well tolerated and resulted in weight loss in routine clinical care similar to that seen in randomized controlled trials.

KEYWORDS

antiobesity drug, bariatric surgery, liraglutide

1 | INTRODUCTION

Obesity is a major global health problem and has reached epidemic proportions worldwide with ~600 million adults currently classified as obese and another 1.9 billion as overweight.[1] Options for treatment of obesity include lifestyle changes, pharmacotherapy and bariatric surgery.[2,3] Recently, the glucagon-like peptide-1 (GLP-1) analogue liraglutide 3 mg has been licensed for treatment of obesity. The SCALE series of studies involving 5700 patients showed the effectiveness and safety of this drug.[4–8]

There are no published large studies on the use of liraglutide 3 mg in routine clinical practice that can provide insight into whether the findings from randomized controlled trial settings can be translated into real life. Moreover, the SCALE studies were largely conducted in white populations and data on the use of liraglutide 3 mg in obese patients of other ethnicities, including those of Arab descent, are limited. We aimed to assess the real-life efficacy and tolerability of liraglutide 3 mg as a treatment for obesity in Arab patients attending routine clinical care.

2 | RESEARCH DESIGN AND METHODS

The prospective data collection was performed as a clinical audit at the Imperial College London Diabetes Centre (ICLDC) in Abu Dhabi and Al Ain, United Arab Emirates. All patients attending the ICLDC are assessed by a multidisciplinary team who record body weight, height, waist circumference, pulse and blood pressure.

In December 2016, liraglutide 3 mg (Saxenda, Novo Nordisk, Bagsvaerd, Denmark) was licensed as a treatment for obesity in the United Arab Emirates as an adjunct to a reduced calorie diet and increased physical activity. Patients were considered eligible for treatment if they followed lifestyle advice for at least six months and had either a body mass index (BMI) of ≥30 kg/m^2 or a BMI of ≥27 kg/m^2

together with prediabetes, dyslipidaemia, hypertension or obstructive sleep apnoea.

Liraglutide was started at the dose of 0.6 mg daily with increments of 0.6 mg every week up to the maximum maintenance dose of 3 mg daily. Patients were counselled that the drug would be stopped if they did not achieve body weight loss of ≥5% of their baseline weight after 16 weeks from the start of titration. Patients were asked to return after 16 weeks at which their body weight response was assessed and a decision taken as to whether to continue treatment.

The patient database at ICLDC prospectively includes all patients attending the centre. It was accessed in May 2018 to identify all patients who received liraglutide 3 mg for treatment of obesity from 1 January 2017 to 30 April 2018. The database includes updated information on all ICLDC patients, each of whom signs a consent form upon registration, enabling their anonymized information to be used for data analysis. We used the ICLDC pharmacy records to determine the duration of treatment for which each patient received liraglutide 3 mg. We gathered the post-treatment assessment data consisting of body weight and other criteria performed for each patient at their final clinic visit.

2.1 | Statistical analysis

Values are presented as median (interquartile range) and non-parametric statistical tests were used except where indicated. We performed a modified intention-to-treat (ITT) analysis, including all patients who were dispensed liraglutide 3 mg and received follow-up on at least one occasion.

3 | RESULTS

During 1 January 2017 to 30 April 2018, 2092 Arab patients were dispensed liraglutide 3 mg and had records of both pre- and post-treatment body weight. One hundred and eighty-eight (9%) had previous bariatric surgery, a median of 4 years before starting liraglutide [63% sleeve gastrectomy (SG), 25% Roux-en-Y gastric bypass (RYGB) and 12% other procedures]. Table 1 shows the baseline characteristics of the ICLDC whole cohort and those who completed ≥16 weeks treatment compared with the SCALE obesity and prediabetes study (Supplementary Information File S1).[6]

3.1 | Patients treated for ≥16 weeks

In 787 patients who were treated with liraglutide 3 mg for ≥16 weeks, the median duration of treatment was 213 (162-303) days. Median body weight loss for the group was 6.0 (2.4-9.4) kg, equivalent to 6.4% (2.5%-9.7%) of baseline weight. In this group, 474 (60%) patients achieved >5% weight loss and 182 (23%) patients achieved >10% weight loss.

Median weight loss in the participants with no history of bariatric surgery was 6.4% (2.5%-9.8%) of baseline weight ($P < 0.0001$, n = 711), while that of the postsurgical group was 6.1% (3.1%-8.7%) ($P < 0.0001$, n = 76).

3.2 | Patients treated for ≥28 weeks

Three hundred and forty patients were treated with liraglutide 3 mg for ≥28 weeks; median duration of treatment was 296 (245-342) days. Median body weight loss in this group was 7.4 (3.5-11.0) kg,

TABLE 1 The baseline characteristics of the ICLDC whole cohort and those who completed ≥16 weeks treatment compared with the SCALE obesity and prediabetes study[6] on liraglutide 3 mg

Variable	Pi-Sunyer et al[6]	ICLDC (whole cohort)	ICLDC (≥16 weeks Rx)
Type of study	Randomized, placebo-controlled study	Clinical audit	Clinical audit
Number treated with liraglutide 3 mg	2487	2092	787
Ethnic origin	85% white 15% other ethnicities	93% Emirati Arabs	93% Emirati Arabs
		7% other Arabs	7% other Arabs
Women/men (%)	79/21	75/25	80/20
Mean age (years)	45	38	39
Treatment duration (weeks)	56	16 (10-28) (median and interquartile range)	30 (23-43) (median and interquartile range)
Mean baseline weight (kg)	106.2	98.6	97.9
Mean baseline BMI (kg/m^2)	38.3	37.5	37.5
BMI categories no. (%)			
27-29.9 (overweight)	66 (3)	12 (0.6)	5 (0.5)
30-34.9 (obese class I)	806 (32)	773 (37)	287 (37)
35-39.9 (obese class II)	787 (32)	776 (37)	299 (38)
≥40 (obese class III)	828 (33)	531 (25)	196 (25)
Waist circumference (cm)	115	107	106
Prediabetes at baseline (%)	61	52	55
Baseline HbA1c (%)	5.6	5.4	5.4

Abbreviations: BMI, body mass index; ICLDC, Imperial College London Diabetes Centre; Rx, treatment.

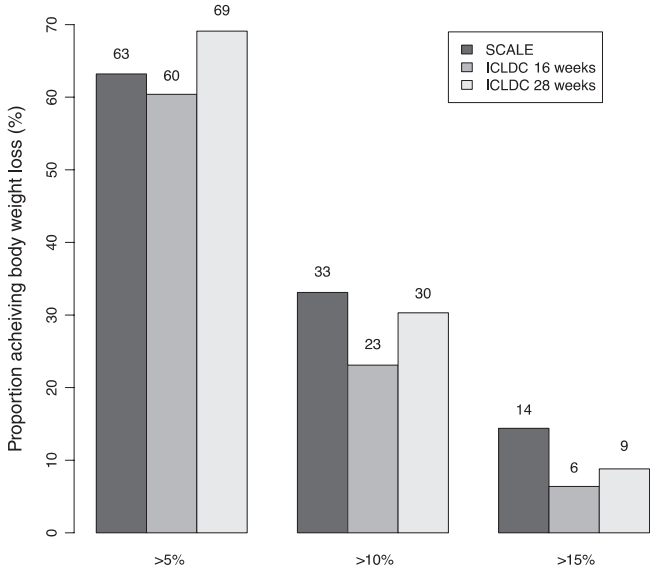

FIGURE 1 Comparison of categorical body weight loss (>5%, >10% and >15% of baseline weight) between the SCALE obesity and prediabetes study[6] (mean treatment period 56 weeks) and the Imperial College London Diabetes Centre (ICLDC) cohort treated for at least 16 weeks (median duration 30 weeks) and 28 weeks (median duration 42 weeks)

equivalent to 7.6% (3.7%-10.9%) of baseline weight; 234 (69%) patients achieved >5% weight loss and 103 (30%) patients achieved >10% weight loss.

Among the postbariatric surgery patients, the RYGB group achieved more body weight loss than the SG group (5.6% vs. 3.3%, $P = 0.025$).

Figure 1 shows the categorical body weight loss with liraglutide 3 mg in the ICLDC patients who completed 16 weeks and those who completed 28 weeks compared with the SCALE obesity and prediabetes study.[6]

3.3 | Patients who stopped treatment

Out of the total cohort of 2092 patients treated with liraglutide 3 mg, 425 patients (20%) stopped the drug after a median period of 108 days. Side effects were the reason for stopping the drug in 140 patients (6.7% of the total cohort).

3.4 | Adverse events

Most of the reported adverse events were mild to moderate gastrointestinal symptoms such as nausea, vomiting and diarrhoea. One 41-year-old woman developed acute pancreatitis. Following 1 month of treatment, she presented with abdominal pain and vomiting. A diagnosis of acute pancreatitis was made based on history and a lipase level of 7575 IU/L (normal range 23-300), and liraglutide was permanently stopped. She made a full, uneventful recovery following conservative treatment and a month later had laparoscopic cholecystectomy to remove gallstones.

4 | DISCUSSION

We have shown in this prospective clinical audit of obese Arab patients that liraglutide 3 mg was effective in reducing body weight by a median of 6 kg (6.4% of baseline body weight) after a median treatment period of 30 weeks. Weight loss of >5% is considered clinically meaningful because of associated metabolic and functional benefits.[2,3] Similar to the SCALE obesity and prediabetes study,[6] 60% of our patients lost >5% of baseline body weight.

The other 40% of our patients did not benefit from treatment with liraglutide 3 mg and were considered non-responders. In a meta-analysis of the studies on the five obesity drugs approved by the US Food and Drug Administration (FDA), Khera et al found non-response rates (defined as <5% body weight loss in 56 weeks) ranging between 25% and 56%.[9] The reasons for the lack of response to treatment are not clear. We used a strict rule of discontinuing treatment if patients did not achieve a benchmark body weight loss of ≥5% after 16 weeks treatment. This cut-off level has been shown to be a good predictor of body weight loss at 1 year.[10]

It was reassuring to observe that our postbariatric surgery patients had responses to liraglutide 3 mg similar to non-surgical patients, as well as similar tolerability. Therefore, our results indicate that liraglutide 3 mg can be a useful adjunctive option in patients who did not have an optimal response to, or have regained weight after bariatric surgery, as shown in previous studies.[11]

Liraglutide at the lower doses of 1.2 and 1.8 mg has been used for treatment of type 2 diabetes since 2009 with no major safety issues. However, more data are needed on the long-term safety of the drug at the higher dose of 3 mg, and users have to be vigilant. Similar to the SCALE series of studies, our prospective audit showed that the majority of side effects leading to treatment discontinuation were gastrointestinal (mainly nausea and vomiting). We identified one case of acute pancreatitis that led to drug withdrawal but the patient made a full recovery. However, the presence of the confounding factor of gallstones precludes a firm conclusion on whether liraglutide treatment was the sole cause of the patient's acute pancreatitis. In 2014, the European Medicines Agency (EMA) and the FDA concluded that an association between the incretin drugs and acute pancreatitis or pancreatic cancer is inconsistent with current data; however, both agencies also agreed that until further information becomes available, pancreatitis will continue to be considered a risk associated with these therapies.[12] Recently, a pooled analysis of four cardiovascular outcomes trials that used GLP-1 receptor agonists, involving 33 457 patients, showed no increased risk of acute pancreatitis or pancreatic cancer with these drugs.[13]

The issue of cost-effectiveness of obesity drug treatment needs to be considered carefully. The cost of pharmacotherapy for obesity must be set against the health economic burden of obesity with its associated complications. For example, diabetes prevention or delay of progression from prediabetes to diabetes shown over 3 years' use of liraglutide 3 mg has to be factored into the equation of cost-effectiveness.[8,14] A potential strategy to further improve the health economic equation would be to have two decision points for continuing medication, i.e. 5% body weight loss after 16 weeks of treatment and

10% body weight loss after 52 weeks of treatment. All patients would thus be given the opportunity to show if they are "responders" at 16 weeks and "super responders" at 52 weeks; the medication would only be continued long-term in those who may benefit most. Future studies with liraglutide 3 mg and other obesity medications will have to assess long-term cost-effectiveness and the budgetary impact of using these medications to address not only body weight loss, but also the effects upon various obesity-related comorbidities.[15]

The strengths of our data include the large number of patients, the detailed documentation of follow-up, and the routine clinical practice setting from a single centre. Thus, the findings are probably generalizable to other routine care clinics. The limitations include the dependence on medical records to ascertain compliance, and not accounting for possible gaps in treatment. A further limitation is the short duration of treatment in our study of 4 to 8 months compared with 1 to 3 years in the SCALE study.[6]

In conclusion, we show that liraglutide 3 mg combined with lifestyle advice is effective in reducing body weight in patients from Arab descent attending routine clinical care. The outcomes achieved as regards the amount of weight lost at 3 months and the percentage of patients achieving 5% weight loss were similar to published randomized controlled trials. Our results show that the treatment is also effective and safe in postbariatric surgery patients. This suggests that data from randomized controlled trials using liraglutide 3 mg can be used to inform clinical practice. The question that now needs to be answered is whether the use of this drug is cost-effective for most patients with obesity, or whether cost-effectiveness will only reach the desired level in a sub-cohort of patients, such as those with obesity and prediabetes.

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CONFLICT OF INTEREST

No potential conflicts of interest relevant to this article were reported.

AUTHOR CONTRIBUTIONS

MS conceived and designed the audit. AA extracted the data from the database. MS, AB, NL and CWR analysed the data and wrote the manuscript. TT and MB contributed to the review and interpretation of results. All authors approved the final version of the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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