Semaglutide treatment for children with obesity: an observational study

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ABSTRACT

Objective To assess efficacy and tolerability of semaglutide as a weight loss treatment for children living with comorbid obesity.

Design Retrospective observational study of the first 50 children from a weight management service treated with semaglutide for at least 6 months.

Setting A tertiary paediatric multidisciplinary weight management clinic in a UK hospital.

Patients Aged 10–18 years old with a body mass index (BMI) SD score (SDS) >2 with a weight-related comorbidity (including insulin resistance (defined as homeostatic model assessment for insulin resistance >4), type 2 diabetes, metabolic-associated fatty liver disease, obstructive sleep apnoea or hypertension).

Interventions Once-weekly injectable semaglutide titrated over 8 weeks to a final dose of 1 mg in addition to dietary and lifestyle advice.

Main outcome measures Primary outcome measures were change in weight, BMI SDS and percentage body weight. Secondary outcomes were side effects and cessation of treatment.

Results After 6 months of treatment, statistically significant decreases in BMI SDS (0.32±0.27, p<0.001) and body weight (7.03±7.50 kg, p<0.001) were seen. Mean percentage total weight loss was 6.4±6.3% (p<0.001). For the 14 patients for whom 12-month data were available, statistically significant decreases were seen in mean BMI SDS (0.54±0.52, p<0.001). Mean body weight decreased by 9.7±10.8 kg (p<0.001). Percentage total weight loss at 12 months was 8.9±10.0% (p<0.001). Mild gastrointestinal side effects were common. One patient developed gallstones. Five patients discontinued treatment due to side effects.

Conclusion Semaglutide appears to be a safe and effective weight loss adjunct when used in a multidisciplinary weight management clinic.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Childhood obesity is associated with significant comorbidity including type 2 diabetes, metabolic-associated fatty liver disease, obstructive sleep apnoea and hypertension.
⇒ Treatment of childhood obesity presents a significant challenge with dietary and exercise-based treatments only having limited effectiveness and current medications only having a modest effect on weight.
⇒ Data from recent trials in adults and adolescents show semaglutide to be a safe and effective weight loss agent.

WHAT THIS STUDY ADDS

⇒ We report the first real-world data looking at use of semaglutide in children aged 10 years or older with comorbid obesity.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Semaglutide appears to be a safe and highly effective weight loss treatment for children living with comorbid obesity alongside support with dietary and lifestyle changes from a multidisciplinary clinic and should be considered for children in this context.

BACKGROUND

A quarter of UK children now leave primary school obese.[1] Childhood obesity is associated with significant comorbidity including type 2 diabetes mellitus (T2DM), metabolic-associated fatty liver disease (MAFLD), obstructive sleep apnoea, hypertension and depression.[2 3] Children with obesity are at higher risk of social exclusion, poor school attendance and lower economic status.[4–6] Treatment of childhood obesity remains challenging, with dietary and lifestyle interventions having limited sustained effect[7] and until recently few effective medication options being available.[2]

Semaglutide is a glucagon-like peptide-1 receptor agonist (GLP-1RA). It acts on brain GLP-1 receptors to increase satiety and reduce central hunger signals as well as working on gastrointestinal receptors to delay gastric emptying. This results in weight loss with fat mobilisation which is greater for visceral fat than subcutaneous fat.[8] GLP-1RAs also stimulate insulin secretion and lower glucagon secretion, resulting in lowering of post-prandial glucose thereby improving glycaemic control in an insulin-resistant state.

We report our experience of using semaglutide, a weekly subcutaneous GLP-1RA, as a weight loss adjunct for obese children in combination with dietary and lifestyle support from a specialist multidisciplinary team.

METHOD

Data from all children in our tertiary weight management service treated with semaglutide (Ozempic) were reviewed retrospectively. Referral criteria for the clinic at the time were any child with a body mass index (BMI) SD score (SDS >3) (which would correspond to an adult BMI >35 kg/m^2) or a weight-related comorbidity. Those who had been started on semaglutide longer than 6 months ago were included in the analysis.

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Patients were titrated to the full dose subcutaneously over 8 weeks, starting at 0.25 mg once weekly for 4 weeks, then 0.5 mg for 4 weeks before increasing to the final 1 mg dose. Patients were treated with Ozempic, which was the only available brand of subcutaneous semaglutide in the UK, with a maximum dose of 1 mg and not yet licensed for children. Wegovy, the current option licensed for adolescent obesity at the higher dose of 2.4 mg, had not yet been launched in the UK at the time.

Demographic data including age, gender, medical diagnoses and comorbidities associated with obesity were collected. Primary outcomes were changes in weight, BMI, BMI SDS and change in % body weight after 6 and 12 months of treatment. Percentage excess weight was calculated by subtracting target weight from actual weight, dividing this excess weight by the target weight and multiplying by 100 (where target weight is defined as the weight at the corresponding centile to height for age and gender). Secondary outcomes were side effects and tolerability. Data analysis was conducted in R V.4.2.1. Normality of continuous variables was assessed graphically and with the Shapiro-Wilk test, with parametric and non-parametric statistics conducted as appropriate. Statistical testing for within-patient changes at 6 and 12 months was conducted using the paired-sample t-test.

RESULTS

Data were available for 50 patients who were prescribed 6 months of treatment with semaglutide including 14 patients who were prescribed 12 months of treatment. Median age at presentation was 14.5 years (IQR 13–16), with a range of 10–18 years (patients under 12 years were only offered semaglutide if there was a genetic mutation associated with hyperphagia and dietary, exercise and psychosocial support already been offered). 26 patients were female (52%). Five patients had a diagnosed genetic cause of obesity or insulin resistance (including Prader-Willi syndrome, Smith-Magenis syndrome, two with MC4R reception mutations and one with an HNF1beta mutation). 21 patients had MAFLD (defined as raised alanine transaminase (ALT) and fatty infiltration on ultrasound). 23 patients had autism and 11 were diagnosed with attention deficit hyperactivity disorder (ADHD). One of the 11 patients with ADHD was prescribed methylphenidate and this was started in the same month as semaglutide. One patient with ADHD was taking guanfacine. Among females, polycystic ovarian syndrome was seen in four patients (14.8%). At presentation, the mean weight was 118.4 kg in males and 99.6 kg in females. Similarly, mean BMI SDS and percentage excess weight were elevated at 3.5 and 88.8% for males and 3.2 and 76.5% for females, respectively. BMI SDS was >3 in 40 patients (80%). A further nine patients had BMI SDS between 2 and 3 with a weight-related comorbidity. One patient with a BMI SDS of 1.8 with complex chronic conditions and weight-related comorbidities also received treatment. Baseline characteristics and comorbidities stratified by gender are further illustrated in table 1.

After 6 months of treatment with semaglutide, statistically significant decreases in BMI (38.3 vs 35.5, $p<0.001$), BMI SDS (3.33 vs 3.01, $p<0.001$), absolute weight (108.6 kg vs 101.6 kg, $p<0.001$) and percentage excess weight (82.4 kg vs 67.9 kg, $p<0.001$) were seen (table 2). This corresponds to an absolute fall in BMI (mean±SD) of 2.8±2.44, BMI SDS of 0.32±0.27 and absolute weight of 7.03±7.50 kg. This corresponds to a mean percentage total weight loss of 6.4±6.3% and percentage excess weight loss of 14.4±14.6%.

For the 14 patients for whom 12-month data were available, similar trends were seen (table 3), with statistically significant decreases at 12 months of mean BMI SDS (3.49 vs 2.95, absolute reduction of 0.54±0.52, $p<0.001$), BMI (38.4 vs 34.2, $p<0.001$) and percentage excess weight (81.9 vs 57.3, $p<0.001$). Absolute weight decreased from 107.8 to 98.0 kg ($p<0.01$, mean reduction of 9.7±10.8 kg). Percentage total weight loss at 12 months was 8.9±10.0% and percentage excess weight loss was 17.8±21.9%. Change in BMI SDS, absolute weight, total percentage and excess percentage weight are illustrated in figures 1–3.

Side effects were reported in 23 patients. 21 of 23 patients reported mild to moderate gastrointestinal side effects with nausea and diarrhoea being most common and the majority of

Table 1 Baseline characteristics

	Overall	Female	Male
	50	26	24
Age	14.5 (13.0–16.0)	15.0 (13.3–16.8)	14.0 (13.0–16.0)
Weight-related comorbidities			
Obstructive sleep apnoea (OSA)	5 (11.1)	3 (12.0)	2 (10.0)
Type 2 diabetes mellitus	6 (12.0)	5 (19.2)	1 (4.2)
Metabolic-associated fatty liver disease	21 (42.0)	8 (30.8)	13 (54.2)
Hypertension	2 (4.0)	2 (7.7)	0 (0.0)
Medical history and medications			
Autistic spectrum disorder	23 (46.9)	9 (36.0)	14 (58.3)
Attention deficit hyperactivity disorder	11 (22.4)	5 (19.2)	6 (26.1)
Metformin	30 (60.0)	16 (61.5)	14 (58.3)
Insulin	3 (6.0)	3 (11.5)	0 (0.0)
Anthropometric measurements at presentation			
Weight	108.63 (28.13)	99.59 (26.82)	118.42 (26.67)
BMI	38.34 (7.33)	37.32 (8.25)	38.41 (9.48)
BMI SDS	3.33 (0.65)	3.15 (0.76)	3.53 (0.45)
Percentage excess weight	82.38 (36.54)	76.50 (38.40)	88.75 (34.06)

Data presented as median (IQR), mean (SD) and absolute count (%). OSA was diagnosed by polysomnography sleep study. Hypertension was defined as mean systolic BP >95th centile for age and height, confirmed by 24-hour BP reading.
BMI, body mass index; BP, blood pressure; SDS, SD score.

Table 2 Change in anthropometric measurements at 6 months of treatment

	Presentation	6 months of semaglutide	P value*
n	50	50	
BMI	38.34 (7.33)	35.51 (7.28)	**<0.001***
BMI_SDS	3.33 (0.65)	3.01 (0.76)	**<0.001***
Weight	108.63 (28.13)	101.59 (27.23)	**<0.001***
Percentage excess weight	82.38 (36.54)	67.94 (37.03)	**<0.001***

*P<0.05.
*Paired-sample t-test.
BMI, body mass index; SDS, SD score.

symptoms settling within the first 3 months of initiation of medication (due to being titrated in four weekly steps). Tiredness, hair loss and a local reaction were all reported by one patient each. Five patients stopped the medication due to side effects. No patients developed pancreatitis (including one who had had prior treatment for severe necrotising pancreatitis). Two patients with a history of gallstones were treated with semaglutide and did not have recurrent symptoms while on medication. One patient developed symptomatic gallstones after 5 months of treatment and semaglutide was discontinued.

DISCUSSION

Our experience shows that semaglutide is a highly effective weight loss adjunct in children with comorbid obesity. These are the first real-world data we are aware of reporting experience of this drug in children. The STEP TEENS trial reported a mean BMI SDS reduction of 1.1 and mean total weight reduction of 15.3 kg after 68 weeks of treatment with a higher dose of semaglutide (2.4 mg). Our results in a real-world multidisciplinary weight management clinic using the lower dose of 1 mg showed a clinically significant mean weight reduction of 9.7 kg and BMI SDS reduction of 0.54 after 12 months (52 weeks) of treatment. This exceeds the effects of liraglutide (the first available GLP-1RA licensed in this age group) reported by Kelly *et al* who report a BMI SDS reduction of 0.22 and absolute weight reduction of 4.5 kg in adolescents taking this medication for 52 weeks.[9]

Our group of patients included a high proportion of children with neurodiversity, learning difficulties and complex social circumstances. The reasons for the high proportion of children with neurodiversity in this clinic are likely to be multitudinous and include difficulties with sensory processing and lack of satiety, higher rates of social exclusion and emotional eating and dysregulated sleeping patterns linked to increased appetite.

Table 3 Change in anthropometric measurements at 12 months of treatment

	Presentation	12 months of semaglutide	P value*
n	14	14	
BMI	38.36 (4.72)	34.16 (5.36)	**<0.001***
BMI_SDS	3.49 (0.42)	2.95 (0.67)	**<0.001***
Weight	107.76 (19.86)	98.04 (20.99)	**<0.001***
Percentage excess weight	81.86 (26.16)	57.29 (29.36)	**<0.001***

*P<0.05.
*Paired-sample t-test.
BMI, body mass index; SDS, SD score.

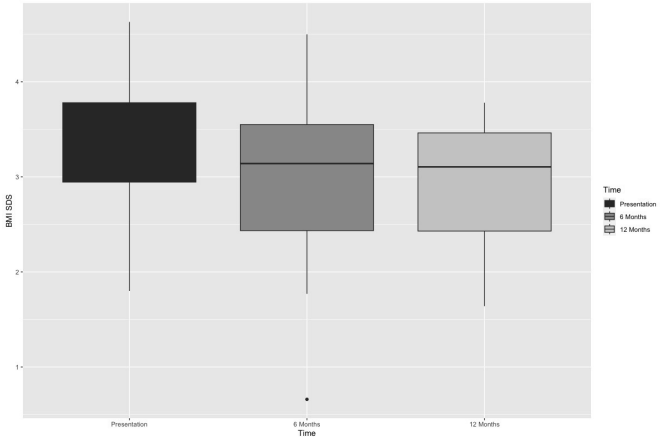

Figure 1 Change in BMI SDS with semaglutide at 0, 6 (n=50) and 12 (n=14) months. BMI, body mass index; SDS, SD score.

These children are not typically represented in drug trials and so it was encouraging to see effective results in this cohort of patients. Anecdotally, many patients reported a dramatic reduction in food-seeking behaviours which was often accompanied by an improvement in quality of life.

A BMI SDS reduction of 0.2–0.25 is thought to be clinically significant[10] and so a reduction of 0.32 at 6 months and 0.54 at 12 months is likely to confer significant benefits to cardiovascular and metabolic health. Of note, three of the six patients diagnosed with T2DM achieved diabetes remission within 6 months of treatment with semaglutide, as evidenced by HbA1c below 48 mmol/mol. Reversal of weight-related comorbidity is likely to confer significant long-term benefits to health as well as cost-savings to healthcare providers.

Semaglutide has recently been licensed in the UK for children aged 12 years and older in the form of Wegovy.[11] Prior to this, the only GLP-1RA licensed for obesity in this age group in the UK was liraglutide. However, adult data demonstrated that semaglutide is better tolerated and more effective at a high dose of 2.4 mg weekly compared with liraglutide 3 mg for weight.[12 13] Semaglutide is also given as a weekly rather than daily injection, making it a more tolerable option for many patients. As evidenced by the shortages in supply of GLP-1RA in 2023–2024,[14] the global demand for such therapies currently exceeds the manufacturing capacity, with a noticeable impact on patient access to treatment. In addition to cost and licensing, clinicians

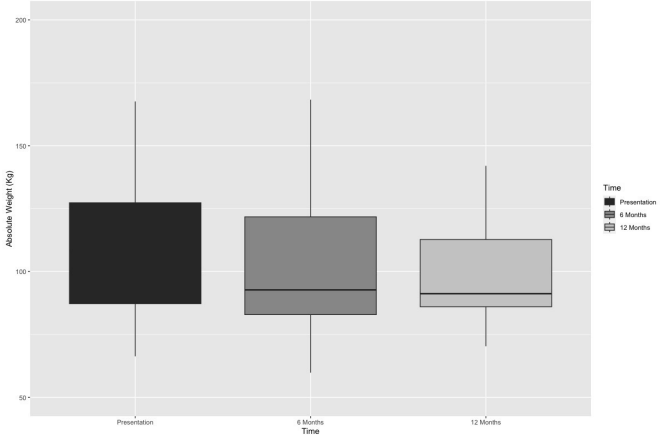

Figure 2 Change in absolute weight with semaglutide at 0, 6 (n=50) and 12 (n=14) months.

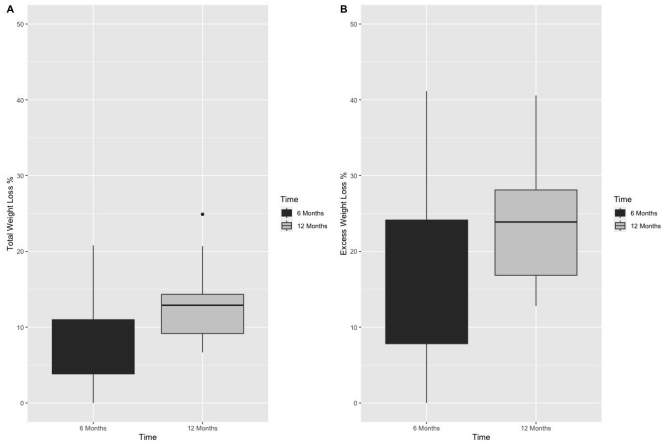

Figure 3 (A) Total and (B) percentage excess body weight loss with 6 (n=50) and 12 (n=14) months of semaglutide.

should be aware of the implications of such global shortages on children living with obesity.

In a small number of patients, semaglutide did not induce weight loss. At 6 months, nine patients had not lost any weight on this medication, although for six of these, their rate of weight gain slowed significantly and actual weight remained within 2 kg of baseline weight. It is possible, given the slowing of rate of weight gain at 1 mg of semaglutide, that this group of patients may respond to the higher 2.4 mg dose trialled in adults and adolescents.[11 15] Within the group of patients without weight loss, one child had a hypothalamic malformation, one had Prader-Willi syndrome and one had autism with complex social and mental health problems.

Our study reports outcomes in terms of change in BMI as this was recorded in the clinical setting. There are well-documented limitations in validity of BMI to describe body composition in children,[15] and further studies looking at bioimpedance measurements or dexa scan results would be useful. Further paediatric long-term studies examining whether the weight loss effect plateaus and potential rebound weight gain after stopping are needed. In addition, studies evaluating reversal of weight-related comorbidity as well as associated cost-savings are indicated.

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