Addition of very low calorie diet (VLCD) during initiation of semaglutide in individuals with type 2 diabetes – interim results

Authors: Oluwaseun Anyiam,[A] Katie Quinn,[A] Bethan Phillips,[A] Daniel Wilkinson,[A] Kenneth Smith,[A] Philip Atherton[A] and Iskandar Idris[A]

Obesity is a chronic metabolic disease which threatens to adversely affect the wellbeing of many people in the UK and globally. In the UK, 28% of adults are classified as obese[1] with this figure expected to rise to 60% by 2050.[2] It is one of the leading causes of preventable death, and is known to be the main risk factor for several non-communicable diseases, in particular type 2 diabetes (T2D), which is also rising in prevalence. Thus, interventions to induce effective weight loss are anticipated to help reduce the prevalence and potential morbidity of both obesity and T2D.

One of the most widely used strategies to produce weight reduction in T2D is the glucagon-like peptide-1 (GLP-1) receptor agonist semaglutide. It requires an 8-week dose escalation period and has demonstrated 4.5 kg weight loss over 30 weeks.[3] It is approved by NICE guidelines for long-term management of T2D, and the higher dose formulation (Wegovy) is awaiting formal approval for treatment of obesity in the UK. Maximising weight reduction is crucial for individuals with T2D in order to achieve optimal glycaemic control, as well as potentially higher rates of diabetes remission. We present the interim results of a study investigating the effect of combining semaglutide with a very-low calorie diet (VLCD) during the initial dose escalation period on weight, glycaemic and insulin sensitivity outcomes.

Nineteen individuals with T2D and BMI $>$ 27kg m^2 were randomly assigned to receive one of three interventions for 12 weeks: semaglutide gradually titrated up to 1mg ($n = 7$), 800 kilocalorie/day VLCD ($n = 7$) and combination of semaglutide and VLCD ($n = 5$). Measures of weight were taken weekly, while glycated haemoglobin (HbA1c), fasting glucose and fasting insulin were measured at baseline and follow-up. Statistical analysis was performed using GraphPad Prism v9.5.0.

All groups demonstrated significant weight reduction, with significantly greater weight loss with VLCD and combination of VLCD and semaglutide, than with semaglutide alone (14.0kg & 14.9kg vs 6.4kg respectively, $p<0.01$ for both). The combination demonstrated the greatest percentage weight loss (14.2%) which was significantly greater than semaglutide alone (6.3%, $p<0.01$). VLCD was also associated with greater percentage weight loss compared with semaglutide (11.6%, $p<0.05$) but not significantly different from combination of VLCD and semaglutide. HbA1c levels were significantly reduced in all groups, with a trend towards significantly greater reduction in HbA1c in the combination group versus the semaglutide group (21.2mmol/mol v 11.3mmol/mol, $p = 0.065$). Fasting glucose was reduced significantly in all groups with no significant between-group differences. Fasting insulin and HOMA-IR reduced significantly in the VLCD group only ($p<0.01$).

These data suggest that addition of an 800 kilocalorie/day VLCD to semaglutide for the initial 12 weeks may induce greater weight loss and improvements in glycaemic control in individuals with T2D, thus facilitating a greater chance of diabetes remission. Further studies are required to determine the long-term outcomes of this approach for managing T2D, as well as obesity. ■

Authors: [A]Centre of Metabolism, Ageing and Physiology, University of Nottingham, UK

References

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