Patient Adherence to Glucagon-like Peptide-1 Receptor Agonists – A Hidden Obstacle in Obesity Management

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Abstract

Glucagon-like peptide-1 receptor agonists (GLP-1RA) are drugs intended for the chronic management of obesity. Short-term use with sudden discontinuation is associated with weight regain and increased metabolic risk. Despite this, adherence to these medications is poor. Several factors such as cost and intolerable gastrointestinal side effects are the cause of poor compliance. This is concerning, especially in low resource settings. Physicians should keep the possibility of discontinuation in mind when prescribing these drugs.

Keywords: GLP-1RA, adherence, compliance, discontinuation

Glucagon-like peptide-1 receptor agonists (GLP-1RA) have emerged as very promising weight loss medications since their advent in 2014[1]. However, the main determinant of a successful weight loss program is adherence. This not only includes adherence to diet and exercise, but also adherence to drugs. Obesity is a chronic, relapsing condition requiring continued treatment. Therefore, it is important to ensure ongoing treatment with antiobesity medications and lifestyle intervention.

Early discontinuation of GLP-1RA is associated with weight gain and an increased cardiovascular risk[2-4]. The STEP-1 trials showed that adults with obesity who had lost weight with 2.4 mg semaglutide regained two-third of the lost weight over 120 weeks after discontinuing semaglutide and lifestyle intervention. There was a similar increase of cardiovascular risk factors as well[4]. The SURMOUNT-4 trials showed a 14% weight regain after discontinuing tirzepatide[3]. Weight loss is followed by a hypometabolic state which leads to a natural tendency to regain weight. This occurs due to down regulation of thyroid hormones, leptin, and the sympathetic nervous and an increase in growth hormone and cortisol, leading to reduced energy expenditure and increased appetite[5]. Therefore, continued treatment has been recommended to avoid weight regain, and maintain lost weight. However, it is not always possible to continue these medications for a prolonged period of time. In that case, patients can be maintained on the lowest effective dose or be given the drug intermittently[6]. If treatment is discontinued, then the drug should be stopped gradually and lifestyle intervention reinforced 2 to 3 months beforehand[4].

Trials show substantial weight loss of 14 to 20% with the newer GLP-RA. However, the picture may not be the same in clinical practice, as drug compliance and adherence are not optimal in the real world. Real world studies showed only 28.2 to 61% patients continued treatment with liraglutide at 12 months[7,8]. Overall discontinuation rates for daily and weekly GLP-1RA were 50.1% and 44.1%, respectively[9]. The reasons behind this picture were adverse effects, cost, inaccessibility to medication, lack of patient education, and perceived ineffectiveness[10]. On the other hand, good adherence was reported in older, more affluent, female individuals[9].

Data from the Obesity Clinic in the Department of Endocrinology, Bangladesh Medical University showed that only 44.7% patients who were prescribed semaglutide continued the drug for more than 6 months. A total of 47 patients were advised semaglutide in the clinic over a period

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of 7 months, from January to July, 2025. The indications were obesity with complications, obesity with weight regain, or obesity not losing weight after 3 months of diet and exercise. Each patient was counseled on the need to continue the drug, the cost and side effects. They were explained how to use the medication by trained doctors. The mean age and body mass index of the patients who were not compliant was 32.1 ± 8.2 years and 40.9 ± 8.1 kg/m^2, respectively. Fourteen patients were females. Out of 47, 26 (55.3%) did not start or discontinued the drug. Eight (17%) patients never started semaglutide because their family did not give permission to take an injectable medication. Eighteen (36.2%) patients started the drug, but discontinued it after an average of 2 months. The reasons were cost (10 patients), adverse drug reactions (3 patients had gastrointestinal symptoms, 1 patient had allergic reaction), pregnancy (2 patients), family problem (1 patient), busy schedule (1 patient). Two patients could not be contacted as their phones were turned off.

Poor compliance and low adherence should be recognized as obstacles in achieving the optimum benefits of nutrient-stimulated hormone-based weight loss medications. Short-term use of these expensive medications is not only a waste of time and money, but also detrimental to health. Patient selection and education are important factors to overcome this problem. Patients should be explained about the need and importance of using these drugs continuously. They should be counseled on the cost, expected efficacy and adverse effects. It is important to make the patient understand that these are not magic drugs, and weight loss occurs gradually. Moreover, efficacy is not uniform, but subject to individual variation. Knowing these facts will help patients set realistic goals of weight loss. Use of GLP-1RA is a challenge in terms of cost, especially in low resource settings like South Asia. Misuse of these medications will only increase health costs without any health benefits. Therefore poor compliance and factors contributing to this should be kept in mind when prescribing GLP-RA.

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