Clinical and Experimental Health Sciences

Comparison of Oral Versus Injectable Semaglutide in Patients with Type 2 Diabetes Mellitus at Liaquat University Hospital, Hyderabad and Jamshoro

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Abstract

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder with increasing prevalence in Pakistan. Despite multiple therapeutic options, many patients fail to achieve target glycemic control and remain overweight or obese. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) such as semaglutide offer combined benefits of HbA1c reduction, weight loss, and cardiovascular protection. Semaglutide is available in injectable (0.25 mg, 0.5 mg, 1 mg weekly) and oral (3 mg, 7 mg, 14 mg daily) forms. Aim of the study is to compare the mean change in HbA1c (%) after three months between oral and injectable semaglutide groups.**:** A prospective observational comparative study conducted over three months among adult patients with T2DM attending the outpatient departments of LUH Hyderabad and Jamshoro. Total duration: three months following ERC approval. Each participant will be followed for 12 weeks (±2 weeks) from initiation of semaglutide therapy. A prospective consecutive sampling technique will be used. All eligible and consenting patients who meet inclusion criteria and are newly prescribed semaglutide during the three-month recruitment period will be enrolled sequentially until the required sample size is reached. No randomization or allocation by the investigators will occur; treatment choice (oral vs injectable) will follow physician prescription and patient preference, reflecting real-world practice.Sample size was calculated using OpenEpi version 3.01 for comparison of two independent means (change in HbA1c %). Assumptions: expected mean difference = 0.5%, standard deviation = 1.2%, confidence level = 95%, power = 80%. The calculated sample was 91 patients per group (182 total); after adjustment for an anticipated 20% attrition rate, the final required sample size is approximately 230 participants. This software-based calculation corresponds with the manual formula for two-sample comparison of means.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder with increasing prevalence in Pakistan. Despite multiple therapeutic options, many patients fail to achieve target glycemic control and remain overweight or obese. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) such as semaglutide offer combined benefits of HbA1c reduction, weight loss, and cardiovascular protection.[1] Semaglutide is available in injectable (0.25 mg, 0.5 mg, 1 mg weekly) and oral (3 mg, 7 mg, 14 mg daily) forms. The oral preparation provides a non-invasive option that may improve acceptance and adherence.[2] However, there is limited local evidence comparing real-world effectiveness, tolerability, and compliance between the two formulations.[11] This study will prospectively evaluate both forms in patients attending the outpatient departments of Liaquat University Hospital (LUH), Hyderabad and Jamshoro, to generate indigenous data on early glycaemic and metabolic responses to semaglutide therapy.

Rationale

Most published studies comparing oral and injectable semaglutide originate from Western populations with different genetics, diet, and body composition.[4-10] There are few studies on real-world experience and short-term metabolic outcomes in Pakistani patients.[11-12] A locally conducted, prospective study will help determine whether oral semaglutide achieves comparable glycemic and weight effects, clarify its side-effect and compliance profiles, and support evidence-based treatment selection for patients in our setting.

Objectives

Primary Objectives

1. To compare the mean change in HbA1c (%) after three months between oral and injectable semaglutide groups.
2. To compare the mean change in body weight (kg) after three months between both groups.

Secondary Objectives

1. To assess changes in BMI, liver function tests (ALT, AST, bilirubin), lipid profile (TC, LDL, HDL, TG), and urine complete examination (UCE) after 12 weeks.
2. To compare the frequency of adverse effects, compliance, and drug discontinuation between the two groups.
3. To determine the proportion of patients achieving HbA1c < 7% and ≥ 5% weight loss at 12 weeks.

Study Design

A prospective observational comparative study conducted over three months among adult patients with T2DM attending the outpatient departments of LUH Hyderabad and Jamshoro.

Study Duration

Total duration: three months following ERC approval. Each participant will be followed for 12 weeks (±2 weeks) from initiation of semaglutide therapy.

Study Population

Adults diagnosed with T2DM who are newly prescribed either oral semaglutide (3 mg or 7 mg daily) or injectable semaglutide (0.5 mg or 1 mg weekly) as part of their routine diabetes management at LUH OPDs.

Inclusion Criteria

- Age ≥ 18 years.
- Diagnosed with Type 2 diabetes mellitus.
- Initiating treatment with oral (3 mg or 7 mg) or injectable (0.5 mg or 1 mg) semaglutide.
- Willing to provide informed written consent and return for 12-week follow-up.

Exclusion Criteria

- Type 1 diabetes or gestational diabetes.
- Concurrent use of any other GLP-1 RA or weight-reducing medication.
- Advanced liver or renal disease, malignancy, or pregnancy.
- Non-consenting or non-compliant individuals.

Sampling Method

A prospective consecutive sampling technique will be used. All eligible and consenting patients who meet inclusion criteria and are newly prescribed semaglutide during the three-month recruitment period will be enrolled sequentially until the required sample size is reached. No randomization or allocation by the investigators will occur; treatment choice (oral vs injectable) will follow physician prescription and patient preference, reflecting real-world practice.

Sample Size

Sample size was calculated using OpenEpi version 3.01 for comparison of two independent means (change in HbA1c %). Assumptions: expected mean difference = 0.5%, standard deviation = 1.2%, confidence level = 95%, power = 80%. The calculated sample was 91 patients per group (182 total); after adjustment for an anticipated 20% attrition rate, the final required sample size is approximately 230 participants. This software-based calculation corresponds with the manual formula for two-sample comparison of means.

Data Collection

After obtaining informed consent, baseline data—including demographics, medical history, concomitant medications, HbA1c, weight, height (BMI), LFTs, lipid profile, and UCE—will be recorded on a structured proforma at enrolment.

Participants will receive their prescribed semaglutide formulation through standard care. Follow-up evaluations will be performed at 12 weeks (±2 weeks) to record repeat HbA1c, weight, BMI, biochemical tests, adverse effects, compliance (via pill count or injection record), and any discontinuation.

No additional intervention beyond usual clinical care will be introduced.

Variables

Independent variable: type of semaglutide (oral 3 mg / 7 mg vs injectable 0.5 mg / 1 mg). **Dependent variables:** HbA1c, weight, BMI, LFTs, lipid profile, UCE, adverse effects, compliance, discontinuation, achievement of HbA1c < 7%.

Statistical Analysis

Data will be analyzed using IBM SPSS Statistics version 25.0. All entries will be checked for completeness and normality. Continuous variables will be summarized as mean ± SD or median (IQR); categorical variables as frequencies and percentages.

Within-group changes from baseline to 12 weeks will be compared using the paired t-test or Wilcoxon signed-rank test. Between-group comparisons (oral vs injectable) will use the independent t-test or Mann–Whitney U test, depending on data distribution. Associations among categorical variables will be assessed using chi-square or Fisher's exact test.

To identify predictors of response, multivariable linear regression will analyze continuous outcomes (e.g., HbA1c reduction) and logistic regression will examine binary outcomes (e.g., HbA1c < 7%), adjusting for age, sex, baseline HbA1c, BMI, and concomitant therapy. All tests will be two-tailed with $p < 0.05$ considered statistically significant. Missing data will be handled using complete-case analysis; sensitivity analysis will be performed if missingness exceeds 10%.

Ethical Considerations

Ethical approval will be obtained from the LUMHS Ethical Review Committee. Written informed consent will be obtained from all participants before enrolment. Each participant will be assigned a unique study code to ensure confidentiality.

As the study observes standard clinical care without experimental intervention, it is considered minimal risk. Participants may withdraw at any time without affecting their medical treatment. Data will be stored securely in password-protected files and used only for research purposes.

Potential Benefits

- **Participants:** improved follow-up and individualized treatment decisions based on observed responses.
- **Society:** local evidence to guide rational semaglutide use and optimize diabetes outcomes in Pakistani patients.
- **Institution:** contribution to clinical research output and better insight for hospital diabetes management protocols.

Limitations

- Short follow-up period (3 months) may not capture long-term metabolic effects.
- Non-randomized design may introduce selection bias.
- Some laboratory parameters may not be repeated for all patients due to routine-care constraints.

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