"Comparative study of the effectiveness of lipid nanoparticles in oral insulin delivery on blood sugar control in type 1 diabetic patients: a double-blind clinical trial"

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Introduction:

Type 1 diabetes is a chronic autoimmune disease that makes patients dependent on lifelong insulin injections. In addition to causing pain and stress, frequent injections are associated with complications such as lipodystrophy, injection-induced hypoglycemia, and reduced patient adherence to treatment. Oral delivery of insulin has always been a major challenge due to enzymatic degradation in the gastrointestinal tract and low permeability of the intestinal mucosa. Nanotechnology has opened a new horizon to overcome these obstacles by providing lipid nanocarriers. The aim of this study is to compare the effectiveness of lipid nanoparticles containing oral insulin versus conventional injectable insulin on blood sugar control in type 1 diabetic patients.

Methods:

This study will be a randomized, double-blind clinical trial conducted on 90 patients with type 1 diabetes, aged 18-65 years, attending diabetes clinics. Participants will be randomly divided into two groups of 45: the intervention group will receive capsules containing lipid nanoparticles (nanoliposomes) containing insulin orally, and the control group will receive regular injectable insulin (rapid-acting and long-acting analogues) according to a standard basal-bolus regimen. Lipid nanoparticles will be prepared using a thin-film hydration method with the aim of protecting insulin from enzymatic degradation and increasing absorption through the lymphatic route. The physicochemical properties of the nanoparticles, including particle size (target: less than 150 nm), zeta potential, and entrapment efficiency, will be evaluated. The primary outcome was change in glycosylated hemoglobin (HbA1c) levels after 6 months, and secondary outcomes included fasting blood glucose profile, blood glucose fluctuations, frequency of hypoglycemia, health-related quality of life, and body mass index.

Results:

It is anticipated that the results of this study will show that lipid nanoparticles containing insulin, due to their small size (150-200 nm) and lipid nature, are able to protect insulin from proteolytic enzymes in the stomach and intestines and increase the oral bioavailability of insulin through absorption by senile plaques and the lymphatic pathway. A significant reduction in HbA1c levels is expected in the intervention group (at least 1%) compared to the control group. It is also likely that a more stable blood sugar profile with fewer fluctuations and a significant reduction in

the frequency of nocturnal hypoglycemia will be recorded in the group receiving the oral nanoformulation. Improved adherence to treatment and patient satisfaction are other expected findings.

Conclusion:

Lipid nanocarriers, with their unique ability to protect sensitive molecules such as insulin and enhance their absorption through alternative (lymphatic) pathways, have the potential to transform oral insulin from a dream into a clinical reality. The results of this study could be a fundamental step towards transforming the therapeutic approach for type 1 diabetes and eliminating daily injections. The clinical application of this nanoformulation, while reducing the complications caused by injections, improves the quality of life of patients and increases adherence to treatment, draws a bright future in diabetes nursing care. Conducting phase III clinical studies with a larger sample size is recommended to finally confirm the effectiveness and safety of this new therapeutic approach.

Keywords:

Lipid nanoparticles , Oral drug delivery , Type 1 diabetes , Blood sugar control