



Inhaled Insulin – An Overview on Current Direction of Insulin Research

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Abstract— Diabetes Mellitus (DM) is a metabolic disorder characterized by relative or absolute deficiency of insulin, resulting in hyperglycemia. Subcutaneous insulin and Oral Hypoglycaemic Agents (OHA) constitute the main treatment option for DM. Insulin is administered by injection or continuous infusion to control glucose levels mainly in Type I diabetes. Newer routes both oral and non oral, for insulin administration are current direction of insulin research as insulin injection therapy is burdensome and painful for many patients. Inhalational insulin is an attractive alternative for systemic administration of insulin given its accessibility and large alveolar-capillary network of lungs for drug absorption. Inhaled insulin has proven to be viable and, in some aspects, a more effective alternative to subcutaneous insulin. Past and present insulin inhaler devices have not found clinical or commercial success. Insulin inhalers create a dry powder or soft mist insulin aerosol, which does not provide the required uniform particle size or aerosol volume for deep lung deposition. **Methods:** The primary focus of this review is to investigate the potential treatment of diabetes with a wet insulin aerosol. Afrezza, inhaled insulin has been recently approved by Food and Drug Administration (FDA). It is a new, quicker acting inhalable insulin with a different and safer pharmacokinetic profile in comparison to previously failed inhaled form of insulin.

Keywords— Afrezza, Diabetes, Glycemic control, Hemoglobin A_{1c}, Inhalation, Insulin, Type 1 diabetes, Type 2 diabetes

INTRODUCTION

In 2021, there were approximately 8.4 million (95% uncertainty interval 8.1 million to 8.8 million) people with type 1 diabetes worldwide. Of these, 1.5 million (18%) were under the age of 20, 5.4 million (64%) were between the ages of 20 and 59 and between the ages of 20 and 20, and 1.6 million (19%) were over the age of 60. Bottom. That year, 500,000 were newly diagnosed (median age at diagnosis was 29 years) and approximately 35,000 undiagnosed people died within 12 months of symptom onset. 1 in 5 of her with type 1 diabetes (1.8 million) live in low- and middle-income countries. In 2021, she was diagnosed with type 1 diabetes. Life expectancy for her 10-year-old child ranged from an average of 13 years in low-income countries to an average of 65 years in high-income countries. The broader missing persons count for 2021 was estimated at her 3.7 million. We project that the prevalence will increase to 13.5-17.4 million by 2040 (up 60-107% from 2021), with the largest relative increase from 2021 in low- and middle-income countries. (1).

The burden of type 1 diabetes in 2021 is enormous and is expected to grow rapidly, especially in resource-constrained countries. Most incidents and most common cases involve adults. The remarkably low prevalence highlights the early mortality rate of type 1 diabetes and the opportunity to save and prolong the lives of people with type 1 diabetes. The new model, released as the Type 1 Diabetes Index Model, will be an important tool to support type 1 diabetes care, advocacy, and funding decisions (2). Diabetes can be broadly divided into her two categories:

Type 1 diabetes (T1DM) and type 2 diabetes (T2DM). Patients with type 1 diabetes rely on insulin for survival by injection or subcutaneous injection by continuous infusion. People with type 2 diabetes can control their disease for some time with lifestyle interventions and oral therapy. However, those who fail these strategies require insulin to achieve adequate disease control. Administration of insulin by inhalation is a potential alternative to subcutaneous insulin in the management of diabetes. This review describes the rationale for the development of pulmonary-delivered

insulin and the role inhaled insulin may play in improving long-term diabetes care.(3)

Insulin is currently a treatment option for both type I and type II diabetes. Insulin therapy should be added to type II diabetics who are unable to maintain blood glucose levels with lifestyle or OHA. The UK Prospective Diabetes Study (UKPDS) showed that it could control type II diabetes (HbA1c <7%). Insulin was required by approximately 50% of diabetics within 6 years [4].

Inhaled insulin/inhaled insulin is powdered insulin delivered to the lungs in an inhaler. This is seen as a paradigm shift in insulin delivery due to different routes of administration, dosage units, patient suitability, and the need for regular safety testing. A 2007 review of inhaled insulin concluded that it appeared to be as effective as, but no better than, injectable insulin. It's also not very cost effective as the additional costs are much higher. The additional costs are very high and probably unprofitable [5].

Intensive insulin therapy for type I diabetes includes multiple daily subcutaneous insulin injections (3–5 times daily) using both long-acting basal insulin and short-acting prandial insulin [6,7] contains [7,8,9]. Current strategies for subcutaneous insulin administration mimic this first-pass effect of insulin on hepatic glucose control, a phenomenon in which hepatic absorption causes insulin levels to drop significantly before it reaches the general circulation. [10,11]. Patients resist transitioning to subcutaneous insulin delivery due to anxiety [12,13,14], the need to accurately correlate carbohydrate intake and insulin delivery, and concerns about hypodermic needle proficiency [15,16]. often do. These concerns may lead to delayed intensification of insulin therapy and suboptimal adherence to injection schedules in patients with type 1 diabetes [17].

Innovative new means of insulin delivery may significantly increase the use of insulin as a method of controlling blood glucose levels. Administration of inhaled insulin has the potential to significantly improve the quality of life of diabetic patients by overcoming the burden and perceptions associated with traditionally administered subcutaneous insulin. Administration results in loss of biopotency due to gastric collapse. Several parenteral routes of insulin administration other than subcutaneous and intravenous routes have been investigated, including transdermal, buccal, nasal, and pulmonary administration. The lung offers an attractive option for insulin therapy because of its accessibility and extensive alveolar-capillary network for drug deposition [18].

Several studies have been conducted in patients with T1 and T2DM to evaluate the efficacy of inhaled insulin in controlling diabetes. Inhaled insulin was compared to regular insulin or short-acting insulin analogues in people with type 1 diabetes. Studies in people with type 2 diabetes have examined the effects of inhaled insulin on diabetes control when combined with oral therapy and compared it with short-acting insulin. Outcome measures

included HbA1c, lung function, weight gain, and patient satisfaction. [19]

One proposed advantage of inhaled insulin therapy, as opposed to injections, is that it is more acceptable to patients when insulin therapy needs to be intensified or when oral therapy is not meeting glycemic targets. is. Fremantle et al. The availability of inhaled insulin as a hypothetical treatment option has been shown to increase the likelihood that patients with poorly controlled type 2 diabetes will accept the addition of insulin to their therapy. [20]

CONCLUSION

Several important questions remain regarding the potential clinical use of inhaled insulin in the future. Although the concept of inhaled insulin is attractive, the availability of subcutaneous insulin therapy to enable intensive diabetes management and concerns about lung function and health will greatly influence future developments in this field.

In summary, inhaled insulin is a novel route of insulin delivery that may become a therapeutic option in the treatment of both type 1 and type 2 diabetes. Overall, clinical studies have shown that inhaled insulin is not inferior to subcutaneous insulin in terms of improving glycemic control. Additionally, inhaled insulin serves as a suitable adjunctive therapy for her type 2 diabetic patients who are not optimally controlled with oral therapy. The most notable advantage of inhaled insulin over subcutaneous insulin therapy is better patient tolerability and improved overall satisfaction scores. Therefore, the availability of inhaled insulin may improve diabetes control and reduce the risk of long-term diabetic complications.

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