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REVIEW

Insulin inhalation for diabetic patients: Nursing considerations

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Abstract Scientific knowledge has advanced to enable the development of inhaled insulin. It is a form of diabetes medication administered via the pulmonary system that studies have shown to be efficacious in the treatment of both type 1 and type 2 diabetes. Inhaled insulin is a new, safe means to deliver insulin that may increase patient compliance with insulin therapy, helping them to achieve optimal glycemic control and possibly reducing their risk of developing cardiovascular complications. However, diabetes is a chronic illness requiring lifetime intervention. Empowering patients with the knowledge of the diabetes disease process may give them the confidence to be more autonomous in managing their diabetes. HIIP gives nurse practitioners a new option that may improve their patients' acceptance of insulin therapy, and improve glycemic control.

Contents

Abbreviations: HIIP, Human Insulin Inhalation Powder; FDA, Food and Drug Administration; AUC, area under the curve; FEV, Forced Expiratory Volume; COPD, chronic obstructive pulmonary disease; PFTs, Pulmonary Function Tests; T1DM, Type1 Diabetes Mellitus; T2DM, Type2 Diabetes Mellitus; BG, Blood Glucose

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Introduction

The discovery of insulin in the early 1920 s was considered a milestone in modern medicine, and for good reason. It was a life-saving measure for those with type 1 diabetes. In type 2 diabetes, quality of life also took a quantum leap forward with the use of insulin, and glucose control was now a more realistic expectation [1]. The world heralded the discovery of insulin as the ''miracle cure'' for diabetes that had been sought for years. Insulin therapy has evolved since its inception. Initially, we saw improvements in its purity, as well as new formulations to increase action time and decrease frequency of injections. With time, and a further understanding of the need to replace insulin in a manner that mimicked normal physiology, newer insulin was designed that could accomplish this goal more effectively. Concurrently, methods of insulin delivery have also improved, including disposable syringes, insulin pens, and insulin pumps, all of which have helped to make insulin administration more reasonable and more comfortable [2].

Scientific knowledge has advanced to enable the development of inhaled insulin [3]. It is a form of diabetes medication administered via the pulmonary system that studies have shown to be efficacious in the treatment of both type 1 and type 2 diabetes. Approximately 80 years have been devoted to the modification, purification, and production of human inhaled insulin. The concept of inhaled insulin was first investigated in Germany in 1925 where the use of a nebulizer to deliver insulin was initially explored [4,1]. Insulin is a protein macromolecule with a large particle size that is not easily absorbed into the alveoli of the lung. Many years of research resulting in failures to achieve hypoglycemia with intrapulmonary insulin delivery were likely due to under dosage, probably arising from the loss of drug in the oropharynx or in the delivery device, secondary to large particle size. Since that time, investigators have continued to focus on the development of non-invasive routes to deliver proteins such as insulin. Non-invasive routes include transdermal, oral, intranasal and intrapulmonary [5]. While the nasal cavity is more accessible, it has a decreased surface area for absorption compared to that of the alveolar region of the lung. Intranasal insulin could also be rapidly moved to the back of the nasopharynx by the mucociliary mechanisms in the nose, and swallowed [6,3]. Insulin deposited in the lungs has a longer residence time because mucociliary clearance mechanisms are minimal. Transdermal and oral delivery routes face more challenges due to poor absorption, but continue to be a focus of research. There is currently one FDA approved HIIP that entered the market in late 2006, and at least 6 new pulmonary insulin drugs and delivery systems that are in active development. HIIP gives nurse practitioners a new option that may improve their patients' acceptance of insulin therapy, and improve glycemic control [7].

Physiology of inhaling insulin

The inhalation of insulin into the lungs offers a new method of insulin treatment delivery for people with diabetes. The same features that make the lung so well suited for gas exchange also make it an ideal organ for absorption of small molecules into the bloodstream. The pulmonary alveolar surface area of the lung is 130 m^2, the size of a tennis court, and the pulmonary capillary surface area is nearly as large at 115 m^2. With each breath, air flows into nearly 300 million alveoli. Moreover, the alveolar lining cell is just 1–2 cm^2 from the pulmonary capillary lumen, a distance that favors rapid uptake into the bloodstream [8].

Absorption of a molecule across the alveolar-capillary interface is inversely related to its molecular mass. Small peptides, such as insulin (approximately 6000 Da) are readily absorbed across the very thin, vesiculated, permeable membrane. Molecules that make it to the alveolar level have longer residence time there, because mucociliary mechanisms at this level are minimal (Fig. 1) [3].

There are several factors affecting lower respiratory deposition of an aerosol or dry powder formulation. One of these is particle size. Particles greater than 5 cm^2 in diameter impact and are deposited in the pharynx and large airways. Particles 1–3 cm^2 generally reach the lower airways and alveoli. Particle velocity also affects deposition. Flow rates >35 L/min or <10 L/min will favor upper airway impaction, while flow rates of 15–25 L/min are ideal for lower airway deposition. Even under the best of circumstances, however, only the minority of an aerosol or dry powder usually makes it deep into the lungs [9].

Place of inhaled insulin in diabetes therapy

Insulin-dependent type1 or type2 diabetic patients are heavily dependent on accurate dosing and tight glycemic control to prevent acute, potentially severe hyperglycemia. Since studies based on the ''superiority'' principle were only performed in comparison with oral anti-hyperglycemic agents, there is no clear advantage to replacing traditional insulin delivery systems with inhaled insulin. However, those patients treated with several oral agents with fair-to-poor control and who are resistant to the idea of injection treatment are excellent candidates for inhaled human insulin [10]. Improved glycemic control in type 2 diabetics could be achieved at an earlier stage, when oral anti-hyperglycemic agents and inhaled human insulin combination therapy is considered as a bridge to converting to