VARIOUS EMERGING TECHNOLOGIES IN INSULIN DELIVERY SYSTEM

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ABSTRACT:

In today's era, insulin delivery by alternative route is a area of current interest in the design of drug delivery system. Most of the global pharmaceutical companies are showing encouraging progress in their attempts to develop alternative insulin delivery technologies. For most patients with type 1 diabetes, the tedious part of the treatment is to tolerate needle after needle, both for glucose measurement and to deliver insulin. The introduction of insulin therapy years ago has saved the lives of millions of patients with diabetes. The development of technologies in the last decade have brought to limelight the strategies that hold some promise in turning non-injectable insulin delivery from theory to reality. A rigorous research effort has been undertaken worldwide to replace the authentic subcutaneous route by a more accurate and non-invasive route. Considerable progress has been made to achieve new milestones for effective treatment of diabetes. Peroral, nasal, and pulmonary administration has demonstrated good potential for treatment of diabetes. In addition, transmucosal, buccal, ocular, rectal, and vaginal routes of insulin have also shown to decrease serum glucose concentrations. The transdermal route using various technologies also exhibits success in delivering insulin.

Keywords: type 1 diabetes, insulin therapy, non-injectable, vaginal routes of insulin, transmucosal

INTRODUCTION

The demand for novel drug delivery technologies is ever increasing. These drug delivery technologies can be broadly classified into four principle routes like oral, transdermal, inhalation and parenteral. The main goal for the delivery of any drug therapy is oral administration with once or twice daily dosing. However, there are large number of therapies, particularly protein-based, gene-based, vaccine-based that cannot be delivered by this route for example insulin, growth hormones and other similar biologics[1]. Pulmonary delivery is another non-invasive alternative method that is suitable for small molecules and proteins. However, for drugs with very large molecular weights, such as monoclonal antibodies, penetration through the lung for systemic delivery may require some type of transport enhancement mechanism, of which there are several still at the primordial research stage. Therefore, most protein-based drugs are still being developed as injectables for initial market launch[2].

History about Disease: As reported by the World Health Organization (WHO), 200 million people around the world suffering from diabetes in 2005[3]. Diabetes is a serious condition and its rapidly increasing prevalence on the global scale is a significant cause for concern. By 2030, the WHO estimates that the number of people with diabetes will almost double to 366 million[4]. About 40% of people with diabetes rely on insulin to maintain control of their blood glucose levels. Patients with Type 1 diabetes are completely dependent on insulin injections. For patients with Type 2 diabetes, which comprises 90% of the world's diagnosed cases of diabetes, about one-third of them rely on insulin as part of their regimen for controlling their blood glucose levels. Normal blood sugar is around 90 to 120 mg/dL[5].

Needle Free Technology: The reason this topic fits is that the diabetes market, and particularly insulin development is, by its nature, a hotbed for new ideas in drug delivery. It is difficult to think of one other therapeutic area, let alone another single disease, where so many factors align to drive the development of novel delivery systems[6]. This technology was first described in the 19th century in France, when the French company-H Galante-manufactured an 'apparatus for aquapuncture'. Since then, the demand had increased considerably[7]. It was first commercialised in the US in 1960s. Bioject had summed up the reasons for it in their brochure stating ''Patients hate needles, healthcare professionals fear accidental needle stick injuries, drug companies are looking for new and innovative ways of delivering their products[8]. This technology achieved the Food and Drug Administration approval in 1996 for the subcutaneous delivery of insulin and is CE marked for sale throughout the Europe. This system has been used to give thousands of successful injections without the use of a needle[9].

Factors influencing blood glucose and free insulin levels following insulin delivery: In addition to the delivery system, a wide range of other factors influence blood glucose and free insulin levels following insulin delivery. These include: (1)Delivery site (inter- and intra-site variations) - A primary influence, responsible for large variations in insulin absorption, even between the commonly-used sites, which patients are recommended to rotate sites between successive insulin deliveries. - Insulin delivered in the abdomen is absorbed 86% faster than that delivered in the thigh and 30% faster than in the arm[10]. This variation in absorptions directly affects bl[12]ood glucose levels[11], with 29% lower post-prandial blood glucose levels for deliveries in the abdomen compared with the thigh. -Duration of insulin action varies with delivery site. (2)Liver and kidney function[13]: (3)Skin temperature and fat thickness at injection site[14]: (4)Presence and degree of lipodystrophy - The prevalence of lipodystrophy in diabetic patients has been assessed at as igh as 52%[15]. (5)Exercise: - Absorption is affected in the region of an exercising muscle. (6)Temperature of injected insulin: -Insulin peak also occurs earlier when the insulin is stored in a fridge[16]

New technologies for insulin delivery: Insulin inhalers: Inhaled insulin appears to be a non-invasive, well-tolerated and liked modality of treatment with potential for both type 1 and 2 diabetes[17]. Results of short-term studies indicate that glycemic control achieved with an inhaled insulin regimen is comparable with a subcutaneous insulin regimen in patients with type 1 and type 2 diabetes[18]. It has been determined in patients with type 1 diabetes that improvement in overall patient satisfaction with inhaled insulin is rapid and sustainable compared with conventional subcutaneous insulin, and the reduced treatment burden has a positive impact on psychological well-being[19]. Inhaled insulin greatly enhances patient satisfaction, quality of life and acceptance of intensive insulin therapy in a diabetic patient[20].

Insulin spray: The buccal route is another promising alternative for insulin delivery. With the buccal area having an abundant blood supply, it offers some advantages such as a means to deliver the acid labile insulin, and elimination of insulin destruction by first pass metabolism.The buccal spray formulation being developed by Generex Biotechnology, based in Toronto, delivers insulin to the buccal cavity as a fine spray using company's 'rapidmist' device. The patient does not inhale with the buccal spray device; instead, the drug is sprayed onto the buccal mucosa. The high-speed spray allows the drug to be rapidly absorbed into the bloodstream. The deposition of the drug onto the buccal mucosa also allows the developers to bypass earlier concerns about any risks to lung tissue that have been raised regarding investigative inhaled insulin formulation.[21]

Insulin pill: To adequately control postprandial glycemia, several daily injections of insulin are necessary. However, insulin therapy via subcutaneous or other parenteral route is known to result in peripheral hyperinsulinemia. In addition to the risk of hypoglycaemia, some studies have suggested that peripheral hyperinsulinemia may be associated with coronary artery disease, hypertension, dyslipidemia and weight gain[22].

Insulin analogues: Traditional insulin preparations such as NPH (Neutral Protamine Hagedom) insulin have duration of action 14 h and plasma insulin peak level 4-6 h after administration. As a consequence, NPH insulin may need to be administered up to three times daily in type 1 diabetic patients to provide sufficient insulin supply throughout the day[23]. Insulin complement: Apart from the new insulin, one new drug, Symylin, is ready to be launched by Gibard Pharma, San Diego. Symylin is a synthetic version of the human hormone amylin, which moderates the glucose lowering effect of insulin. Symylin has been designed to complement insulin action and has been shown to reduce blood glucose without causing an increase in hypoglycemic episodes[24].

Implantable insulin pumps: An implantable insulin pump works the same way as an external insulin pump with two major differences: It is implanted just under the skin (usually in the abdominal area) and insulin is delivered into the peritoneal cavity not into the subcutaneous tissue.

Transdermal patch: The Altea Therapeutics PassPort™ System was the first product in development shown in US FDA clinical trials to provide a non-invasive, controllable and efficient way to deliver insulin via a patch on the skin. The PassPort™ System enables fast, controlled drug delivery without the pain of an injection or the possible complications associated with inhaled medications. It also avoids the first-pass gastro-intestinal and liver metabolism that occurs often after oral administration. It creates and effective, economical

and patient-friendly delivery of insulin as well as the delivery of drugs for a wide variety of conditions[26].

Islet cell transplant: In contrast to conventional insulin treatment, islet transplantation is far superior for achieving a constant normoglycaemic state and avoiding hypoglycaemic episodes. Insulin-producing beta cells are taken from a donor's pancreas and transferred into a person with diabetes. Once transplanted, the donor islets begin to make and release insulin, actively regulating the level of glucose in the blood[28]. Successful transplantation can provide the following benefits: (1)It can eliminate the need for frequent blood glucose measurements and the need for daily insulin injections. Although only a few are free of insulin injections a year after transplantation. (2) It can provide more flexibility with meal planning. (3) It can help protect against the serious long-term complications of diabetes, including heart disease, kidney disease, stroke and nerve and eye damage[29].

CONCLUSION

The advanced methods of insulin delivery systems would gradually progress toward physiological insulin replacement and reduce the long-term complications of diabetes mellitus. Thus, a feasible alternative route for insulin delivery is likely to emerge in the future. This new millennium promises a revolutionary change in the delivery of insulin, which is not too far off for billions of sufferers who are reliant on subcutaneous administration. The approaches that seem to hold potential must be consolidated and converted to a working protocol. Among the various alternative delivery systems, each have their own set of favourable and unfavourable properties. Some unfavourable aspects have to be circumvented to make this alternative insulin delivery system a reality and make them to reach the market

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