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Advantages and Disadvantages of Different Insulin Administration Methods for the Treatment of Diabetes

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Abstract. The prevalence of diabetes has been on the rise in recent years, with a significant increase in China. 1980 epidemiological data on 300,000 people in 14 provinces and cities across the country showed that the prevalence of diabetes was 0.67%. By 2013, the prevalence had skyrocketed to 10.4%. Subcutaneous injection is the main route of insulin administration, however, patient compliance is poor and there are many adverse effects. This paper analyzes the advantages and disadvantages from both non-injectable and injectable delivery perspectives through a literature review. This paper finds that insulin pumps and insulin needle-free syringes are both good treatments for diabetes, but they are expensive and not easily accessible on a large scale, while oral administration is also a good treatment, but with low bioavailability. This paper provides researchers with new developments and perspectives on the future of insulin delivery and provides patients with a painless and efficient way to administer insulin.

Keywords: diabetes mellitus, insulin, rout of administration, insulin pumps

1. Introduction

The diabetes mellitus is the One of the most common chronic diseases, and has many feature.Such as, noncommunicable, the process of the disease, as well as it hard to recover [2]. There are two main types of diabetes mellitus in the word, type 1 diabetes mellitus and type 2 diabetes mellitus. The etiology and pathogenesis of type 1 and type 2 diabetes mellitus are not known, but the pathology and pathophysiology of type 1 diabetes mellitus characterized by a significant decrease or absence of insulin secretion due to a significant decrease and loss of pancreatic islet beta cells, and The distinctive pathophysiological feature of type 2 diabetes mellitus is the reduced ability of insulin to regulate glucose metabolism (insulin resistance) accompanied by reduced (or relatively reduced) insulin secretion due to defective pancreatic beta-cell function[1]. There are a lot of factors that relate to the development of the diabetes. Such as, the life style, diet and heredity. Type 2 diabetes mellitus (T2DM) accounts for 85% of the total number of people with diabetes and is on the rise as people's lifestyles change, the prevalence is increasing year by year [3]. The diabetes mellitus can lead to many complications, even lead to death. So the Early treatment of diabetes mellitus is a very important. The main treatment way of diabetes is the insulin. In 1921, Banting and Best discovered insulin, which was used in clinical medicine the following year [4]. Insulin has been used for 100 years, is still the most important tool for controlling blood sugar in the treatment of diabetes mellitus. Today, there are various route of administration of insulin for diabetes patient. The essay will use the method that is the literature review to analyze the advantage and disadvantage of the different routs of administration.

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The Insulin is the only hormone secreted by the beta cells of the human pancreas that directly lowers blood sugar. And the insulin is a small protein containing 51 amino acid residues, consisting of an A chain containing 21 amino acid disabilities and a B chain containing 30 amino acid residues, the two chains being linked by two disulfide bonds [5]. The insulin has three types,

Animal insulin, Human insulin and Insulin analogues. Animal insulin, which also known as regular insulin, is originally extracted from the pancreas of animals, often from the pancreas of pigs or cattle, and is produced through a process of isolation, extraction, crystallization and purification. Animal insulin was already widely used in clinical practice by the end of 1923. Human insulin, which using genetic engineering and DNA recombination, is produced by fermenting bacteria and yeast. 1982 Recombinant human insulin is approved for clinical use. Insulin analogues, which use recombinant DNA technology to modify the amino acid sequence of human insulin, have different structural, physicochemical and pharmacokinetic characteristics from those of regular insulin [6, 7]. And the main routs of administration are non-injection and injection.

This paper analyzes the advantages and disadvantages from both non-injectable and injectable delivery perspectives through a literature review, hopes to provide researchers with new developments and perspectives on the future of insulin delivery and provides patients with a painless and efficient way to administer insulin.

2. The injection devices

2.1. Insulin injection pens

The advantages of the insulin pen are that the pen is graduated for more accurate dosing, eliminates the need for tedious insulin extraction, is easy to carry and use, and the needle is small enough to reduce injection pain.The disadvantage of insulin pens is that when different types of insulin are used they cannot be freely dispensed unless pre-mixed insulin is used, then split injections are required [8].

2.2. Insulin syringes

The advantage of insulin syringes is their low price.However, the disadvantage of insulin syringes is that insulin needs to be withdrawn for use, which makes them less convenient to carry and inject [8].

2.3. The insulin pumps

Insulin pump therapy is a form of insulin therapy that uses an artificially intelligent insulin input device to control hyperglycemia through continuous subcutaneous infusion of insulin, mimicking the physiological secretion pattern of insulin. The DCTT study in the United States and the study by Yiming Mu et al. both confirmed that compared to multiple insulin injections, insulin pumps can more effectively control the level of glycated hemoglobin and also improve the quality of life of patients. Currently, insulin pumps are widely used in China and abroad. Numerous studies have demonstrated that continuous insulin pump therapy provides effective and smooth glycemic control without increasing the risk of hypoglycemia, and can improve quality of life. There is also evidence that insulin pump therapy may reduce microvascular and macro-vascular diabetes-related complications [9]. Intensive insulin pump therapy also can rapidly correct blood glucose and lipid abnormalities and improve islet β-cell function in patients with primary T2DM [3]. The insulin pump also has the advantage of simulating the physiological secretion of human insulin, effectively lowering blood sugar while reducing the occurrence of nighttime hypoglycemia, and is easy to operate and has a large degree of freedom of life, especially for people with an irregular lifestyle. The disadvantages of insulin pumps are that they are expensive, they need to be worn 24 hours a day and they are too demanding for the user (e.g. I test my own blood glucose, I take care of myself and I am financially capable)[8].

2.4. Insulin needle-free syringes

The concept of the needle-free syringe, also known as the jet syringe, dates back to the 19th century and is fundamentally different from the traditional syringe in that it does not require a sharp needle to

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be fitted and propels different forms of drugs into the body by converting different forms of energy into kinetic energy and thus into the body. The device uses high voltage power sources, such as spring force, laser force, Lorentz force, high pressure gas force, shock wave force, through which the drug is injected ultra-fine, at high speed (150-200 m/s) and in a straight line from a good nozzle into the skin, diffusing it into the skin, subcutaneous or muscular, to exert its action. It was not until the 1940s that the first needle-free insulin syringe was introduced, but at that time the device needed to be filled with insulin before each use, making delivery inefficient, dosing unadjustable and very inconvenient to use. Research by domestic and international scholars has led to a more scientific and rational design. Based on the original work of the needle-free syringe, a disposable nozzle and cannula were developed, and the drug could only be used once, greatly reducing the incidence of cross-contamination and making the needle-free syringe increasingly perfect. Some studies have shown that needle-free injections reduce systemic and adverse reactions in insulin-allergic patients, which may be related to the way insulin is absorbed in needle-free syringes. Needle-free insulin syringes have no foreign bodies other than the insulin solution entering the body and avoid the risk of needle cuts and breakage that can occur with traditional insulin pens. This shows that needle-free syringes can save the dose of basal insulin, improve the bioavailability of insulin, reduce the probability of hypoglycemia, improve patients' blood glucose control level, reduce insulin resistance and protect the function of the pancreas [10]. Needle-free syringes also have the advantage of wide distribution of the drug, fast diffusion and even absorption, as well as the elimination of pain and pain caused by needle injections. However, The disadvantages of insulin needle-free syringes are that they are expensive, they are cumbersome to remove and install, and they often cause skin bruising in thin people [8].

3. The non-injection administrations

3.1. Oral administration

Oral administration is by far the most desirable and simplest of the various delivery methods. It has been found that insulin molecules are absorbed into the intestinal environment through the intestinal wall, with the highest absorption rate in the small intestine and high absorption rates in the colon and rectum, and it has been shown that insulin molecules are transported into the intestinal environment by the upper intestinal pericardium, which then penetrates the inner cell membranes of the urinary bladder and enters the circulation. As part of the digestive system, the gastrointestinal tract is responsible for the digestion of proteins, fats and sugars. As part of the digestive system, the gastrointestinal tract is responsible for digesting substances such as proteins, fats and sugars into small, structurally simple substances and then absorbing them. It is absorbed. To be effective when taken orally, insulin must pass through the gastrointestinal tract and remain there before it reaches the systemic circulation [4]. However, there are three main problems with this route of administration: chemical, enzymatic and osmotic barriers [11].

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3.1.1. Chemical barriers. The pH of the gastrointestinal tract varies over a wide range. In the fasted state, the pH in the stomach pH in the stomach is approximately 1.55, in the proximal small intestine 6.72, in the terminal small intestine 7.5, in the cecum 6.05, in the right colon 5.88 and in the left colon 6.12. Thus, weakly acidic drugs are more readily absorbed in the stomach, while the left colon is more readily absorbed. Thus, weakly acidic drugs are more readily absorbed in the stomach, while weakly alkaline drugs are more readily absorbed in the small intestine. It has been shown that changes in the protonation state of particle components (e.g. polysaccharides, proteins or lipids) in different pH environments can lead to dissociation of the nanoparticles, resulting in abrupt release and degradation of bioactive substances. To prevent premature degradation of the drug in the stomach, and prevent premature degradation in the stomach, formulations are often enteric-coated. Commonly used cellulose acetate-phthalate, methacrylate methacrylic acid copolymers (e.g. Eudragit®) and hydroxypropyl methylcellulose o-phthalate [11].

3.1.2. Enzyme barriers. The enzyme barrier consists of the gastric and intestinal enzyme systems.The addition of enzyme inhibitors enhances the oral action of insulin. The main hydrolases in the gastrointestinal tract that degrade insulin are aminopeptidases and trypsin-like enzymes. However, whether excessive use causes dysfunction of the intestinal system needs to be studied [12].

3.1.3. Osmotic barriers. The permeability barrier of the intestine consists of an epithelial barrier and a mucosal barrier. The cells of the intestine can be broadly divided into four categories: epithelial cells, cup cells, pannus cells and M cells. Epithelial cells are the most abundant and are responsible for the absorption of nutrients. The cupped cells are the second most abundant and produce mucus, which forms the mucosal barrier. The mucus reduces the diffusion capacity of the drug and does not facilitate its entry into the epithelial cells. Since mucins are negatively charged, hydrophilic and near-electrically neutral particles are more likely to penetrate the mucus barrier, while positively charged particles are more likely to be trapped by the mucus. As positively charged, hydrophobic drugs are more likely to interact with negatively charged epithelial cells. These two barriers have conflicting physicochemical requirements for drugs and particles, making drug delivery more difficult [11].

3.2. Nasal administration

The nasal mucosa is rich in capillaries and has a large surface area of epithelial cells (approximately 150 cm), making it a promising non-invasive drug delivery system for protein-based drugs with rapid absorption and no first-pass effect, and improved patient acceptance [12].

The nasal administration has the significant advantage of being non-invasive, but further development would need to consider the effect of nasal mucosal ciliary clearance on drug retention; in addition, although the enzymatic activity of the nasal cavity is lower than that of the digestive tract, it may still cause insulin degradation; many osmogenic agents can damage the nasal mucosa and are not suitable for long-term use [12].

3.3. Pulmonary administration

The total surface area of the alveoli is larger than that of the small intestinal cavity, and the alveoli are very thin and permeable. The proteinase activity is lower than that of the gastrointestinal tract and there is no first pass effect, so pulmonary absorption may be a route for absorption of the majority of drugs into the systemic circulation [4]. In January 2006, the first inhaled insulin, Exubera, was approved for marketing in the United States, only to be withdrawn a year later because of its high price and increased risk of bronchial cancer in smokers who quit. However, research into the pulmonary delivery of insulin has not stopped [12].

3.4. Intraocular administration

Insulin can be absorbed through the lens or diffused through the lenticular spaces of the lens to the site of application. Recent studies have shown that insulin for ocular use enters the iris ciliary body and is

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then absorbed by the sclera. Intraocular administration of insulin in the conjunctival sac of diabetic eyes at a dose of 15 U/kg or more has been shown to have a hypoallergenic effect for more than 7 hours, using a natural or synthetic hydrophilic, high molecular weight material that is not harmful to the eye [4]. However, the ocular administration of insulin requires consideration of the small intraocular volume, the ability of the ocular formulation to achieve an effective concentration, the inaccuracy of the dose due to tear loss and the irritating effect of the formulation on the eye [12].

4. Conclusion

Insulin plays an irreplaceable role in the treatment of diabetes. Subcutaneous injection is the main route of insulin administration. However, there are many other rout of insulin administrations, which can be used to cure the diabetes mellitus. Such as, the insulin pumps, insulin needle-free syringes and the oral administration. However, the insulin pumps and insulin needle-free syringes are very expensive. That can not yet fully universal. The oral administration has many problems, but the researcher find the solution in pharmaceutical manufacturing process. The effect of improved bioavailability is still limited, with most still below 20%. Future research objectives should focus on improving the bioavailability of oral insulin drugs and on new and more effective ways of administering them, as well as cheaper and newer ways of administering insulin by injection. What's more, clinical promotion is also essential.

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