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Beyond Insulin.

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ABSTRACT

Type 1 diabetes is one of the global health problems specially targeting children and young adults. This disease was initially a terminal illness but since the discovery of insulin this has become a chronic illness. However, the cure for this debilitating illness has been a mystery. The researchers have come up with whole organ transplant and pancreatic beta cell transplant, but these procedures are far from being perfect. This review article is about a novel concept which if successful is going to revolutionize the field of type 1 diabetes.

Keywords: Encapsulation, diabetes, stem cells.

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INTRODUCTION

Even though type 1 diabetes is just 5 -10% of all diabetes cases, it is a serious problem affecting children and young adults with long term implications. A type 1 diabetic is on lifelong continuous glucose monitoring, screening for complications and meal planning[1].

There are three ways to treat type 1 diabetes. Either put the patient on insulin injections or a whole organ transplant or an islet cell transplant. Insulin therapy remains the main stay for treatment of diabetes mellitus. The problem with this treatment modality is that the patient has to take multiple insulin shots daily and lifelong, which is painful, and an expensive affair. In addition, when the dose of insulin is inadequate the patient is hyperglycemic and when overdone, the patient might develop hypoglycemia, which may jeopardize life. Thus, it is difficult to maintain euglycemia in these patients and since most of the type 1 diabetics are young their chances of developing micro and macro vascular complications on a long run are significant[2].

The next alternative, which is the whole organ transplant, is an expensive and impractical affair. In this case a whole organ that is pancreas is required, the source being cadavers or live donors, the supply of which is less than the demand. During the process of whole organ transplant, laparotomy has to be done which can lead to serious complications like peritonitis, pancreatitis etc. In addition, the patient post-surgery patient has to be put on life long immunosuppression, which increases pill burden, cost and side effects like increased susceptibility to infections[3].

The third and the most recent option is the islet cell transplantation. Here, the islet cells are infused into the portal vein, which carries it to the liver. The source for beta cell islets is cadavers which are scarce. Similar to whole organ transplant, these patients have to be pharmacologically immunosuppressed for their entire life and thereby are associated with its demerits as stated before[4].

Keeping all of these in mind, an ideal way to manage type 1 diabetes would be to find an unlimited source of islet cells and to ensure adequate measures to protect them from immune reactions, without the need for lifelong immunosuppression therapy.

The encapsulation device

The acute shortage of donor pancreatic cells led to the search of alternate sources such as the stem cells. Pancreatic endodermal stem cells are an unlimited source of functional pancreatic cells. Researchers have sketched a way to convert these stem cells into cells of pancreatic lineage by exposing them to appropriate culture conditions. So much so that these stem cells can be converted to beta cells that produce insulin, alpha cells that produce glucagon and delta cells that produce somatostatin[5].

These stem cells are then encapsulated. The capsule is semipermeable device with multiple pores on its surface. The pores are big enough to let the entry of glucose and exit of insulin and glucagon. At the same time, they are small enough to prevent the immune cells from entering and damaging the cells contained inside. Let's put it this way, while at one end it's like a tea bag which holds the tea powder inside and lets out only the essence, at the same time it is robust like a shark cage thereby preventing the immune cells from entering and damaging the cells inside. The concept is simple; it is immune containment or immunoisolation[6].

How does it work?

This device is to be placed in the back on a subcutaneous plane through a minor day care procedure. As the device contains stem cells it takes time to differentiate to mature cells. The type 1 diabetic is continued with his regular insulin shots meantime. Once the cells are mature, glucose entering the device is sensed by the beta cells which produce insulin. In case of hypoglycemia the alpha cells within the device produces glucagon. In short it is glucose dependent insulin and glucagon release which is physiological and the chances of hypoglycemia are minimal. The device is placed on the back because it takes time for the cells to mature and the insulin injections when taken might puncture/damage the device if the device is placed in front of the abdomen. The shelf life of this device is at least one year to at most 5 years[7].

The macro encapsulation device by Viacyte who are the pioneers in the field of encapsulation research called VC01 are of 2 types. The first one called the EN 20 sentinel that is slightly smaller than a coin is used for rodent studies and the second one called the EN dose ranging device is half the size of a credit card and is used for clinical trials. These two devices are robust and cadaveric testing has shown that a baseball thrown at up to 60 miles per hour is not going to shatter the device[7].

Animal studies have shown promising results where diabetic mice maintained euglycemic status without any exogenous insulin or immunosuppression. It is at present undergoing phase 1 and 2 clinical trials[7].

CONCLUSION

The encapsulation research is a breakthrough in the field of diabetes. If the researchers are able to reproduce the pre-clinical success in humans, this blockbuster device is going to be a breakthrough in the field of type 1 diabetes.

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