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Brief Communication

Is Insulin like Growth Factor a new wonder drug?

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ABSTRACT

Insulin has been used since a long time to treat Diabetes Mellitus. Little is known about the potential new uses of insulin due to its structural similarities with Insulin Like Growth Factors (IGFs). This brief communication aims to throw light on the potential uses of this hormone and its future prospects.

Keywords: Insulin, Growth factor, CTGF, Restenosis, Spinal injury, Fibrosis.

Introduction

Since the time insulin was discovered, it has been of tremendous use to mankind in the treatment of morbid condition of diabetes [1, 2]. However, the role of insulin and insulin like growth factors (IGFs) is little understood while studying other pathological conditions of the body [3]. In recent years, there have been a number of studies which discuss the role of insulin and insulin like growth factors in other pathological ailments besides diabetes mellitus (DM) [4, 5, 6]. Though, a clear understanding of the mechanism of action and human clinical trials are still lacking. This brief review discusses the possible potential benefits of insulin and IGFs in treating various ailments besides diabetes.

Insulin is secreted by pancreas and allows the body to utilize glucose from carbohydrates from the food that is consumed. It helps to prevent hyper or hypoglycaemia in body. After the food is consumed, the blood sugar rises and beta cells in pancreas secrete insulin into the blood stream. This hormone then attaches and signals cells to absorb sugar from bloodstream [5, 7].

Insulin like growth factors have structure similar to insulin [8, 9]. Though they are not secreted by beta cells of pancreas and their origin is limited to liver, they have shown to perform similar functions like insulin in various in-vitro models.

Insulin like Growth Factors I and II

IGFI is the mediator of growth hormone (GH) which is secreted from the anterior pituitary. GH stimulates liver to secrete IGF I which enhances body growth in muscle, cartilage, bones, nerves and lungs. IGFII has the effect in growth promotion during the gestation period.

The structure of insulin and insulin like growth factor 1 and II is almost similar and these drugs have been shown to be interchangeable in performing various activities in in-vitro conditions.

Role of Insulin in Diabetes

The role of insulin in Diabetes Mellitus is well known. Insulin is secreted by the beta cells of pancreas and helps in regularizing the sugar levels in body. After the food is eaten,

Article Details

Date Received: 29/04/2017
Date Accepted: 04/05/2017
Date Published: 04/05/2017
DOI: 10.5281/zenodo.574853
Editor(s): Varshil Mehta

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Financial or Comepeting Interest: None

Cite as:

Goel, S. (2017). Is Insulin like Growth Factor a new wonder drug?. Journal Of Medical Research And Innovation, 1(2), AX4-AX6. doi:10.5281/zenodo.574853

insulin is released by pancreas which allows the body to utilize glucose from the carbohydrates. It thus helps to prevent hypo or hyperglycaemia [1]. This is the most widely used method

Role of Insulin and IGFs in Vascular Restenosis

An important finding in the recent studies is the role of insulin and insulin like growth factors in preventing vascular restenosis after angioplasty. It is well known that a majority of patients undergo re-stenosis after the primary angioplasty procedures within 6 months of the treatment [10]. A number of laboratories have been working to understand the mechanism for the same. The restenosis of vessels has been attributed to two factors; increased smooth muscle cell hyperplasia and decreased adaptive vessel remodelling [11].

Though insulin has little effect in reducing the smooth muscle cell hyperplasia, it has been shown to cause increased vessel diameter and adaptive remodelling in vessels. In a recent patent, it has been shown that insulin along with connective tissue growth factor (CTGF) causes overall expansion of vessel size without the risk of aneurysm [12].

In another study, it has been shown that IGFII interacts with CTGF and leads to stimulation of a cascade that causes adaptive remodelling [4]. As per their study, it is the differential secretion of collagen III versus collagen I which is responsible for elasticity of the vessels. Since collagen I is more rigid, it leads to vessel constriction whereas collagen III is responsible for adaptive remodelling due to its elasticity [4].

In another in-vitro study, it has been shown that TGF beta and Smad3 treated smooth muscle cells (in vitro model for vascular injury) lead to increased secretion of CTGF and IGFII from vascular smooth muscle cells which in-turn stimulated collagen III more than Collagen I from vascular fibroblasts thus leading to adaptive vessel remodelling [4, 10].

Though the exact interaction of connective tissue growth factor and insulin like growth factor is little understood, a few studies have laid emphasis on the mechanism. It is believed that CTGF has a number of domains for Insulin like growth factor I/II and the complex activates after the attachment (figure 1). The domain then starts a cascade of events which leads to collagen synthesis.

Clinical trials are being done to validate the role of insulin and insulin like growth factors in vascular stenosis.

Role of Insulin and IGFs in fibrosis

An interesting finding about insulin's role in vascular stenosis has come up after its interaction with connective tissue growth factor was notices. Sharing the similar structure as insulin like growth factors, insulin can bind with the domain site of CTGF and activate the cascade for increased synthesis of fibrous tissues (Fig 1). This may help in increased wound healing and faster growth of skin. A property which can be of tremendous use in defence and plastic surgery [10].

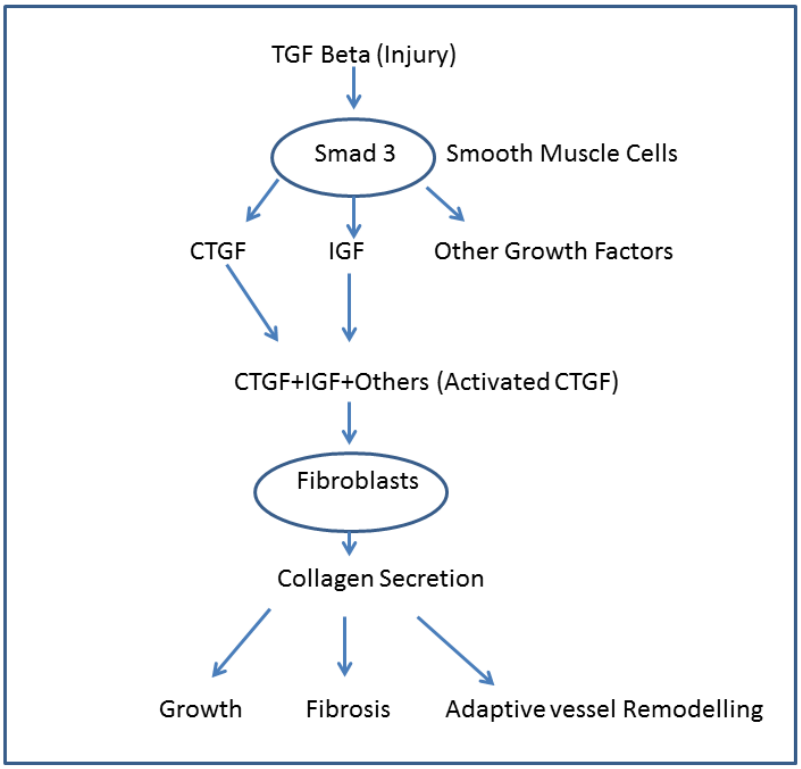

Figure 1. Possible pathway of fibrosis by interaction of IGF and CTGF

TGF beta (injury) leads to activation of SMAD3 in smooth muscle cells which leads to the secretion of various growth factors from the SMCs. The growth factors interact and activate CTGF after binding to the respective domain. The activated CTGF acts on fibroblasts and secretion of collagen takes place (Figure 1).

Role of insulin in spinal injuries

A recently conducted study has even discussed the role of insulin like growth factors in acute spinal cord injury. After an acute injury to spinal cord, a subacute inflammatory process usually begins. The repair and modulation of the spinal cord begins under the mediation of growth factors like IGF1 and II. These growth factors have been shown to be of neuroprotective nature and its role has not only been confirmed in animals but also humans. In another study conducted on 45 individuals, the levels of insulin like growth factors were significantly high in blood after acute spinal cord injury. These findings may throw a light on the use of insulin or insulin like growth factors in spinal cord regeneration after an acute spinal cord injury. IGFs may hold future in acute spinal injuries with limb paresis and replace steroids as the drug of choice in golden period [11].

Insulin and Insulin like growth factors definitely hold a lot of promise for future. Their role in liver dysfunctions and other ailments is still being explored [13]. A number of studies are thus warranted to explore the potential that these agents hold. This brief communication is just to highlight a few new explorations being done by laboratories all around the world. More studies are thus warranted.

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