PAPER TITLE:

WHY IS INSULIN INJECTED, INSTEAD OF TAKEN BY MOUTH?

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ABSTRACT: WHY IS INSULIN INJECTED, INSTEAD OF TAKEN BY MOUTH?

KEY WORDS: Diabetes, Dipeptidyl-peptidase inhibitor (DPP-4 inhibitor), Sitagliptin, Linagliptin, Vildagliptin, BIRDEM

INTRODUCTION:

Diabetes is a very common disease among the adult people in Bangladesh and all over the world now-a-days. This is becoming the major cause of death and disability. To treat diabetes different antidiabetic drugs prescribed by the doctors and prescribers. The purpose of this study was to determine the frequency of use of Dipeptidyl-peptidase inhibitor (DPP-4 inhibitors) in the prescription by the doctors. Doctors are not so convinced and familiar with this class of antidiabetic drugs. Therefore, this class especially Sitagliptin, Linagliptin and Vildagliptin require more promotion to increase its market. Another objective was to determine whether this new class of drug is required or the older class is enough to fill up the requirements of the diabetic patients. To work on these two objectives, a survey was performed by collecting 500 prescriptions from Bangladesh Institute of research & Rehabilitation in Diabetes, Endocrine and Metabolic Disorders.

Diabetes mellitus is a leading cause of death and disability around the world. Diabetes has recently become a major public health issue in our country. There are different types of diabetes such as- type-1, type-2 & diabetes insipidus. For the treatment of type-1 diabetes insulin is used and there are so many oral anti-diabetic agents which are used to treat type-2 diabetes like: Metformin, Vildagliptin, Linagliptin, Sitagliptin etc. Older molecules or generics are more likely to be prescribed by the physicians till now. But, in recent times it is seen that DPP-4 inhibitors (Sitagliptin, Saxagliptin, Linagliptin, and Vildagliptin) are prescribed by the physicians.

Here, it can be mentioned that these newer molecules are discovered around 2005 and marketed in Bangladesh after 2010. The objective of my survey is to analyze how frequently these newer generics (like: Vildagliptin, Linagliptin & Sitagliptin) are prescribed by the physicians for the patients who is suffering from diabetes. Another objective of this survey is to observed wheather these newer molecules are required to treat the patients suffering from diabetes or the older molecules are sufficient enough to treat these patients?. My focus for analysis is on the generic Sitagliptin. For this purpose 500 prescription data is collected from the outpatients of BIRDEM hospital with the prior approval from hospital authority. Then these prescription data is analyzed. Diabetes Mellitus: (McCanceet al., 1994, Metzgeret al., 2010) a heterogeneous group of disorders characterized by high blood glucose levels. A metabolic

Type 1 Diabetes:

An autoimmune disease, body's own immune system attacks and destroys the beta cells. This type involves the processes of beta–cell destruction, which results in absolute insulin deficiency. It occurs at the age of less than 30 years. This is also called insulin dependent diabetes or juvenile diabetes mellitus. Different symptoms with elevated blood glucose levels will develop. If it is not diagnosed properly, ketoacidosis may occur.

Type 2 diabetes:

It is the most common form of diabetes. Type 2 diabetes is often undiagnosed and sometimes when a patient consult with doctor for another medical problems or for the eye or physical examination, suddenly it appeared. Diabetes develops most often in middle-aged and older people who are also overweight or obese. It is also called non-insulin dependent diabetes mellitus (NIDDM). Causes: • Insulin resistance: when body do not use insulin properly although sufficient quantity of insulin is produced • sometimes body cannot produce sufficient quantity of insulin. Risk Factors: • Age 45 or older • Overweight or obese, physically inactive, Family background • History of gestational diabetes • High blood pressure: 140/90 or above, High-density lipoprotein (HDL) level Table 1: Clinical Features of Type 1 and Type 2 diabetes mellitus (Genuth et al., 2003, Ozougwu.

Signs and symptoms of Diabetes Mellitus:

The most common signs and symptoms of diabetes are: • Frequent urination • Excessive thirst • Disproportionate thirst • Intense hunger • Weight gain • Unusual weight loss • Increased fatigue • Irritability • Blurred vision • More skin and/or yeast infectionsDrug interactions(Reutter, 2002) • Plasma concentration of sitagliptin may be increased with the interaction of cyclosporine. • Digoxin plasma levels may be increased slightly • Care should be taken with drugs that can potentially lower blood sugar such as: Probencid, NSAIDs, MAO inhibitors, β- blockers Contraindications: (Reutter, 2002) • Dosage adjustment is needed in patients with moderate or severe renal impairment • should be used cautiously during pregnancy • It is Contraindicated in diabetic ketoacidosis Insulin is an enzyme produced by the pancreas. There are a couple of options for taking insulin orally:

Take insulin as a pill, and
Use a spray to take insulin nasally

Insulin pill:

Insulin is an enzyme and cannot survive the harsh acidic environment in the stomach. If taken as a pill, it would get destroyed in the stomach.

Scientists have tried placing insulin in a protective covering so that it gets absorbed in the intestines. However, this is not very efficient. I have read a recent article that suggests that this assumption may change.

Nasal insulin:

It is possible to take insulin in powdered form and delivered to the lungs via a nebulizer. However, this has not been successful commercially.

Oral insulin is a reality:

It is simply a matter of when Issue with Oral Insulin is that it gets decomposed within the gastric juices of the stomach so best way to make it bio available is via Injection directly to blood stream.

Many alternative delivery systems, although they work to some extent, leave the insulin broken down by digestive juices, usually too much for it to be of significant use to the body. Furthermore, the complicated environment within the stomach means that simple tablets would be unpredictable and ineffective.

The solution will come, and may have already, when a pharmaceutical research company creates a tablet in which insulin can be enclosed and yet still pass through the stomach wall.

Nose, Mouth and lungs:

Three principal target areas are obvious in developing alternative insulin delivery systems:

Nose, Mouth & Lungs

Nasal delivery issue:

Nasal delivery into the upper airway presents severe problems primarily that the transport system is too convoluted and would require massive, expensive quantities of insulin to reach the target area.

Insulin delivery via the lungs

Insulin into the lungs is a promising area: the insulin can be directly absorbed into the bloodstream through the thin walls of the lung.

Insulin via the mouth

Effective oral insulin is extremely difficult to create due to the thickness of the stomach wall.

Oral insulin research: expensive

This is by no means an impossible hurdle, but it is a very complicated and costly one. Several companies across the globe are solely concerned with the creation of effective oral insulin delivery mechanisms, and many major pharmaceutical companies are at the research and development stage.

Insulin is a peptide hormone, meaning it is essentially a protein. If you were to take it orally, your stomach enzymes would break it down into amino acids, causing it to lose its functional capacity.

This is the reason it is injected, so that it directly enters the blood stream, thus bypassing the stomach and the entire gastrointestinal tract, thereby avoiding digestion by enzymes.

It is noteworthy however, that since injectable insulin is inconvenient for the patients, oral preparations of insulin are currently under development and trial.

Blood sugar levels are subject to great change throughout the day. What foods were consumed, exercise, stress, illness, even time of day – all of these impact glucose levels. If this were not so, there would be no need to monitor levels with a finger prick multiple times each day.

Insulin is needed to ensure that glucose is properly utilized and that levels of glucose remain stable. In order to work properly, insulin must enter the bloodstream intact.

By injecting it into the subcutaneous tissue in our bodies, it is designed to be absorbed into the bloodstream without changing its properties and within a proscribed amount of time. Insulin should not be injected directly into muscle or into the bloodstream, as both will increase the speed of absorption.

How fast absorption happens is also a function of what type of insulin is being used: rapid-acting, short-acting, intermediate-acting, long-acting or a mix of some of these. Each is designed to be absorbed and active over certain time frames, in order to cope with different glucose control needs, like consuming a meal or sleeping all night.

Our natural body insulin is in our blood, so it has to be directly mixed to blood, Orally it will take time to get mixed in blood, and the diabetic patient take insulin from outside, Because they have more sugar level and they have no production of insulin in their body or very less amount of insulin are produced which are not sufficient for one's

body and if in that case we give orally to them then it will take time to mix, influence on body will be no immediate.. So what is the use of that insulin, which is given orally, so if it is injected then it will go directly to our veins blood?

Oral delivery of insulin may significantly improve the quality of life of diabetes patients who routinely receive insulin by the subcutaneous route. In fact, compared with this administration route, oral delivery of insulin in diabetes treatment offers many advantages.

However, insulin is a hormone, which is digested in the stomach and gut and in order to be effective at controlling blood sugar, cannot be taken orally in its current form.

The oral delivery of insulin remains a challenge because its oral absorption is limited. The main barriers faced by insulin in the gastrointestinal tract are degradation by proteolytic enzymes and lack of transport across the intestinal epithelium.

Several strategies to deliver insulin orally are proposed, but without much clinical or commercial success. Protein encapsulation into nanoparticles is regarded as a promising alternative to administer insulin orally because they have the ability to promote insulin paracellular or transcellular transport across the intestinal mucosa.

The reasons are as follows:

Our body cells store food items. It’s obvious that it has quite amount of glucagon in it. Insulin is a peptide hormone which is intra dermal in nature i.e. it is always injected into the skin and not blood or muscles. Thus insulin is given to its exact place if. Injected but it is not the case if taken orally. Moreover being a peptide hormone, if it were to be taken orally, it would break into amino acids (keeping in mind the general concept of proteins) and thus destroy the purpose of taking it to decrease sugar level.

Insulin is destroyed by the digestive system. There has been new development in an oral insulin. But is still in testing phase.

Because being a protein insulin when taken from mouth gets acted by several enzymes and in simple terms you can say gets digested

While when injected it's able to perform its function of uptake of glucose by Gut receptors

Another controversial subject and disputable:

The best that I can understand it is with the injection it enters the blood stream directly and quicker; with pills, they claim is not as effective and take too much time. This is another subject that is as big as an ocean

Insulin cannot be taken orally because it would break down in the digestive process:

Insulin is a poly-peptide protein, which can be broken down by enzymes in the digestive system. By the time it reaches the small intestine, where it is absorbed, it is only a single peptide and can no longer function as insulin.

Besides the chemical reasons for not ingesting insulin, there are other reasons that have more to do with the management of diabetes.

Why Injection Is Better:

Blood sugar levels are subject to great change throughout the day. What foods were consumed, exercise, stress, illness, even time of day – all of these impact glucose levels. If this were not so, there would be no need to monitor levels with a finger prick multiple times each day.

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How Inhaled Insulin Works:

The idea of inhaling insulin has been around for decades. It wasn't until the 1990s that researchers made it possible.

With an inhaler much like the ones people with asthmatic use, you breathe a fine insulin powder into patient's lungs. There, it enters into blood through tiny blood vessels.

Inhaled Insulin Today:

In June 2014, the FDA approved Afrezza. it's an inhaler with pre-measured, rapid-acting insulin people should use before meals.

These inhaled products have so far been found to be slightly less effective than injected insulin. However, the advantage of not having to inject oneself, it is believed, will increase compliance with insulin treatment. This will help prolong the health of patients.

CONCLUSION:

There is active research to develop alternatives to injections. One of the most promising is inhaled insulin.
There was an inhaled insulin product, Exubera, on the market for about a year between 2006 and 2007. The manufacturer withdrew it from the market because of poor sales. The product was extremely expensive, and did not provide any better results than injectable insulin.
Another potential entry into this market is called Afrezza. It is presently teetering on the edge of possible FDA approval, with a ruling currently anticipated by July 15, 2014.

Diabetes mellitus (DM) is a chronic metabolic disorder caused by an absolute or relative deficiency of insulin. Absence, destruction, or loss of beta cells of the islets of Langerhans causes an absolute deficiency of insulin, leading to type 1 diabetes (insulin-dependent diabetes mellitus [IDDM]). Most children with diabetes have IDDM and a lifetime dependence on exogenous insulin.

Researchers, doctors, and people with diabetes agree that injected insulin works well to manage the disease. They'll probably also say that getting insulin into people's body through something other than a needle would be even better.

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