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A Review Article on Protease Inhibitor and Glucose Transport Inhibition

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A B S T R A C T

Protease inhibitors (PIs) for the human immunodeficiency virus (HIV) are known to impact glucose homeostasis during HIV treatment. PIs function as reversible, noncompetitive inhibitors of GLUT4 with low micromolar binding affinities. Using HIV1 protease inhibitors (PIs) in clinical settings has significantly reduced HIV-related morbidity and death. But it's now known that these medications directly cause a number of metabolic alterations that greatly raise the risk of diabetes mellitus and cardiovascular disease. Peripheral insulin resistance and reduced glucose tolerance are the results of HIV protease inhibitors (PIs) abruptly and reversibly inhibiting the insulin-responsive glucose transporter Glut 4. A reduced insulin secretory response has been found using minimal modelling analysis of glucose tolerance tests performed on individuals receiving PI, which may indicate increased pancreatic β-cell dysfunction.

Keywords: HIV, Glucose, Protease, Protease Inhibitors

A class of drugs known as protease inhibitors (PIs) is used to treat or prevent viral infections, such as Hepatitis C. PIs stop the spread of viruses by blocking HIV-1 protease, an enzyme the viruses utilize to cut developing proteins before assembling new virions. Antiretroviral protease inhibitors (saquinavir, ritonavir, indinavir, nelfinavir, etc.) are protease inhibitors that have been created or are now undergoing testing for the treatment of numerous viruses, including HIV/AIDS. Protease inhibitors all function in the same way. They prevent newly formed viral particles or human cells' protease enzyme from working. The new viruses are still able to exit the cell when the PIs attach to the enzyme, but they are unable to infect other Impact of Protease Inhibitors on HIV Patients' Serum Glucose Levels.

The amount of glucose in the blood is known as blood sugar. The body's cells use glucose, which is carried throughout the circulation, as their main energy source. The glucose level, often known as blood sugar concentration, is strictly controlled in the human body. Blood glucose levels are normally kept between 4 and 6 mmol/L. Homoeostasis, or normal blood glucose, is approximately 90 mg/100 ml, or 5 mm Therefore, assuming an average adult blood volume of 5 litres, the total measurement of glucose in the circulating blood is approximately 3.3 to 7g. Blood glucose levels typically peak in the morning, just before the first meal of the day, and then decline after meals. Conditions where blood sugar levels are consistently high (hyperglycaemia) or low (hypoglycaemia) result from failing to keep blood glucose levels within the normal range. Insulin and glucagon regulate just blood glucose levels.

HIV-1 protease inhibitor (PI) treatment, when combined with highly active antiretroviral therapy (HAART), has been shown to significantly lower HIV viral loads and boost CD4+ lymphocyte counts in HIV-infected patients. These improvements have slowed the development of the disease and improved patient life. Nevertheless, in spite of this therapeutic success, it is now known that PI-based therapy is associated with some important metabolic side effects, such as insulin resistance, hyperlipidaemia, and lipodystrophy. Up to 80% of patients on PIs experience insulin resistance, which in people with a genetic predisposition can result in overt diabetes. The frequency of PI-associated aberrations in glucose homeostasis has come to light, but a complete knowledge of the molecular mechanisms underlying these metabolic alterations has proven difficult to achieve.

1.MATERIALS AND METHOD

- SAMPLE COLLECTION

200 samples in all were taken from the Jos Plateau State's Faith Alive Foundation. Of the samples, which were from people between the ages of 20 and 60, 100 came from HIV patients using protease inhibitors while the remaining 100 came from those without such a prescription. After preventing venous stasis and disinfecting the Cubital Fossa with methylated spirit, 2 ml of venous blood was obtained by venipuncture. Every sample was moved into a clean, dry sample vial with the proper label. This was left in place for thirty minutes in order for it to retract and clot. After that, it was centrifuged for five minutes at 3000 revolutions per minute (rpm).

- INCLUSION CRITERIA

1. HIV patients only

2. HIV patients on protease inhibitor only
3. HIV patients who has not developed AIDS
4. HIV patients on protease inhibitor from two weeks and above.
5. HIV patients with CD4+ count of two hundred and fifty and above

- EXCLUSION CRITERIA

1. Non HIV positive patients HIV patients on drugs other than protease inhibitor
2. HIV patients who has developed AIDS
3. HIV patients less than two weeks on protease inhibitor
4. HIV patients with CD4+ count of less than two hundred and fifty

2.METHOD:

Estimation Of Serum Glucose Using Dia lab Liquid Reagent.

2.1PROCEDURE

Pipetted 1000µl of the reagent into each of the three test tubes, Sample, Blank, and Standard, after they had been cleaned and dried. The reagents were mixed with 100µl of the sample and standard, while the blank was made out of distilled water. After mixing and incubating it for ten minutes at 37°C, a reading of the absorbance at 500 nm was obtained.

2.2 CALCULATION:

Glucose concentration = Abs. of Test × Conc. of Std. Abs. of Std.

3.RESULT

The result indicate that HIV patients who are on treatment have greater blood glucose levels than those who are not. The mean glucose levels for the male and female subjects were 4.97 and 4.94 for the male test and 5.43 and 4.84 for the female test, respectively. As a result, the test male and female had greater glucose levels than the control. The research reported that insulin resistance developed rather quickly following the start of protease inhibitor therapy and that, upon evaluation, fasting insulin and glucose levels as well as insulin resistance increased markedly. The female test and female control showed a significant difference in pairwise comparison and post hoc tests, but the male test and male control showed no such significant difference ($p>0.05$) . This could be because men showed higher rates of insulin clearance and increased peripheral tissue sensitivity to insulin in comparison to non-HIV-positive controls.

More significantly, though, people with diabetes mellitus are two to five times more likely to develop cardiovascular disease than people without the condition, and the majority of diabetic patients pass away from cardiovascular disease. Additionally, due to reports of hyperglycaemia and diabetes mellitus linked to protease inhibitor usage, the Food and Drug Administration advised physicians to closely monitor patients using these drugs. Following this warning, doctors kept reporting cases of diabetes mellitus and hyperglycaemia related to protease inhibitors.

According to two retrospective investigations, between 6% and 7% of those with new-onset diabetes mellitus develop the condition after starting protease inhibitor medication.it is found that after using the protease inhibitor indinavir for a short while, HIV-positive individuals experienced impaired insulin sensitivity and hyperglycaemia during fasting, which are common indicators of developing diabetes mellitus in the future.

4.CONCLUSION

According to the data, HIV patients receiving a protease inhibitor had higher blood glucose levels than HIV patients not receiving the medicine. This could lead to metabolic problems such diabetic mellitus, ketoacidosis, atherosclerosis, and other ailments that can be prevented.

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