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Elevated Intact Proinsulin Levels Are Indicative of Beta-Cell Dysfunction, Insulin Resistance, and Cardiovascular Risk: Impact of the Antidiabetic Agent Pioglitazone

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Abstract

Background:

Insulin resistance (IR) and deterioration of beta-cell secretion are main features in the development of type 2 diabetes, which is reflected in increasing serum intact proinsulin levels in later disease stage. Introduction of stable assays that are able to distinguish between intact proinsulin and its specific and unspecific cleavage products has resulted in the finding that serum intact proinsulin values can serve as a direct marker for beta-cell dysfunction, are a highly specific indicator of IR, and can predict cardiovascular risk.

Method:

Determination of fasting intact proinsulin may be used to monitor and optimize antidiabetic therapeutic approaches. Our study group has been involved in a variety of clinical studies investigating drug effects on beta-cell secretory capacity, IR, and intact proinsulin levels. One focus was on the impact of insulin-sensitizing therapy with pioglitazone on the pancreatic beta-cell load.

Results:

Treatment with pioglitazone resulted in significant decreases in elevated proinsulin levels in type 2 diabetes patients. This effect was independent from glycemic control.

Conclusions:

Measurement of fasting intact proinsulin values allows a staging of beta-cell dysfunction and evaluation of IR, thus providing an interesting diagnostic tool for both selection of appropriate therapy and monitoring of treatment success.

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Abbreviations: (ELISA) enzyme-linked immunosorbent assay, (HbA1c) hemoglobin A1c, (HOMA) homeostasis model assessment, (IR) insulin resistance, (T2DM) type 2 diabetes mellitus

Keywords: beta-cell dysfunction, cardiovascular risk, diabetes, insulin resistance, pioglitazone, proinsulin

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