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Marker for the diagnosis of an insulin resistance

Marc Beineke

■ HOMA Index and intact proinsulin

An important mechanism for the lowering of the blood sugar level is the adsorption of glucose via insulin into the fatty tissue and muscles. A decreased insulin effect at the target cell which is followed by an increased insulin need is called insulin resistance.

The insulin resistance represents an important pathogeneic mechanism in the development of type 2 diabetes and is often already observed years before the manifestation, in the context of a metabolic syndrome. Beyond that one finds reduced insulin sensitivity frequently in female patients with fertility disorders and a polycystic ovary syndrome (PCO).

In the pathogenesis of the PCO syndrome the insulin resistance represents an important cause. Particularly for young women it is indirectly a frequent cause of sterility and cycle disturbances (17).

An improvement of the insulin sensitivity and/or the metabolic situation either by a change of life-style (weight reduction, increased physical activity) or medication is the basis for the therapy of female patients with polycystic ovary syndrome.

Due to the improvement of the metabolic situation it comes to an increase of the SHBG and to a decrease of the androgen levels whereby the cycle disturbances in most cases improve and the fertility rises.

■ HOMA Index

The direct measurement of the insulin effect on the blood sugar concentration is not possible at present, however, due to the high laboratory costs. Alternatively, therefore, other indices are used for determining an insulin resistance.

In doing so the determination of fasting insulin (= control variable) and fasting blood sugar values (= actuating variable) in plasma plays an important role. One of the most common indices is the HOMA index (Homeostasis Model Assessment), which is calculated according to the following formula:

HOMA index = fasting insulin (µU/ml) X fasting blood sugar (mg/dl) /405

The HOMA index consists of the analysis of insulin and glucose and is calculated from these two parameters. An affirmation of the diagnosis of an insulin resistance is possible by the additional measurement of the intact proinsulin (sensitivity 48 %, specificity 98 %).

Intact proinsulin

Clinical relevance of proinsulin

Proinsulin is a forerunner molecule of insulin and is formed in the beta cells of the pancreas. During insulin formation, proinsulin is split over different reaction steps into two dipeptides and equimolar into the peptide hormone c-peptide (= connecting peptide) and active insulin. This proteolysis happens almost completely and only traces of intact proinsulin get into the blood circulation. In case of a (chronic) increase in the secretion rate of the pancreas, e.g. with an insulin resistance, hyperglycaemia or by secretion-stimulating drugs (e. g. sulphonylurea) it comes after some time to an incomplete processing of proinsulin, as the catalytic capacity of the proteases is limited. Thereby it comes to an increased secretion of incompletely processed proinsulin into the blood circulation, linked to a decrease of the effective insulin levels. Therefore, raised intact proinsulin levels can be seen as an indication of functionally impaired ß-cells.

Intact proinsulin and diabetes type 2

The type 2 diabetes mellitus is characterised by a malsecretion of the pancreas and a genetically determined insulin resistance. In particular, the insulin resistance is closely linked to the appearance of macrovascular illnesses such as cardiac infarction and stroke. Hence, the clinical diagnosis and classification of the insulin resistance is of great importance. The intact proinsulin is a highly specific marker for the diagnosis of insulin resistance (9-12).

Intact proinsulin as a cardiovascular risk factor

An arteriosclerosis or coronary heart disease is favoured by increased serum levels of intact proinsulin and the degredation products of proinsulin Des-31, 32-Proinsulin (1, 3).

Indications

HOMA index

- Adiposis (BMI > 28 kg/m²)
- Suspected insulin resistance (metabolic syndrome, diabetes mellitus type 2)
- Suspected polycystic ovary syndrome (PCO-S)
- Cycle disturbances (e. g. amenorrhea)
- Infertility

Intact proinsulin as a diagnostic marker

The secretion condition of the pancreatic beta-cell is specifically described and classified by the analysis of intact proinsulin. Thus, a decision concerning specific therapy concepts can be made and the quality of the therapeutic medication can be examined (9-12).

■ Reference ranges

■ HOMA index

> 2.0 indication for insulin resistance

> 2.5 insulin resistance probable

> 5.0 average value in patients with diabetes mellitus type 2

■ Intact proinsulin

Interpretation of results in type 2 diabetes patients:

- ■ Intact proinsulin < 11 pmol/l (questionable insulin resistance)

  With values in the upper reference range (7–11 pmol/l), repeat analysis after 3–6 months is recommended (9–12).

- ■ Intact proinsulin > 11 pmol/l (presence of a secretion disturbance)

  In these patients an insulin resistance with secretion disturbance is probably present: Therapeutically, treatment of the insulin resistance is now recommended. A decrease in the intact proinsulin level should be observed under successful therapy (after approximately 3 months) (9–12).

Interpretation of results in patients without diabetes mellitus:

- ■ Intact proinsulin > 11 pmol/l

  The exclusion of a diabetes mellitus or an insulinoma as well as a cardiovascular risk status is recommended (9–12).

■ Sample collection and sample material

■ HOMA index

1 ml serum, FROZEN – for insulin analysis 1 ml plasma with sodium fluoride (request special tube), NOT FROZEN – for glucose analysis

Draw the blood in the morning following 12 hours of fasting.

■ Intact proinsulin

2 ml Serum, FROZEN. Draw the blood in the morning following 12 hours of fasting.

■ Author:

Dr. Marc Beineke, M. D., MSc.
clinical pathologist

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