Diabetologia (2001) 44: 783–789

Diabetologia

Letters

Comments

– to: Albareda M et al. (2000) Assessment of insulin sensitivity and beta-cell function from measurements in the fasting state and during an oral glucose tolerance test. Diabetologia 43: 1507–1511

To the Editor: Dr M. Albareda et al [1] have recently published a study of the various methods used to assess insulin sensitivity and insulin secretion from baseline and Oral Glucose Tolerance Test (OGTT) plasma glucose and plasma insulin concentrations. They concluded that the hyperbolic relation between insulin sensitivity and beta-cell function can best be measured using the fasting values of plasma glucose and plasma insulin. The authors correctly give Homeostasis model assessment (HOMA) beta-cell function as $20 \cdot I/(G - 3.5)$, where I stands for plasma insulin in mU/l, and G stands for plasma glucose in mmol/l (Table 1). In Figure 1 of their study, the HOMA beta-cell function is compared with the glucose-to-insulin ratio, which is used to assess insulin sensitivity (IS), according to the following formula: beta-cell function = K/IS, where K is a constant. Not surprisingly, the authors note this to be a hyperbolic function. Mathematically, this is a comparison between two (almost) reciprocal formulas. The comparison is I/(G-3.5) to G/I, which will render any set of data hyperbolic. When G approaches 3.5, (G-3.5) approaches zero; the division of I/(G-3.5) will therefore approach infinity (∞). When G is considerably higher than 3.5, the division of I/(G + 3.5) is almost equivalent to I/G; therefore the line comparing G/I with I/(G + 3.5) becomes asymptotic.

Physiologically, the hyperbolic relation between beta-cell function and insulin sensitivity suggests that beta cells adapt to insulin action. Interestingly, the authors observe that most OGTT-derived indices do not fit a hyperbolic function. This might be because OGTT-derived indices are better suited to measuring the first phase insulin secretion than the second phase: and indeed, the authors only used the first phase formula from the "Stumvoll index" [2]. It could well be that the relation between beta-cell function and insulin sensitivity is more complex. We recently studied first and second phase insulin secretion with hyperglycaemic glucose clamps in a large number of subjects (185 subjects with normal glucose tolerance and 98 with impaired glucose tolerance) [3]. Both first and second phase insulin secretion were lower in the subjects with impaired glucose tolerance than in the subjects with a normal glucose tolerance. Further multiple linear regression analysis indicated that both first and second phase secretion were positively correlated with BMI, in both subjects with normal glucose tolerance and in subjects with impaired glucose. Because BMI (a measure of excess weight) is strongly correlated with insulin resistance, these findings argue that beta-cell function can adapt to insulin resistance. In order to substantiate this, we plotted the insulin sensitivity index (assessed using a clamp) against first phase and second phase secretion; this should yield the "hyperbolic relation". The data did indeed point to a hyperbolic relation for second phase secretion when compared with insulin sensitivity. But for the first phase, secretion appeared to reach a maximum in the most insulin resistant subjects arguing against a hyperbolic function for the first phase.

In physiological terms, this could imply that the ability of beta cells to "adapt" their secretory function to insulin sensitivity could have reached their limit in the most insulin-resistant subjects, apparently even in subjects with normal glucose tolerance. Of note is that the "hyperbolic" functions of subjects with impaired glucose tolerance and subjects with normal glucose tolerance appeared to be different: for a given (level of) insulin sensitivity, beta-cell function was on average approximately 30 % (second phase) to 50 % (first phase) lower in subjects with impaired glucose tolerance than in subjects with normal glucose tolerance. This could point to a change in the adaptation process of the beta cell to insulin sensitivity as impaired glucose tolerance develops.

The relation between insulin sensitivity and beta cell function becomes more and more intriguing.

T.W. van Haeften, M. Stumvoll

References

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Corresponding author: T.W. van Haeften, MD, Dept Internal Medicine G 02.228, University Medical Center Utrecht, PO Box 85500, NL 3508 GA Utrecht, The Netherlands