What kind of simple fasting index should be used to estimate insulin sensitivity in humans?

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S U M M A R Y

The hyperinsulinemic euglycemic glucose clamp method is the gold standard for measuring insulin resistance. However it is complex, and simple indexes have been developed. Some of them are based on formulae that calculate the product or the addition of fasting plasma insulin and glucose values whereas others are based on their ratios. We calculated several simple indexes of insulin resistance and compared them to hyperinsulinemic euglycemic clamp data in 111 subjects with a wide range of insulin resistance. We showed that indexes using insulin and glucose ratios in their formulae are poorly correlated with clamp measurements and give false evaluations, particularly in glucose-intolerant and type 2 diabetic subjects. Thus, whatever the glucose profile of study subjects, we suggest the use of a simple index based on the product or the addition of fasting plasma insulin and glucose values instead of their ratios to obtain insulin resistance evaluations close to the hyperinsulinemic euglycemic clamp technique.

Key-words: Insulin resistance - Hyperinsulinemic euglycemic clamp - QUICKI - HOMA - FIRI.

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R É S U M É

Quel type d’index simple devrait-on utiliser chez l’homme pour évaluer la sensibilité à l’insuline à jeun ?

Le clamp hyperinsuliniémique euglycémique est la méthode de référence de mesure de l’insulino-résistance. Cependant, cette méthode est complexe et plusieurs index simples ont été développés dont certains sont basés sur le produit ou l’addition des valeurs de glycémie et d’insulinémie à jeun et d’autre sur leur rapport. Nous avons utilisé plusieurs de ces index et comparé les résultats à ceux obtenus au cours d’un clamp hyperinsuliniémique euglycémique chez 111 sujets présentant des degrés variables de résistance à l’insuline. Nous avons montré que les index utilisant les rapports étaient peu corrélés aux données du clamp et donnaient des résultats erronés en particulier chez les patients intolérants au glucose et diabétiques de type 2. Ainsi, quelque soit le profil glycémique des sujets, nous proposons d’utiliser un index simple de mesure de l’insulino-résistance basé sur le produit ou l’addition des valeurs de glycémie et d’insulinémie à jeun plutôt que sur leur rapport afin d’obtenir une estimation de la résistance à l’insuline la plus proche possible de celle obtenue au cours du clamp.

Mots-clés : Insulino-résistance - Clamp hyperinsulinémique euglycémique - QUICKI - HOMA - FIRI.

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Insulin resistance is associated with several diseases: type 2 diabetes, obesity, metabolic syndrome, lipodystrophies and polycystic ovary syndrome (PCOS). The hyperinsulinemic euglycemic glucose (IS) clamp method is the gold standard for measuring insulin resistance in these diseases [1]. However, it is complex, time-consuming and cannot be used in large populations. For this reason, simple indexes obtained from fasting plasma glucose and insulin have been developed. Some of them, such as homeostasis model assessment (HOMA) [2], the fasting insulin resistance index (FIRI) [3] and the quantitative insulin sensitivity check index (QUICKI) [4], are based on formulae that calculate the product or the addition of fasting plasma insulin and glucose values whereas others measure their ratios [5].

Recently, using a pedagogic example, M.J. Quon, reported the limitations of the fasting glucose to insulin (G/I) ratio as an index of insulin sensitivity compared to HOMA and QUICKI [6]. However, although they could be erroneous in several situations, G/I and I/G ratios have been and are still being utilized by several investigators [7-9]. These ratios are acceptable in normal glucose-tolerant subjects, but when fasting plasma glucose increases, they underestimate the insulin-resistant state and become misleading. Since it does not seem to be fully integrated, we tested Quon’s theory [6] by adding data obtained from IS clamp studies.

We analysed the results in 111 subjects investigated between 1995 and 2002. This study group consisted of 28 controls, 16 PCOS patients, 10 obese non-diabetics, 28 glucose-intolerant and 29 type 2 diabetics. All subjects underwent hyperinsulinemic (75 mU/m²/min) euglycemic clamp, conducted with the same methodology [10]. We calculated HOMA, FIRI, QUICKI, the G/I ratio and the Raynaud index (40/I) [11] from both fasting plasma glucose and insulin obtained from basal values of the IS clamp. These data were compared to those obtained with insulin sensitivity measured during IS clamp.

As expected, the IS clamp results showed that PCOS, obese non-diabetic, glucose-intolerant and type 2 diabetic subjects were more insulin-resistant than the controls, with type 2 diabetics being the most insulin-resistant and PCOS patients being the least insulin-resistant. HOMA, FIRI and QUICKI estimates of insulin resistance or insulin sensitivity gave the same results (Tab I). By contrast, the G/I and I/G ratios presented quite different values, for example, with G/I, only PCOS and non-diabetic obese subjects were found to be more insulin-resistant than the controls whereas glucose-intolerant and type 2 diabetic subjects were as insulin-sensitive as the controls, type 2 diabetes being the most insulin-sensitive group. Intermediate results were obtained with the Raynaud index which showed that all groups were more insulin-resistant than the controls, with

Table I

<table>
<thead>
<tr>
<th>Table I</th>
<th>Insulin sensitivity measured by hyperinsulinemic normoglycemic clamp and by simple indexes of insulin sensitivity.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>PCOS</td>
</tr>
<tr>
<td>N = 28</td>
<td>N = 16</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>22.7 ± 0.4</td>
</tr>
<tr>
<td><strong>Glucose (mmol/l)</strong></td>
<td>4.7 ± 0.1</td>
</tr>
<tr>
<td><strong>Insulin (µU/ml)</strong></td>
<td>5.5 ± 0.5</td>
</tr>
<tr>
<td><strong>HOMA</strong></td>
<td>1.16 ± 0.10</td>
</tr>
<tr>
<td><strong>FIRI</strong></td>
<td>1.04 ± 0.09</td>
</tr>
<tr>
<td><strong>QUICKI</strong></td>
<td>0.384 ± 0.006</td>
</tr>
<tr>
<td><strong>G/I (mg/10⁴U)</strong></td>
<td>18.4 ± 1.5</td>
</tr>
<tr>
<td><strong>I/G (pmol/mmol)</strong></td>
<td>7.07 ± 0.58</td>
</tr>
<tr>
<td><strong>40/I (ml/µU)</strong></td>
<td>8.88 ± 0.78</td>
</tr>
<tr>
<td><strong>IS clamp</strong></td>
<td>8.44 ± 0.55</td>
</tr>
</tbody>
</table>

PCOS: polycystic ovary syndrome; BMI: body mass index; HOMA: homeostasis model assessment (fasting plasma insulin [µU/ml] X fasting plasma glucose mmol/L)/22.5; FIRI: fasting insulin resistance index (fasting plasma insulin [µU/ml] X fasting plasma glucose [mmol/L])/25; QUICKI: quantitative insulin sensitivity check index (1/(ln fasting plasma insulin [µU/ml]) + ln fasting plasma glucose [mg/dl]); G/I: glucose to insulin ratio; I/G: insulin to glucose ratio; 40/I: Raynaud index; IS clamp: insulin sensitivity during euglycemic hyperinsulinemic clamp (GIRss/Gss x ΔIAU expressed in 10⁻⁴ dl/kg x min per µU/ml) where GIRss is the glucose infusion rate during steady state of the clamp (mg/kg x min), Gss is the steady state blood glucose concentration (mg/dl) and ΔIAU is the difference between the steady state and basal insulin concentration (µU/ml).

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obese non-diabetics being the most insulin-resistant instead of type 2 diabetics as clearly demonstrated by IS clamp. Table II illustrates that HOMA, FRI and QUICKI (Fig. 1a) were highly correlated with the IS clamp. G/I (Fig. 1b) and I/G ratios were less correlated with the IS clamp than the other indexes; similarly, the correlation between the Raynaud index and the IS clamp was intermediate (Tab II).

We thus proved with this study, performed in a large population, including subjects with a wide range of insulin resistance states, that HOMA, FRI and QUICKI give insulin sensitivity evaluations corresponding to those measured with IS clamp. On the other hand, G/I and I/G ratios produced contrasting results, especially for type 2 diabetics and glucose-intolerant subjects, despite their moderate but significant correlation with IS clamp data. Our findings clearly demonstrated that G/I and I/G ratios could be erroneous, whereas HOMA, FRI and QUICKI avoided such misleading outcomes, although they were calculated from the same data, i.e., fasting plasma glucose and insulin.

![Figure 1](image_url)

Figure 1
Correlation between IS Clamp and
a) QUICKI.
 b) G/I ratio.
We clearly established that indexes using insulin and glucose ratios in their formulae are poorly correlated with clamp measurement of insulin sensitivity (Tab I), and evoke false evaluation, particularly in glucose-intolerant subjects (Tab I). Since these subjects are likely to be included as normal controls in large epidemiological studies where this pathologic situation is not always diagnosed, G/I and I/G ratios should be abandoned.

In conclusion, whatever the glucose profile of study subjects, we suggest the use of one of three simple indexes (HOMA, FIRI or QUICKI) instead of G/I and I/G ratios for clinical and epidemiological investigations to obtain insulin resistance evaluations close to the hyperinsulinemic euglycemic clamp technique.

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References