Comparison of insulin sensitivity values using the hyperinsulinemic euglycemic clamp: 2 vs 3 hours

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Insulin sensitivity is one of the major determinants of the progression and development of type 2 diabetes and cardiovascular disease [1]. The hyperinsulinemic euglycemic clamp is considered the “gold standard” in the assessment of insulin sensitivity because it directly measures insulin action on glucose utilization under steady-state conditions [2, 3]. It is performed by infusing insulin at a constant rate to achieve high physiological levels of plasma insulin. In addition, glucose is monitored frequently while 20% dextrose is administered at variable rates to maintain near-constant glycemia (~5 mmol/l). There is no present consensus as to the duration of the clamp that is appropriate for the measurement of insulin sensitivity. Investigators use different lengths and types of clamps depending on the research question [4, 5]. Therefore, given the central importance of insulin sensitivity in several diseases, including type 2 diabetes, obesity, hypertension, dyslipidemia, and cardiovascular disorders, we compared the values of glucose disposal determined at 120 and 180 min and its correlation with several cardiovascular risk factors.

We examined results from an ongoing study in our laboratory in 51 obese postmenopausal women. These women had an average age of 57.4 ± 5.6, fasting glucose of 5.0 ± 0.5 mmol/L, BMI of 33.2 ± 4.8 kg/m² and percentage body fat of 46.4 ± 4.9%. The mean glucose infusion rate in the last 30 min of insulin infusion (75 mU/m²/min~2 mU/kg/min) was used to determine the insulin sensitivity index and was then expressed in relative levels (per kg of fat free mass). Results showed that insulin sensitivity at 180 min was 10% higher than at 120 min, whereas glycemia at 180 min was not significantly different from glycemia at 120 min (Tab I). Forty-one out of the 51 subjects (~80%) had higher insulin sensitivity values at 180 min than at 120 min. Insulin sensitivity at 120 min was significantly correlated with insulin sensitivity at 180 min (r = 0.893; P < 0.01), whereas glycemia at 120 min was not related to glycemia at 180 min (r = 0.127; NS). Finally, insulin sensitivity values at 120 and 180 min were significantly correlated with HOMA (r = -0.582 and r = -0.519, respectively) and triglycerides (r = -0.386 and r = -0.401, respectively), however, waist circumference and percentage of body fat were not significantly correlated with insulin sensitivity at min 120 and 180.

These results suggest that 2 and 3 hours clamp values are different and cannot be used interchangeably. It is not our intention to convey the notion that a 3 hour clamp is the most accurate duration for the determination of insulin sensitivity, but rather that higher values (10%) are observed at 3 hours than at 2 hours. Researchers should consider the duration of the clamp as a potential variable responsible for the variation in glucose disposal. Standardization for the glucose clamp technique could be essential in the attempt to define threshold values for the metabolic syndrome as a potential cardiovascular risk factor [5]. Until prospective studies are conducted the most pertinent clamp duration will remain unknown.

Table I
Insulin sensitivity and glycemia at 120 and 180 min.

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<tr>
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<th>120 min</th>
<th>180 min</th>
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<tbody>
<tr>
<td>Insulin Sensitivity (mg/min/FFM)</td>
<td>10.25 ± 2.9</td>
<td>11.19 ± 2.9*</td>
</tr>
<tr>
<td>Glycemia (mmol/l)</td>
<td>4.82 ± 0.41</td>
<td>4.78 ± 0.38 *</td>
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Values are means ± SD.
*Significantly different from min/20 (P < 0.01).

References

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