Background

Insulin resistance occurs as a reaction to surgery. Its magnitude is, in part, related to the degree of injury (1). Post-operative insulin resistance and its accompanying hyperglycemia are independent risk factors for several complications in surgical patients, most notably infections, and cardiopulmonary disorders (2,3,4,5). Several readily available perioperative treatments, including many of the components of the Enhanced Recovery or ERAS programs, reduce postoperative insulin resistance (6).

The challenge

In studies of insulin resistance, several publications of similar kind have rendered conflicting results (7,8). A probable reason for this is the use of different measurement methods. The hyperinsulinemic euglycemic clamp (clamp) is well documented as the “gold standard” for measurement of insulin resistance (9).

The HOMA (Homeostasis Model Assessment) method, since cheaper and easier to use, often is used as an alternative (10) and several authors using this method tend to draw direct comparison with data on insulin resistance using the clamp.

The question

Do HOMA and Clamp capture the same metabolic phenomenon and are they interchangeable?

Methods

- 113 non-diabetic elective surgery patients.
- To insure a wide range of insulin resistance, the surgical procedures, both open and laparoscopic, were varied, with procedures of colorectal-, upper GI-, general- and orthopaedic surgery represented.
- Insulin resistance quantified using clamp and HOMA, both before and after surgery.
- Pre and postoperative clamp and HOMA values were compared using regression- and correlation-analysis. The degree of agreement and interchangeability was studied both using kappa, K, and the Bland-Altman test (11) for the relative change pre vs. post operatively using absolute values.
- The hyperinsulinemic euglycemic clamp, technique. After an overnight fast, insulin is infused intravenously at a constant rate to yield a hyperinsulinemic steady state at insulin levels seen after a normal meal.
- The resulting fall in blood glucose levels is countered by infusing glucose intravenously thereby maintaining blood glucose levels within the normal, or euglycemic, range (5.5 mmol/l). After approximately 60 minutes, plasma insulin, blood glucose and the glucose infusion rate all reach steady state. With blood glucose levels now constant and with the hyperinsulinemic state, the glucose infusion rate is therefore a measure of the whole body insulin sensitivity at that given time (M-value, expressed as mg glucose infused/kg body weight and minute). Consequently, the lower the M-value the greater the resistance to insulin.
- HOMA was calculated as; HOMA = Go x Io / 22.5, where Go = fasting glucose concentration (mmol/L), Io = fasting plasma insulin concentration μU/ml. The higher its value the greater the resistance to insulin.
- The clamp result was treated as the reference method.

Results

When comparing clamp to HOMA there was a significant but poor correlation for both pre- and postoperative results as well as for relative difference after surgery. Analyzing the degree of agreement for the relative change in insulin sensitivity after surgery using the Bland-Altman test gave a large range for “limits of agreement” (±2SD) and a proportional error where low degree of insulin resistance was underestimated by HOMA and a high resistance overestimated. Figures 1-4. This poor intermethod agreement was further consolidated by a kappa value of 0.07.

Comments

Previous studies using tracer techniques, showed that 85-90 % of the insulin resistance seen after surgery is accounted for by the reduction of glucose uptake, while the remaining 10-15% is due to lowered inhibition of liver glucose production. They also showed that the effect of insulin resistance on glucose uptake is only evident at higher physiological insulin concentration levels (12). Figures 5-6.

Therefore the main portion of postoperative insulin resistance can only be detected when raising insulin to levels after meals. At basal (fasting) levels, only the small change due to increased glucose production is detectable.

Conclusion

- HOMA does not determine the same physiological or metabolic measure as the clamp.
- The clamp studies insulin at levels when the hormone is active, while HOMA does not.
- Data using the HOMA method should be interpreted as something different from and not be immediately compared with data using the clamp, which remains the gold standard method.

References

7. Mathur et al. BJS 2010 ;97:485-494