Methods

Evaluation of insulin sensitivity during a two-step hyperglycaemic clamp  The M/I index of insulin sensitivity [1] was calculated at steady state (last 40 minutes of each step of the hyperglycaemic clamp) by dividing the glucose infusion rate by the plasma insulin level.

Evaluation of beta cell function during a two-step hyperglycaemic clamp  The C-peptide response was taken as an index of absolute insulin secretion, as the insulin secretion rate cannot be calculated in rats. This is because rat C-peptide kinetics have not been determined as the species-specific rat C-peptide is unavailable for injection. Insulin secretion in vivo has to be evaluated in the context of insulin sensitivity, since the normal beta cell compensates for insulin resistance. In normal subjects, the relationship between insulin sensitivity and insulin secretion is hyperbolic [2, 3], i.e., the product of insulin sensitivity and insulin secretion is a constant defined as Disposition Index (DI) and considered as a measure of beta cell function. We have shown that the relationship between C-peptide and M/I index is indeed hyperbolic in control rats [4]. Therefore, we calculated DI during the last 40 minutes of each step of the hyperglycaemic clamp.

References

