Weight versus Pre-Insulin-Treatment Assessment of Insulin Sensitivity to Determine the Starting Basal Insulin Dose: A Faster Way to Get to Goal?

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According to product inserts, the recommended starting doses for basal insulin in type 2 diabetes is 10–20 U or 0.1–0.2 U/kg. Although usually not causing hypoglycemia, these are far short of the eventual dose at the glycemic goal, prolonging the period of titration and increasing the chance of failure to reach goal. We postulated that larger initial doses determined by the patient's insulin sensitivity (IS) would accelerate goal attainment without increasing the risk of hypoglycemia.

Days-to-glycemic goal were compared between two methods of determining the starting dose of basal analog insulin, weight (W) versus a pre-insulin-treatment assessment of IS.

In uncontrolled insulin-naïve type 2 diabetes subjects, IS was determined by the fasting plasma glucose (FPG) decline in 4 h following subcutaneous insulin aspart, 0.1 U/kg. The IS dose was calculated from the formula $500/((FPG_{BASELINE} - FPG_{4th\,HOUR})/U_{ASPART})$. Once-nightly insulin detemir, 0.1 U/kg, was titrated every 3 days to achieve a 3-day mean FPG of <110 mg/dl. On the third day, subjects were randomized (1:1) to begin titration (W group) or to increase to the IS dose over 3 days. On the ninth day, the IS group began titration. Compliance was supported by weekly telephone calls and clinic visits every 4 weeks during the 12-week study.

Without an increase in the hypoglycemia incidence, the IS group (n = 9) achieved target FPG in 27.8 ± 23.7 versus 38.2 ± 25.6 days (p = .186) for the W group (n = 10). The mean IS dose at start and at goal was significantly higher than in the W group, 60.7 ± 23.6 versus 11.0 ± 2.4 U (p < .001) and 79.0 ± 35.7 versus 45.0 ± 25.9 U (p = .0142) despite similar baseline IS, 8.06 ± 3.18 versus 8.19 ± 3.52 mg/dl/U, respectively (p = .456). The titration course of both approaches is seen in **Figure 1**.

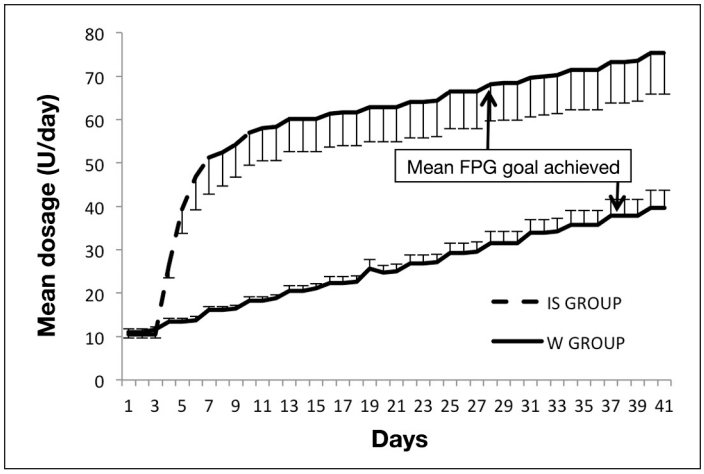

Figure 1. The mean once-nightly insulin detemir dose (and standard error) in that group starting dose determined by W (0.1 U/kg; n = 10) compared with that dose determined by a pretreatment test of IS (n = 9).

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Abbreviations: (FPG) fasting plasma glucose, (IS) insulin sensitivity, (W) weight

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Although our investigation demonstrated that the IS-derived dosing did not increase hypoglycemia and did achieve the goal in fewer days, the results were not statistically significant. This failure could be due to the small number of the study subjects or due to the large initial starting dose inducing insulin resistance. Brief and modest increases in insulin levels do increase insulin resistance.[1–3] In fact, Shanik and coauthors[4] have proposed that hyperinsulinemia is the cause, not the result, of insulin resistance.

If we had used a smaller numerator in the formula for calculating the IS-determined dose, e.g., 400 instead of 500, the smaller initial dose may have lessened the possible insulin-induced insulin resistance and achieved target dose sooner.

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