Glycemic Response and Attainment of A1C Goals Following Newly Initiated Insulin Therapy for Type 2 Diabetes

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OBJECTIVE—To identify the characteristics associated with glycemic response to newly initiated insulin therapy.

RESEARCH DESIGN AND METHODS—We identified 1,139 type 2 diabetic patients who initiated insulin therapy between 1 January 2009 and 30 June 2010. Outcomes of interest were the proportion of patients achieving A1C <7% and mean change in A1C within 3–9 months.

RESULTS—Mean A1C at insulin initiation was 8.2 vs. 9.2% among those who did and did not attain A1C <7% (P < 0.001). Within a mean of 5 months, 464 (40.7%) patients attained A1C <7%. In multivariable analyses controlling for insulin regimen, dose, and oral agent use, pre-insulin A1C was responsible for nearly all the explained variance in A1C change. Each one percentage point of preinsulin A1C reduced the probability of attaining <7% by 26% (odds ratio 0.74 [95% CI 0.68–0.80]).

CONCLUSIONS—Insulin initiation at lower levels of A1C improves goal attainment and independently increases glycemic response.

Most type 2 diabetic patients require ongoing therapy intensification that eventually includes exogenous insulin administration (1). Despite the theoretical ability of insulin to correct any amount of hyperglycemia, in clinical practice only 30–37% of insulin patients achieved A1C <7% in any given quarter over 7 years of observation (2). Our objective was to examine the characteristics associated with better glycemic response to insulin and achievement of A1C targets.

RESEARCH DESIGN AND METHODS—The data for this observational study were extracted from the pharmacy, laboratory, and electronic medical record systems of Kaiser Permanente Northwest (KPNW). Details of KPNW and its data systems have been recently described (3). For the current observational study, we selected 1,139 KPNW members who met the following inclusion criteria: 1) entered the diabetes registry prior to 1 January 2008; 2) had no insulin dispensed in 2008; 3) had a new dispense of insulin between 1 January 2009 and 30 June 2010; 4) were aged ≥45 years as of the date of dispense; 5) had continuous health plan membership for at least 9 months following the first insulin dispense; 6) had at least one A1C measurement in the year prior to initiating insulin; and 7) had at least one A1C measurement 90–270 days following insulin initiation. The study observation period for each patient began on the date of insulin initiation and ended on the date of the first A1C measured 90–270 days later.

Outcomes of interest were the proportion of patients who achieved A1C <7% within 3–9 months of initiating insulin and mean change (decline) in A1C, calculated by subtracting the value of the first A1C measure taken 90–270 days following insulin initiation from the A1C value preceding insulin initiation. We identified three insulin regimens: long-acting alone (glargine, detemir, or NPH); short-acting alone (regular or rapid insulins); and combinations of long- and short-acting insulins.

RESULTS—Of 1,139 patients, 464 (40.7%) attained A1C <7% following insulin initiation (Table 1). Patients who attained A1C <7% were older (aged 66.1 vs. 62.6 years; P < 0.001), were less likely to be of a nonwhite race (7.1 vs. 12.2%; P = 0.006), and had slightly shorter duration of diabetes (8.5 vs. 9.0 years; P = 0.050) compared with patients who did not attain A1C <7%. Mean A1C at insulin initiation was 8.2% among those who subsequently attained <7% compared with 9.2% among those who did not (P < 0.001). Mean decline in A1C with insulin was greater among patients who attained the 7% goal (1.9 vs. 1.3%; P < 0.001). Patients who achieved A1C <7% did so with fewer mean units of insulin per day (47.4 vs. 53.2 units/day; P < 0.001) and less use of any oral agent (67.2 vs. 73.0%; P = 0.035). The majority of patients used a combination of insulin types (55.6%), whereas 33.3% used only long-acting and 11.2% used only short-acting insulins.

In multivariable analyses, A1C prior to insulin initiation was the dominant factor in goal attainment; each one percentage point of A1C prior to insulin reduced the probability of attaining A1C <7% by 26% (odds ratio 0.74 [95% CI 0.68–0.80]). Although other variables were statistically significant, A1C prior to initiation accounted for 96% of the discriminatory power of the model. Likewise, A1C prior to insulin initiation was responsible for nearly all of the explained variance of change in A1C. Relative to a regimen of long-acting insulin only, short-acting insulin only or combination regimens were significantly associated with goal attainment and glycemic response. Micro- and macrovascular complications and the use of other non-diabetes medications were not associated with glycemic response.
medications were not statistically significant covariates in either model.

**CONCLUSIONS**—With sufficient doses and appropriate lifestyle management, insulin can reduce any level of elevated A1C to the therapeutic goal (4). In our observational study of 1,139 patients in a clinical practice setting, we found that only 41% achieved A1C < 7% within a mean of 5 months after initiating insulin. Our findings were remarkably similar to a recent observational study in five European countries (5) and to the Treating To Target in Type 2 Diabetes (4-T) study (6). Thus, even in a rigorous clinical trial setting, A1C goal attainment is intensifying therapy quickly and is a shareholder of Merck and currently is employed by Regeneron. T.D.K. and K.G.B. are employees and shareholders of Merck. No other potential conflicts of interest relevant to this article were reported.

G.A.N. contributed to the study conception, design, and interpretation of the results; researched the data; and developed the first draft of the manuscript. T.M.K. contributed to the study conception, design, and interpretation of the results and researched the data. J.B.H. and T.D.K. contributed to the discussion and reviewed and edited the manuscript. K.G.B. contributed to the study conception, design, and interpretation of the results; contributed to the discussion; and reviewed and edited the manuscript. The final draft for submission was approved by all authors. G.A.N. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**References**


