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Towards Prediction of Type 1 Diabetes Patients Who Fail to Achieve Glycemic Target

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Abstract. In this study, we investigated which predictors from people with type 1 diabetes at initiation of intensive treatment that increase the risk of not achieving glycemic target. Data from a clinical trial with type 1 diabetes people (n=460) were used in a logistic regression model to analyze the effect of the predictors on achievement of glycemic target. Results indicate that age, smoking, glycated hemoglobin, 1,5-anhydroglucitol and fluctuation from continuous glucose monitoring are predictors of achievement of glycemic target, which can be used in an algorithm to predict people who fail to achieve glycemic target.

Keywords. Type 1 diabetes, prediction, continuous glucose monitoring

1. Introduction

Today's guidelines, such as, American Diabetes Association's Standards of Medical Care in Diabetes – 2019[1] recommend intensive treatment for diabetes patients to achieve a glycated hemoglobin (HbA_{1c}) level of less than 7% (54 mmol/mol). However, it is challenging for people with type 1 diabetes to achieve this glycemic target, and a too aggressive treatment increases the risk of severe hypoglycemia[2]. Prediction at initiation of intensive treatment of those who will fail to achieve target would enable an alternative personalized treatment with the potential of being more effective and safer. This study sought to investigate which predictors from people with type 1 diabetes at initiation of intensive treatment that increase the risk of not achieving glycemic target.

2. Method

Data from people with type 1 diabetes (n=460) enrolled in the Onset 5® trial by Novo Nordisk. Participants were on average 43 years old, 57% male, had a diabetes duration of 24 years, a body mass index of 26 kg/m^2 and an HbA_{1c} of 7.5% (58.5 mmol/L) at baseline. 359 (78%) of the participants did not achieve HbA_{1c} < 7% after 16 weeks of treatment. Time of randomization defined baseline and initiation of intensive insulin

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treatment. A logistic regression model was constructed to analyze the effect of a variety of predictors at baseline on achievement of HbA_{1c} < 7% (Y/N) after 16 weeks of treatment. Predictors at baseline included age (stratified in 18-25, 25-35, 35-50, 50-65 and >65 years), gender, diabetes duration, body mass index, HbA_{1c}, smoking status, fluctuation from continuous glucose monitoring, 1,5-anhydroglycitol (1,5-AG) and fasting plasma glucose. Odds ratios (OR) are presented with 95% confidence intervals (CI).

3. Results

Higher age resulted in an increased risk of not achieving target (50-65 vs 18-25 years OR: 3.5, 95% CI: 1.3-9.6). Not surprisingly, higher HbA_{1c} at baseline increased the risk as well (OR: 14.7, 95% CI: 7.2-30.0). Being a smoker resulted in a 4-fold increased risk of not achieving target (OR: 4.0, 95% CI: 1.2-13.4). Increase in 1,5-AG resulted in a decreased risk (OR: 0.89, 95% CI: 0.87-1.01), whereas increased fluctuation in CGM increased the risk (OR: 1.34, 95% CI: 0.77-2.33), however, none of them were statistically significant. An analysis without fluctuation resulted in a statistically significant association between 1,5-AG and achieving glycemic target (OR: 0.87, 95% CI: 0.77-0.99).

4. Discussion

In this study, higher age affects ability to achieve glycemic target irrespective of diabetes duration. Furthermore, being smoker is associated with not achieving target, which is confirmed by Peng et al.[3]. Higher 1.5-AG level decreased the risk of not achieving target. Blood concentrations of 1,5-AG decreases during time of hyperglycemia, and a higher 1,5-AG level at baseline is thus a reflection of a better control with less glycemic variability. Furthermore, findings about fluctuation in CGM strengthen the indication of glycemic variability as a predictor of achievement of glycemic target.

5. Conclusion

Both age, smoking status, HbA_{1c}, 1,5-AG and CGM fluctuation are at baseline for people with type 1 diabetes who succeed or fail to achieve glycemic target after 16 weeks of treatment. These are valuable findings prior to development of an algorithm to predict people who do not achieve glycemic target from intensive insulin treatment where alternative treatment options should thus be considered.

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