Association of 1,5-Anhydroglucitol and 2-Hour Postprandial Blood Glucose in Type 2 Diabetic Patients

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Objective To assess the association of 1,5-anhydroglucitol (1,5-AG) with 2-hour postprandial glucose values in type 2 diabetic patients followed over 12 months in an outpatient setting.

Research Design and Methods In 55 patients, self-measured postprandial blood glucose values were correlated with 1,5-AG values over pre-specified preceding time periods (3 days, 1 week, weekly up to 12 weeks).

Results The correlation coefficients were -0.34 (p<0.05) for postprandial glucose values in the preceding three days, -0.38 (p<0.001) for values during the week before a visit, and -0.40 (p<0.001) for the values obtained two weeks preceding the measurement of 1,5-AG. Correlations declined for time periods of ≥ 2 weeks before measurement of 1,5-AG. The correlation was lower with fasting/preprandial plasma glucose levels. There was no time-dependency of the correlation of HbA1c and fasting or postprandial glucose.

Conclusions 1,5-AG best reflected the 2-hour postprandial glucose values of the two previous weeks.
Recent studies found 1,5-anhydroglucitol (1,5-AG) to generally reflect postprandial hyperglycemia (1, 2, 3, 4). However, these studies were either cross-sectional, had a comparably short follow-up, (1, 2, 4) or included patients in the pre-diabetic state (3). The present study assessed the correlation of 2-hour postprandial glucose measurements, frequently recommended in clinical practice, with 1,5-AG and aimed at defining the time interval of glucose values yielding the closest correlation with 1,5-AG in diabetic patients.

RESEARCH DESIGN AND METHODS

This was a prospective study at three large Swiss hospitals assessing the impact of strategies to improve post-prandial glucose by optimizing the combination of oral antidiabetic drugs and/or insulin according to a pre-specified scheme (5). Included patients had type 2 diabetes \( \geq 6 \) months with HbA\(_1c\) between 7.0% and 12.0%. Patients with renal insufficiency or proteinuria were excluded. Written consent was obtained, and the study was approved by the local ethical committees. The study duration was 12 months with clinical visits every 3 months. Patients regularly monitored their blood-glucose levels before and 2 hours after main meals (Glucotrend Premium\( ^\circledR \), Roche Diagnostics, Mannheim, Germany). 1,5-AG was measured at each time point in a central laboratory (Lana\( ^\circledR \)1.5 Auto Liquid Reagent, InterBiotech Corporation, Tokyo, Japan, automated on a Hitachi 917 Analyser, CV 5.2%). HbA\(_1c\) was measured on a DCA 2000\( ^\circledR \) (Bayer AG, Leverkusen, Germany). Postprandial glucose values were included into the analysis if measured between 110 and 130 minutes after the corresponding preprandial measurement. Correlation coefficients were calculated using standardized linear regression. In sensitivity analyses the models were adjusted for age, gender, treatment modalities, time in study, and time of day. We correlated postprandial glucose values for the following pre-specified time periods preceding a visit with the corresponding 1,5-AG: 3 days, 1 week, then weekly up to 12 weeks. All analyses were performed using Stata 10.0 (Stata Corporation, College Station, TX, USA).

RESULTS

All 55 patients (19 female and 36 male individuals) contributed to the present analysis. Mean age was 61.3±9.6 years (mean ± SD). Average number of self-measurements of blood glucose per patient and year were 405±224 (fasting/preprandial) and 230±122 (postprandial). Mean fasting/preprandial glucose was 155±48 mg/dl at beginning and 133±46 mg/dl at end of study, corresponding values for postprandial glucose were 172±55 and 162±53 mg/dl. Mean HbA\(_1c\) was 8.7±1.3% at baseline and 7.7±1.0% at study end. Mean 1,5-AG was 4.2±3.5 \( \mu \)g/ml at baseline and 6.4±3.5 \( \mu \)g/ml at end. HbA\(_1c\) and 1,5-AG were negatively correlated (\( r=-0.42, p<0.001 \)). The correlation coefficient of postprandial glucose values with 1,5-AG varied across the pre-specified time periods preceding the measurement of 1,5-AG (Figure 1): -0.34 (\( p<0.05 \)) for postprandial glucose values of the previous 3 days, -0.38 (\( p<0.001 \)) for the first week before a visit, and -0.40 (\( p<0.001 \)) for the 2 weeks preceding measurement of 1,5-AG. Afterwards the strength of correlation decreased (\( p<0.001 \) for all remaining correlations). The association of fasting/preprandial glucose and 1,5-AG was lower (-0.19 to -0.23, \( p<0.001 \) for all correlations) and did not reveal a time dependency (Figure 1). Adjusting analyses for age, gender, treatment modalities, time in study, and time of day did not change the observed time dependency (data not shown). Time specific correlation coefficients were between 0.26 and 0.28 for HbA\(_1c\) with fasting/preprandial and between 0.22 and 0.30.
CONCLUSIONS

The present study is the first to longitudinally assess the association of 1,5-AG with 2-hour postprandial glucose values in diabetic patients followed over 12 months in an outpatient setting. Although correlations were moderate (<0.5 in magnitude), 1,5-AG reflected best 2-hour postprandial glucose values of the two preceding weeks. No time dependency resulted for the association of fasting glucose values and 1,5-AG. Correlations were weaker for HbA1c with fasting/preprandial as well as with postprandial glucose.

A comparable albeit slightly stronger correlation of 1,5-AG with postprandial glucose in a population of type 1 and 2 diabetic patients was reported recently (1). Of note, Dungan and colleagues used a continuous glucose monitoring system to measure the area under the curve for glucose levels exceeding 180 mg/dl, while the present study was based on self-measured glucose values. The lower number of postprandial compared with preprandial values reflects the difficulty to motivate patients for additional measurements and substantiates the role of 1,5-AG as a substitute of postprandial glucose measurements, complementing the widely used HbA1c and fructosamine.

A recent cross-sectional study in pre-diabetic Japanese patients found a higher correlation with 2-hour postprandial glucose (3). Noteworthy, 1,5-AG is subject to urinary excretion followed by almost complete reabsorption, which is competitively inhibited by glucose if the renal threshold for glucosuria is exceeded (6). While glucosuria in pre-diabetic individuals mainly occurs in the context of carbohydrate loading, diabetic patients may reveal increased glucose values independently of meals. Moreover, differences in absolute levels of 1,5-AG between Asian and Caucasian individuals were reported before (7). In conclusion, this longitudinal study in an outpatient setting shows that 1,5-AG reflects best the 2-hour postprandial glucose values of the two preceding weeks.

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Figure 1: Correlation coefficients and 95% confidence intervals of 1,5-anhydroglucitol (1,5-AG) with 2-hour postprandial glucose values (▲) and with fasting/preprandial glucose values (●) for the corresponding time periods preceding measurement of 1,5-AG (3 days up to 12 weeks)