

# Association of 1,5-Anhydroglucitol and 2-h 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-h postprandial glucose values in type 2 diabetic patients followed over 12 months in an outpatient setting.

**RESEARCH DESIGN AND METHODS** — In 55 patients, we examined self-measured postprandial blood glucose values for correlations with 1,5-AG values over prespecified preceding time periods (3 days, 1 week, and weekly up to 12 weeks).

**RESULTS** — The correlation coefficients for postprandial glucose values were  $-0.34$  ( $P < 0.05$ ) for 3 days,  $-0.38$  ( $P < 0.001$ ) for 1 week, and  $-0.40$  ( $P < 0.001$ ) for 2 weeks preceding the measurement of 1,5-AG. Correlations declined for time periods  $>2$  weeks before measurement of 1,5-AG. The correlation was lower with fasting/preprandial plasma glucose levels. There was no time dependency for the correlation between A1C and fasting or postprandial glucose.

**CONCLUSIONS** — 1,5-AG best reflected the 2-h postprandial glucose values of the 2 previous weeks.

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Recent studies found 1,5-anhydroglucitol (1,5-AG) to generally reflect postprandial hyperglycemia (1–4). However, these studies were 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-h 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 assess-

ing the impact of strategies to improve postprandial glucose by optimizing the combination of oral antidiabetes drugs and/or insulin according to a prespecified scheme (5). Included patients had type 2 diabetes  $\geq 6$  months with A1C 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 ethics committees. The study duration was 12 months with clinical visits every 3 months. Patients regularly monitored their blood glucose levels before and 2 h after main meals (Glucotrend Premium; Roche Diagnostics, Mannheim, Germany), and 1,5-AG was measured at each time point in a central laboratory (Lana

1.5 Auto Liquid Reagent; InterBiotech, Tokyo, Japan; automated on a Hitachi 917 Analyzer, coefficient of variation 5.2%). A1C was measured on a DCA 2000 (Bayer, Leverkusen, Germany). Postprandial glucose values were included in the analysis if measured between 110 and 130 min after the corresponding preprandial measurement. Correlation coefficients were calculated using standardized linear regression. In sensitivity analyses, the models were adjusted for age, sex, treatment modalities, time in study, and time of day. 1,5-AG measurements were examined for correlations with postprandial glucose values taken over the following prespecified preceding time periods: 3 days, 1 week, then weekly up to 12 weeks. All analyses were performed using Stata 10.0 (Stata, College Station, TX).

**RESULTS** — All 55 patients (19 women and 36 men) contributed to the present analysis. The mean age was  $61.3 \pm 9.6$  years (mean  $\pm$  SD). The average number of self-measurements of blood glucose per patient and year were  $405 \pm 224$  (fasting/preprandial) and  $230 \pm 122$  (postprandial). Mean fasting/preprandial glucose was  $155 \pm 48$  mg/dl at the beginning and  $133 \pm 46$  mg/dl at the end of the study, and corresponding values for postprandial glucose were  $172 \pm 55$  and  $162 \pm 53$  mg/dl. Mean A1C was  $8.7 \pm 1.3\%$  at baseline and  $7.7 \pm 1.0\%$  at study end. Mean 1,5-AG was  $4.2 \pm 3.5$   $\mu\text{g/ml}$  at baseline and  $6.4 \pm 3.5$   $\mu\text{g/ml}$  at study end. A1C 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 prespecified time periods preceding the measurement of 1,5-AG (Fig. 1):  $-0.34$  ( $P < 0.05$ ) for 3 days,  $-0.38$  ( $P < 0.001$ ) for 1 week, and  $-0.40$  ( $P < 0.001$ ) for 2 weeks. Afterward, the strength of the 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 (Fig. 1). Adjusting analyses for

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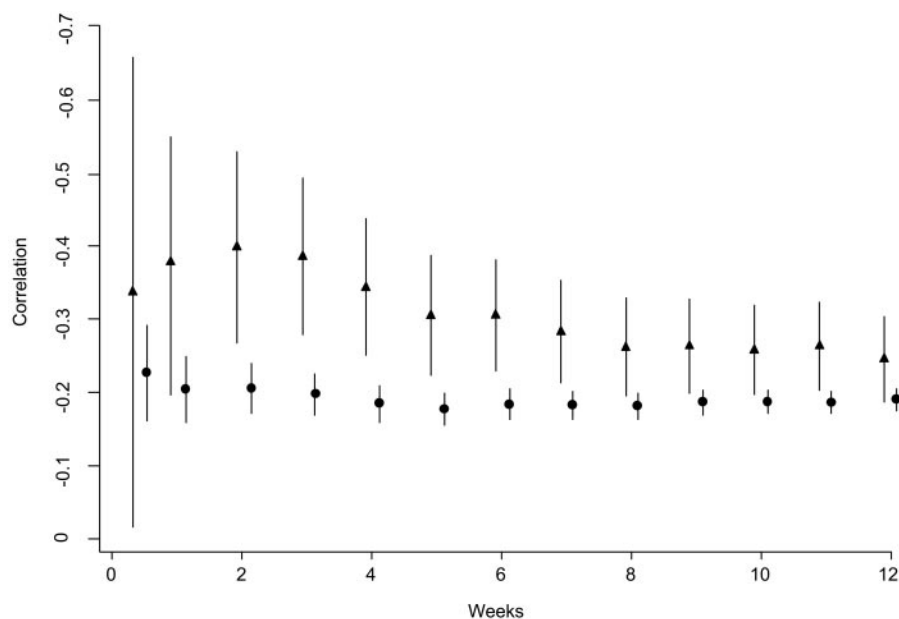
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**Figure 1**—Correlation coefficients and 95% CIs of 1,5-AG with 2-h postprandial glucose values (▲) and with fasting/preprandial glucose values (●) for the corresponding time periods preceding measurement of 1,5-AG (3 days up to 12 weeks).

age, sex, treatment modalities, time in study, and time of day did not change the observed time dependency (data not shown). Time-specific correlation coefficients were 0.26–0.28 for A1C with fasting/preprandial and 0.22–0.30 for A1C with postprandial glucose, without evidence of a time dependency.

**CONCLUSIONS**— The present study is the first to longitudinally assess the association of 1,5-AG with 2-h 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 best reflected 2-h postprandial glucose values in the 2 preceding weeks. No time dependency resulted for the association of fasting glucose values and 1,5-AG. Correlations were weaker for A1C 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 recently reported. Of note, Dungan et al. (1) 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 for postprandial glucose measurements, complementing the widely used A1C and fructosamine measurements.

A recent cross-sectional study in prediabetic Japanese patients found a higher correlation with 2-h postprandial glucose (3). It is noteworthy that 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 prediabetic 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 have been previously reported (7). In conclusion, this longitudinal study in an outpatient setting shows that 1,5-AG best reflects 2-h postprandial glucose values in the 2 preceding weeks.

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