A1C in Children and Adolescents With Diabetes in Relation to Certain Clinical Parameters

The Swedish Childhood Diabetes Registry SWEDIABKIDS

LENA HANBERGER, MSC[1]
ULF SAMUELSSON, MD[1]
BENGT LINDBLAD, MD[2]
JOHNNY LUDVIGSSON, MD[1]

OBJECTIVE — We explored the relationship between A1C and insulin regimen, duration of diabetes, age, sex, and BMI as well as the differences between clinical mean A1C levels at pediatric diabetes clinics in Sweden.

RESEARCH DESIGN AND METHODS — Data from 18,651 clinical outpatient visits (1,033 girls and 1,147 boys) at 20 pediatric clinics during 2001 and 2002 registered in the Swedish Childhood Diabetes Registry SWEDIABKIDS, a national quality registry, were analyzed.

RESULTS — A1C was <7.0% (target value ~8% per Diabetes Control and Complications Trial/National Glycohemoglobin Standardization Program standards) at 35% of the visits. Girls had significantly higher mean A1C than boys during adolescence. High mean A1C was correlated with high mean insulin dose, long duration of diabetes, and older age. Mean A1C varied between clinics (6.8–8.2%). Differences between centers could not be explained by differences in diabetes duration, age, BMI, or insulin dose.

CONCLUSIONS — Adolescents with a high insulin dose and a long duration of diabetes, especially girls, need to be focused on. Differences in mean values between centers remained inexplicable and require further investigation.

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Good metabolic control in type 1 diabetes is crucial (1), but for unclear reasons A1C levels differ greatly between clinics (2). Therefore, we analyzed data from a national quality registry, the Swedish Childhood Diabetes Registry SWEDIABKIDS. Since 2000, all data from outpatient visits are registered locally in a specially designed program for childhood diabetes. Our analysis included each patient's 2-year mean values of A1C, insulin dose, number of insulin injection times per day, duration of diabetes, BMI, number of visits to outpatient clinics per patient-year, sex, and age. The study group consisted of patients <20 years of age (n = 3,195: 1,526 girls and 1,669 boys) registered during 2001 and 2002. Data from 18,651 registered visits (9,177 by girls and 9,474 by boys) were analyzed after excluding 363 incorrectly registered visits. When insulin dose was <0.5 units $\cdot$ kg^{-1} $\cdot$ day^{-1} and diabetes duration was <1 year (n = 682) or not reported (n = 333), subjects were excluded. Of the 42 pediatric departments in Sweden, 22 provided data to the register. Two centers, one reporting data from only one visit per patient and one not reporting insulin dose, were excluded.

The mean ± SD number of visits per patient-year was 2.9 ± 3.4 (range 1–14), after excluding one outlier. The number of patients per center varied from 57 to 474. A1C was measured with the DCA-2000 analyzer (Bayer Diagnostics) or with local laboratory methods. All methods are standardized through EQUALIS (External Quality Assurance in Laboratory Medicine in Sweden) and are traceable to the Mono S method. Swedish A1C values are ~1% lower than Diabetes Control and Complications Trial (DCCT)/National Glycohemoglobin Standardization Program (NGSP) standard values (3).

We used four categories of A1C, referring to different levels of care and clinical interventions at our department in Linköping: <7.0% (target value at the time of data collection), 7.0–7.9% (intensified adjustment of insulin dose, diet, and physical activities), 8.0–9.9% (visits to outpatient clinic once a month), and ≥10% (referred to the diabetic ward). The BMI SD score was calculated and adjusted for age and sex (4), with cut-off points for overweight and obesity according to Cole et al. (5).

Statistical analysis was performed using SPSS, version 14.0. Descriptive statistics are expressed as mean ± SD or SEM where indicated. For comparisons between groups, t test was used, and for comparisons between multiple variables, ANOVA was used. For correlations, the Pearson correlation coefficient was calculated. Results were considered significant at $P < 0.05$. Multivariable linear regression analysis was used to identify significant independent correlates of A1C.

RESULTS — In the analyzed population (n = 2,180: 1,033 girls and 1,147 boys) the mean age was 13.4 ± 3.9 years (range 1.9–19.9); the proportion of overweight (age- and sex-adjusted BMI ≥25 kg/m^2) and obese (age- and sex-adjusted BMI ≥30 kg/m^2) children was 19.8 and 3.0%, respectively; the mean duration of diabetes was 6.0 ± 3.7 years (range 1.0–18.5); the mean insulin dose was 1.00 ± 0.27 units $\cdot$ kg^{-1} $\cdot$ day^{-1} (range 0.50–2.94); the mean number of times insulin was given per day was 4.5 ± 0.7 times per day (range 1–7.6); and the proportion of rapid-acting insulin was 49 ± 13% (range 6–100), after excluding one outlier.

From the [1]Faculty of Health Sciences, Linköping University, Linköping, Sweden; and the [2]Sahlgrenska Academy, Göteborg University, Göteborg, Sweden.

Corresponding author: Lena Hanberger, Division of Pediatrics, Faculty of Health Sciences, S-581 85 Linköping, Sweden. E-mail: lena.hanberger@lio.se.

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Table 1—*Distribution of A1C in relation to age, BMI, duration of diabetes, and insulin regimen for boys and girls, respectively, adjusted by center effect*

	A1C <7.0%	A1C 7.0–7.9%	A1C 8.0–9.9%	A1C ≥10%
n (%)	768 (35%)	760 (35%)	545 (25%)	87 (4%)
Age (years)	12.5 ± 0.1†§¶	13.4 ± 0.1*§¶	14.3 ± 0.2*†¶	16.5 ± 0.4*†§
Sex (male/female)	55/45	52/48	50/50	41/59
Age- and sex-adjusted BMI ≥25 kg/m² (%)	18	21	21	22
Age- and sex-adjusted BMI ≥ 30 kg/m² (%)	2	3	4*	4
Duration of diabetes (years)	5.0 ± 0.1§	5.9 ± 0.1	6.9 ± 0.2*	7.9 ± 0.4
Insulin dose (units · kg^{-1} · day^{-1})	0.89 ± 0.01†§¶	0.99 ± 0.01*§¶	1.09 ± 0.01*†¶	1.25 ± 0.03*†§
Injection times per day	4.3 ± 0.03†§¶	4.4 ± 0.03*#	4.5 ± 0.03*‡	4.6 ± 0.07*
Proportion using fast-acting insulin	49 ± 0.6	50 ± 0.6	50 ± 0.7	53 ± 1.7

Data are means ± SEM unless otherwise indicated. *P* values refer to difference of a category from each of the other categories of A1C and are adjusted for multiple comparisons. *$P < 0.01$ vs. A1C <7.0%, †$P < 0.01$ vs. A1C 7.0–7.9%, ‡$P < 0.05$ vs. A1C 7.0–7.9%, §$P < 0.01$ vs. A1C 8.0–9.9%, #$P < 0.05$ vs. A1C 8.0–9.9%, and ¶$P < 0.01$ vs. A1C ≥10.0%.

Metabolic control

The 2-year overall mean ± SEM A1C (adjusted for center effect) was 7.5 ± 0.1% (n = 2,160); the DCCT/NGSP-corrected value was 8.3%, normally distributed (girls 7.6 ± 0.2%, n = 1,022; boys 7.3 ± 0.2%, n = 1,138; $P = 0.015$). Mean A1C was higher in girls at ages 14 ($P < 0.05$), 16 ($P < 0.01$), 17 ($P < 0.001$), and 18 years ($P < 0.01$). When adjusting for center effect, those with the highest A1C were older and had a longer diabetes duration, a higher insulin dose, and a higher proportion of fast-acting insulin use (Table 1). High A1C correlated with high mean insulin dose in units per kilogram of body weight ($r = 0.341$, $P < 0.001$), somewhat longer duration of diabetes ($r = 0.248$, $P < 0.001$), and older age ($r = 0.222$, $P < 0.001$).

Centers

Mean A1C varied between centers from 6.8% (95% CI 6.8–6.9) to 8.2% (8.1–8.3), $P < 0.001$. Adjusting for age, sex, duration of diabetes, insulin dose, age- and sex-adjusted BMI SD, number of injection times per day, and number of visits per patient-year, mean A1C varied between 6.5% (6.4–6.7) and 8.7% (8.4–8.9), $P < 0.001$. Of the 20 centers, only 1 reported a mean A1C below our target value (7.0%). The number of visits to the centers, mean insulin dose, and duration of diabetes did not correlate with the centers ' mean A1C.

In a multiple regression model, significant predictors of increasing A1C were high insulin dose ($\beta = 1.09$, $P < 0.001$) followed by high numbers of visits per patient-year ($\beta = 0.14$, $P < 0.001$), long diabetes duration ($\beta = 0.05$, $P < 0.001$), and older age ($\beta = 0.03$, $P < 0.001$), most obviously in girls. The mean center A1C varied significantly ($P < 0.001$). The difference remained significant after adjusting for age, sex, duration of diabetes, insulin dose, age- and sex-adjusted BMI SD, number of injections per day, and number of visits per patient-year.

CONCLUSIONS

In Sweden, all pediatric clinics and one primary health care unit treat all children and adolescents with diabetes from defined geographic areas. We thus have data from an unselected population at each center. Clinics from Stockholm did not report data.

Despite the modern treatment and care given by multidisciplinary teams, only 35% of the children and adolescents had A1C <7.0%. Poor glycemic control was associated with older age, high insulin dose, and long duration of diabetes (2), especially during adolescence, suggesting that circumstances during puberty, both physical and psychological, affect metabolic control. High insulin dose, number of visits per patient-year, and long duration of diabetes were the strongest predictors of high A1C level (6). We assume that it is common to prescribe an increased insulin dose when A1C is increasing. A1C increased by 0.045% for each year with diabetes.

There were pronounced differences in mean A1C between centers. Differences in characteristics of the populations did not explain the differences in A1C. According to the Hvidøre study (7), diabetes education, attitudes of the diabetes team, and treatment target values may underlie center differences.

More efforts are required to reduce A1C levels. The pronounced differences in A1C per center cannot be explained by differences in formal treatment.

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