A1C in children and adolescents with diabetes in relation to certain clinical parameters. The Swedish Childhood Diabetes Registry, SWEDIABKIDS

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SWEDIABKIDS was financially supported by the Swedish Child Diabetes Foundation (Barndiabetesfonden) and the National Board of Health and Welfare.

Received for publication 23 September 2007 and accepted in revised form 22 January 2008.
ABSTRACT

Objective: We explored the relation between A1C and insulin regimen, duration of diabetes, age, gender, BMI, and the differences between clinical mean A1C at pediatric diabetes clinics in Sweden.

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

Results: A1C was <7.0 % (our target value, approximately 8% DCCT/NGSP value) at 35% of the visits. Girls had significantly higher mean A1C than boys during adolescence. High mean A1C correlated with high mean insulin dose, long duration and high age. Center mean A1C varied between clinics (6.8-8.2%). Center differences could not be explained by differences in diabetes duration, age, BMI or insulin dose.

Conclusions: Adolescents with high insulin dose and long duration, especially girls need to be focused on. Center differences remained inexplicable and require further investigation.
Good metabolic control in type 1 diabetes is crucial (1) but for unclear reasons A1C differs greatly between clinics (2). Therefore we analyzed data from the national quality registry SWEDIABKIDS. Since 2000 all data from out-patient visits are registered locally in a specially designed programme for childhood diabetes. We used each patient’s 2-year mean values of A1C, insulin dose/kg/day, number of insulin injection times per day, duration of diabetes, BMI, number of visits to out-patient clinics per patient year, gender and age. Our study group consisted of patients <20 years of age (3,195; 1,526 girls, 1,669 boys,) registered during 2001 and 2002. Data from 18,651 registered visits (girls: 9,177, boys: 9,474) were analyzed, after excluding 363 incorrectly registered visits. When insulin dose was <0.5U/kg/day and diabetes duration <1year (n=682) or not reported (n=333), subjects were excluded. Twenty-two of the 42 pediatric departments in Sweden provided data to the register. Two centers were excluded; one reporting data from only one visit/patient, one not reporting insulin dose.

The mean number of visits/patient/year was 2.9, SD 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 approximately 1% lower than DCCT/National Glycohemoglobin Standardization Program (NGSP) values (3).

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

Statistical analysis was performed using SPSS Inc., version 14.0. Descriptive statistics are expressed as mean and SD or SE. For comparisons between groups, t-test was used and for comparisons between multiple variables, Anova. For correlation, 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, 1,147 boys) the mean age was 13.4 years (SD±3.9, range 1.9-19.9), the proportion of overweight (age- and gender-adjusted BMI ≥25kg/m²) and obese children (age- and gender-adjusted BMI ≥30kg/m²), 19.8% and 3.0%, respectively, duration of diabetes 6.0 years (SD±3.7, range 1.0-18.5), insulin dose, 1.00 U/kg/day (SD±0.27, range 0.50-2.94), the number of times insulin was given per day, 4.5 (SD±0.7, range 1-7.6) and the proportion of rapid-acting insulin, 49 % (SD±13, range 6-100 after excluding one outlier).

Metabolic control. The 2-year overall mean A1C (adjusted for center effect) was 7.5 (SE±0.1, n=2160), DCCT/NGSP-corrected 8.3%, normally distributed (girls 7.6, SE±0.2, n=1022, boys 7.3 SE±0.2, n=1138, 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 (p<0.01). When adjusting for center effect, those with the highest A1C were older, had longer diabetes duration, higher insulin dose and higher proportion fast acting insulin (Table 1). High A1C correlated with high mean insulin dose in U/kg body weight (r=0.341, p<0.001), somewhat longer duration (r=0.248, p<0.001 and higher 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 (95% CI 8.1-8.3), p<0.001. Adjusting for age, gender, duration of diabetes, insulin dose, age- and gender adjusted BMI SD, number of injection times per day and number of visits/patient/year, it varied between 6.5% (95%CI 6.4-6.7) and 8.7 (95%CI 8.4-8.9), p<0.001. Of the 20 centers, only 1 reported a mean A1C below our target value (7.0%). The numbers of visits to the centers, the mean insulin dose and duration of diabetes did not correlate with the center’s mean A1C.

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

CONCLUSIONS

In Sweden all pediatric clinics and one primary health care unit treat all children and adolescents with diabetes from defined geographic areas. Thus we 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 high age, high insulin dose and long duration (2), especially during adolescence, which suggests that circumstances, both physical and psychological, during puberty affect metabolic control. High insulin dose, numbers of visits/patient/year and long duration 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 Hvidore 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.

ACKNOWLEDGEMENTS

We thank statistician John Carstensen, steering committee of SWEDIABKIDS: Bengt Lindblad (national coordinator), Leif Blom, Ragnar Hanås, Ulf Samuelsson, and Ingmar Zachrisson. and the local coordinators who provided data: Agne Lind, Borås; Inga-Lena Lödesjö, Eskilstuna; Bengt Lindblad, Göteborg; Nils-Östen Nilsson, Halmstad; Jan Neiderud, Helsingborg; Erik Carlsson,Kalmar; Gudrun Jonsell, Karlstad; Christer Gundewall, Kungsbacka; Bert Thrybom, Lidköping; Ulf Samuelsson, Linköping; Maria Nordwall, Norrköping; Lennart Hellenberg, Nyköping; Henrik Tollig, Skövde; Nils Wramner Trollhättan; Ragnar Hanås, Uddevalla; Ingemar Svenne, Uppsala; Margareta Blomgren, Visby; Carl-Göran Arvidsson, Västerås; Stig Edvardsson, Växjö; Torsten Gadd, Ängelholm; Carina Bodén, Östersund.
REFERENCES

**TABLE 1.** Distribution of A1C in relation to age, BMI, duration of diabetes and insulin regimen, for boys and girls, respectively, adjusted to center effect. P values refer to difference of a category from each of the other categories of A1C and are adjusted for multiple comparisons.

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>A1C (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;7.0 p 7.0-7.9 p 8.0-9.9 p ≥10 p</td>
</tr>
<tr>
<td>n</td>
<td>768 760 (35%) 545 (25%) 87 (4%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>12.5±0.1 †§ 13.4 ±0.1 *§ 14.3±0.2 *† 16.5 ±0.4 *†§</td>
</tr>
<tr>
<td>Male/Female (%)</td>
<td>55/45 52/48 50/50 41/59</td>
</tr>
<tr>
<td>Age and gender</td>
<td>18% 21% 21% 22%</td>
</tr>
<tr>
<td>Age and gender</td>
<td>2% 3% 4% * 4%</td>
</tr>
<tr>
<td>Duration of diabetes</td>
<td>5.0 ±0.1 § 5.9 ±0.1 6.9±0.2 * 7.9 ±0.4</td>
</tr>
<tr>
<td>Insulin dose</td>
<td>0.89 †§ 0.99 ±0.01 *§ 1.09±0.01 *† 1.25 ±0.03 *†§</td>
</tr>
<tr>
<td>Injection times per</td>
<td>4.3 ±0.03 †§ 4.4 ±0.03 *# 4.5±0.03 *‡ 4.6 ±0.07 *</td>
</tr>
<tr>
<td>Proportion fast acting</td>
<td>49±0.6 50±0.6 50±0.7 53±1.7</td>
</tr>
</tbody>
</table>

Data are means ±SE or %.

* different from persons in the <7.0 HbA1c group at p<0.01
† different from persons in the 7.0-7.9 HbA1c group at p<0.01
‡ different from persons in the 7.0-7.9 HbA1c group at p<0.05
§ different from persons in the 8.0-9.9 HbA1c group at p<0.01
# different from persons in the 8.0-9.9 HbA1c group at p<0.05
¶ different from persons in the ≥10.0 HbA1c group at p<0.01