Journal of Diabetes and Its Complications 30 (2016) 917–922

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Teenage girls with type 1 diabetes have poorer metabolic control than boys and face more complications in early adulthood

Ulf Samuelsson [a], Johan Anderzén [b], Soffia Gudbjörnsdottir [c], Isabelle Steineck [d], Karin Åkesson [e], Lena Hanberger [f,*]

[a] Dept. of Clinical and Experimental Medicine, Division of Paediatrics, Linköping University, Linköping, Sweden
[b] Dept. of Paediatrics, Ryhov County Hospital, Jönköping, Sweden
[c] Dept. of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
[d] Dept. of Endocrinology, Copenhagen University Hospital, Hvidovre, Denmark
[e] Dept. of Paediatrics, Ryhov County Hospital, Jönköping, and Futurum - academy for Health and Care, Jönköping County Council, Sweden
[f] Dept. of Medical and Health Sciences, Division of Nursing, Linköping University, Linköping, Sweden

ARTICLE INFO

Article history:
Received 11 December 2015
Received in revised form 5 February 2016
Accepted 6 February 2016
Available online 9 February 2016z

Keywords:
HbA1c
Type 1 diabetes
Gender
Microvascular complications
Quality of care

ABSTRACT

Aims: To compare metabolic control between males and females with type 1 diabetes during adolescence and as young adults, and relate it to microvascular complications.
Methods: Data concerning 4000 adolescents with type 1 diabetes registered in the Swedish paediatric diabetes quality registry, and above the age of 18 years in the Swedish National Diabetes Registry was used.
Results: When dividing HbA1c values in three groups; < 7.4% (57 mmol/mol), 7.4–9.3% (57–78 mmol/mol) and >9.3% (78 mmol/mol), there was a higher proportion of females in the highest group during adolescence. In the group with the highest HbA1c values during adolescence and as adults, 51.7% were females, expected value 46.2%; in the group with low HbA1c values in both registries, 34.2% were females, $p < 0.001$. As adults, more females had retinopathy, $p < 0.05$. Females had higher mean HbA1c values at diagnosis, 11.2 vs. 10.9% (99 vs. 96 mmol/mol), $p < 0.03$, during adolescence, 8.5 vs. 8.2% (69 vs. 66 mmol/mol) $p < 0.01$, but not as young adults.
Conclusions: Worse glycaemic control was found in adolescent females, and they had a higher frequency of microvascular complications. Improved paediatric diabetes care is of great importance for increasing the likelihood of lower mortality and morbidity later in life.

1. Introduction

Type 1 diabetes, TID, is one of the most common chronic diseases of childhood, and the incidence is increasing (Diamond Project Group, 2006). Previous studies (Diabetes Control and Complications Trial Research Group, 1993; Nordwall, Arnqvist, Bojestig, & Ludvigsson, 2009) have shown that improved glycaemic control, measured as HbA1c, is important in preventing, delaying or slowing the progression of long-term complications. A high proportion of adolescents do not reach treatment targets for glycated haemoglobin, HbA1c (Hanberger, Samuelsson, Lindblad, & Ludvigsson, 2008; Holl, Swift, Mortensen, et al., 2003; Levine et al., 2001), and there is evidence that metabolic control deteriorates during adolescence. There is a correlation between metabolic control in late childhood and during adolescence (Cardwell, Patterson, Allen, Carson, & Northern Ireland Paediatric Diabetes Study Group, 2005; Dabadghao & Cameron, 2001; Mortensen & Hougaard, 1997). A gender-dependent difference in metabolic control has also been shown, with females having worse glycaemic control during the clinical course, especially during adolescence (Gerstl, Rabl, Rosenbauer, et al., 2008; Hochhauser, Rapaport, Shemesh, Schmeidler, & Chemtob, 2008; Schwab et al., 2010; Viswanathan, Sneeringer, Miller, Eugster, & DiMeglio, 2011). Girls in the 6–12 year age group presented with higher HbA1c levels than boys and girls of other age groups (Hochhauser et al., 2008; Viswanathan et al., 2011). In addition, a higher incidence of diabetic ketoacidosis (DKA), dyslipidemia and growth problems has been reported in female patients (Samuelsson, Steineck, & Gubbjornsdottir, 2014). In contrast, however, in a review of factors associated with the presence of DKA, no difference due to gender was found (Usher-Smith, Thompson, Sharp, & Walter, 2011). A gender difference in residual beta cell function exists when T1D is diagnosed, which has consequences for treatment (Samuelsson, Lindblad, Carlsson, et al.,

Duality of interest: The authors declare that there are no conflicts of interest associated with this manuscript.

* Corresponding author at: Dept. of Medical and Health Sciences, Division of Nursing, Linköping University, Linköping, Sweden.
E-mail address: lena.hanberger@liu.se (L. Hanberger).

http://dx.doi.org/10.1016/j.jdiacomp.2016.02.007
1056-8727/

2013). Pozelli et al. found a more extensive destruction of beta cells in females than in males during puberty (Pozzilli et al., 2001).

Regarding late complications, there is a higher risk of end-stage renal disease (ESRD) for male than for female patients in Sweden (Möllsten et al., 2010). In the EURODIAB study on the association between HbA1c and all-cause mortality, participants who died during follow-up were more often women than men (Schoenaker et al., 2014). There is also a higher hospitalization rate due to severe diabetic vascular complications among females than among males (Dahlquist, Möllsten, Källén, & Swedish Childhood Diabetes Study Group, 2008).

Data on children and adolescents with diabetes in Sweden are registered in the Swedish paediatric diabetes quality registry, SWEDIABKIDS. After transition to departments of medicine and primary health care centres, data are continuously followed and registered in a quality registry, NDR, for patients above 18 years of age. In this study, data from both registries were used and provided longitudinal information on glycaemic control, offering possibilities to study gender differences in early glycaemic control and the risk of microvascular complications.

The aim of this study was to compare metabolic control, measured as HbA1c, between males and females with type 1 diabetes during adolescence and as young adults. How the expected gender differences in metabolic control related to micro- and macroalbuminuria and retinopathy in early adulthood was explored.

2. Material and Methods

2.1. The Swedish paediatric diabetes quality registry, SWEDIABKIDS

Outpatient attendance data from all Swedish paediatric diabetes centres are registered in SWEDIABKIDS (SWE), established in the year 2000. Since 2007, the registry has included data on almost all (approximately 99%) children and adolescents with diabetes in Sweden. According to Swedish guidelines, children with diabetes visit the diabetes centre at least four times a year. At these visits, HbA1c and other clinical parameters such as insulin dose, weight, length and blood pressure are measured and reported by trained nurses or physicians online (Swedish Paediatric Diabetes Quality Registry).

2.2. The Swedish National Diabetes Registry, NDR

The NDR was introduced in 1996 to collect data on clinical characteristics and various risk factors in diabetic patients over 18 years of age at outpatient clinics of departments of medicine and primary health care centres nationwide (The National Diabetes Registry NDR, 2015). Two visits a year to a department of internal medicine or a primary health care centre are recommended in the guidelines (National Guidelines for Diabetes Care). As with SWE, the completeness of NDR has increased, and in 2013 approximately 90% of adult patients with type 1 diabetes were included (National Diabetes Registry).

Both SWE and NDR have the status of a national quality registry (Swedish Association of Local Authorities & Regions), and the patients are informed about the registry before they consent to be included. None of the registries collect data on ethnicity, socioeconomic status or educational level, as Swedish legislation does not allow this.

2.3. Study population

Data on 4945 patients with T1D, who had been transferred from paediatric to adult care, were collected from SWE. Of these patients, 4239 (85.7%) had HbA1c values registered both in the years 2011 and 2012 in NDR and were included in the study. Of these, 1960 were females and 2279 were males.

As the age at the time for diagnosis differed between the patients, the time period for which data were registered varied. Some of the patients were included in SWE for a long period but only for a short period in NDR, and vice versa. The mean age in SWE was 15.0 ± 1.5 years (range 13–18 years) and the mean age in NDR was 24.8 ± 3.5 years (range 21–41 years); 4.9% of the patients were above 30 years of age. The mean duration of follow-up was 14.7 ± 5.5 years (range 3–38 years). The year of diagnosis of T1D varied from year 1974 to 2009.

From 2007, SWE included data on patients from all paediatric clinics in Sweden. During the years 2000–2007 patients treated at non-participating clinics were diagnosed with, and treated for diabetes but not included in the registry. As adults they can still have data in NDR. At the time of this study there were about 3520 patients with T1D registered in NDR, who were diagnosed during childhood but not registered in SWE. Furthermore, as more than 90% of adults with T1D are included in NDR less than 10% of the patients in SWE are lost to follow-up in NDR.

2.4. Outcome measures

All laboratory methods used in Sweden are standardized through EQUALIS (External Quality Assurance in Laboratory Medicine in Sweden). The data on HbA1c obtained from SWE and NDR were derived from capillary blood samples taken and analysed in connection with the visit to the outpatient clinic. All available HbA1c values from the time in SWE were used. In NDR, values from year 2011 and 2012 were used. The mean value was calculated as follows: first the mean HbA1c value for each patient was calculated, and from that the mean HbA1c value for SWE and NDR, respectively, was derived. HbA1c values will be presented as NGSP (%) and IFCC (mmol/mol) (Hanas & John, 2010). Data on albuminuria, retinopathy, physical activity and smoking habits from NDR were used. Microalbuminuria was defined as urine albumin excretion of 20–200 μg/min, and macroalbuminuria as urine albumin excretion > 200 μg/min in two of three consecutive tests during one year. Retinopathy was assessed locally, i.e. through fundus photography performed by an ophthalmologist, and categorized as yes or no. Physical activity was defined as activity lasting more than 30 min and was divided into five levels: never (level 1), less than once/week (level 2), one–two times/week (level 3), three–five times/week (level 4), and daily (level 5).

The national HbA1c target value at the time for the study was 7.4% (57 mmol/mol). An HbA1c value above 9.3% (78 mmol/mol) was considered as a very high value and the patient requires intensified care. Based on this, the HbA1c values were divided into three different groups, <7.4% (57 mmol/mol) (low HbA1c), 7.4–9.3% (57–78 mmol/mol) (middle HbA1c), and >9.3% (78 mmol/mol) (high HbA1c).

2.5. Statistical analysis

SPSS 18® (SPSS inc., Chicago, IL, USA) was used for the analyses. A student's t-test and one-way analysis of variance (ANOVA) were used. When there were indications of skewed distribution, a Mann–Whitney U-test or Kruskall–Wallis test was used. Groups were compared by crosstabs, and chi-square was used for proportions. To test the relationship between HbA1c in SWE and HbA1c during early adulthood in NDR, Spearman's correlation was used. A multivariate logistic regression model adjusted for duration of T1D, age at diagnosis, BMI-SDS in SWE or NDR, physical activity registered in NDR, and smoking registered in NDR, was used to investigate the risk of high HbA1c levels. A multivariate linear regression model with mean HbA1c in NDR as a dependent variable and mean HbA1c in SWE as independent variables was also used in order to adjust for confounders. A p value <0.05, two-sided, was regarded as statistically significant. The results are expressed as mean ± SD.