Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Change in hemoglobin A1c one year following the 2014 American Diabetes Association guideline update

G. Todd Alonso [a,b,*], Laura Pyle [c], Brigitte Frohnert [a,b]

[a] Department of Pediatrics, University of Colorado School of Medicine, United States
[b] The Barbara Davis Center for Childhood Diabetes, Aurora, CO, United States
[c] Department of Biostatistics and Informatics, Colorado School of Public Health, United States

ARTICLE INFO

Article history:
Received 22 November 2016
Received in revised form
6 March 2017
Accepted 28 March 2017
Available online 10 May 2017

Keywords:
Pediatrics
Type 1 diabetes
HbA1c

ABSTRACT

Aims: In June 2014, the American Diabetes Association lowered recommended hemoglobin A1c (HbA1c) targets from <8.5% (69 mmol/mol) for children <6 years of age and from <8.0% (64 mmol/mol) for children 6–12 years of age to <7.5% (58 mmol/mol). Lower target HbA1c may lead to better glycemic control but could increase the risk of severe hypoglycemia.
Methods: Patients with type 1 diabetes >1 year duration, age 0–12 years and seen in our center between January 1 and June 30, 2014 or between January 1 and June 30, 2015 were included. 1013 unique patients had 2684 encounters. We analyzed first quarterly HbA1c (January-March, April-June) and self-reported severe hypoglycemia at all clinic encounters.
Results: HbA1c across the age span and within the 0–<6, 6–12, and 0–12 year old groups did not differ in the insurance adjusted mixed-effects model. Least squares means for all patients' HbA1c in 2014 was 8.59 ± 0.04 (70 ± 0.5 mmol/mol); for 2015, 8.60 ± 0.04 (70 ± 0.5 mmol/mol) ($p = 0.90$). Severe hypoglycemia data fields were more complete in 2015 (43% vs 50%). Logistic regression adjusting for follow up showed no difference in severe hypoglycemia for all ages ($p = 0.80$).
Conclusions: HbA1c did not change 1 year after the updated guidelines despite adoption of the new targets. Assessing changes in severe hypoglycemia may require larger, prospective datasets or longer observation.

1. Introduction

Hemoglobin A1c (HbA1c), a measure of mean blood sugar, is positively correlated with risk of diabetes related complications [1]. Lower levels, however, have historically been associated with increased risk for severe hypoglycemic events [1]. Therefore, until 2014, the American Diabetes Association (ADA) recommended higher HbA1c targets in patients 0–12 years of age than in older patients [2]. The International Society for Pediatric and Adolescent Diabetes (ISPAD), however,

Abbreviations: HbA1c, Hemoglobin A1c; ADA, American Diabetes Association; ISPAD, International Society for Pediatric and Adolescent Diabetes; CGM, continuous glucose monitor; CSII, continuous subcutaneous insulin infusion; MDI, multiple daily injection; SSI, sliding-scale insulin

* Corresponding author at: Barbara Davis Center, Mail Stop A140, 1775 Aurora Ct, Aurora, CO 80045, United States, Fax: +1 303 724 6779.
E-mail address: guy.alonso@ucdenver.edu (G.T. Alonso).

http://dx.doi.org/10.1016/j.diabres.2017.03.033
0168-8227/

has recommended HbA1c targets of <7.5% (58 mmol/mol) for all pediatric patients since 2007 (Table 1) [3]. Registry studies demonstrate lower HbA1c values for pediatric patients in two countries which follow the ISPAD guidelines, Germany and Austria, compared to the United States [4]. It is unknown to what extent these targets contribute to this difference.

With current technology and insulin regimens, lower HbA1c levels no longer appear to be associated with increased risk of severe hypoglycemia in children [4–7]. In light of these data, the ADA updated the recommended HbA1c targets in June 2014 [8].

The purpose of this study was to test whether these new recommendations have resulted in a measurable difference in HbA1c levels or the rate of severe hypoglycemia in our clinic population.

2. Subjects, materials, and methods

The study was approved by the Colorado Multiple Institutional Review Board. Patients with type 1 diabetes aged 1–12 years seen in the pediatric clinic at the Barbara Davis Center during the first (January through March) or second (April through June) quarter of 2014 and 2015 were included. The patient base was defined for each year to include patients with type 1 diabetes for at least 1 year duration who had established care in our clinic for at least 6 months and whose had had an HbA1c measurement in the preceding 6 months.

The study periods were the first two quarters of 2014 and of 2015. The first HbA1c value for each patient during each of the two study periods was included in the analysis. We also analyzed all self-reported severe hypoglycemia recorded by the healthcare provider in the electronic health record at all ambulatory encounters during those dates. Severe hypoglycemia was defined as seizure, loss of consciousness, emergency room visit, hospitalization, or need for intramuscular glucagon administration for self-reported or documented hypoglycemia. These were abstracted from visit note text or from flowsheet entries.

The Chi-square test was used to compare demographics and insulin regimen between 2014 and 2015. A cross-sectional comparison of HbA1c between the two periods was made with the Kruskal-Wallis test for all patients combined and then by age group (0–5 years, 6–12 years, 0–12 years). This does not take into account the fact that some patients have paired data, and therefore, the two years are not independent. As a sensitivity analysis, a mixed-effects model accounting for insurance coverage and the correlation between years in patients with both HbA1c measures, with age as a time-varying covariate, was used to compare HbA1c values from the two years. Logistic regression, adjusted for patient follow up, was performed to test the relationship between hypoglycemia and year.

3. Results

A total of 1013 unique patients, 530 of whom were included in both treatment periods, and 2684 clinical encounters were available. Patient demographics and insulin regimen are shown in Table 2. There was no difference in race/ethnicity, insurance, or gender between the two years. In 2015 more patients had Medicaid insurance and fewer had private insurance, though this did not reach statistical significance. Insulin regimen changed, with more patients using insulin pumps and fewer on multiple daily injection regimens with NPH insulin or sliding scale dosing.

In the cross-sectional analysis, the median HbA1c value was lower in each of the age groups in 2015 compared to

Table 2 – Characteristics of Subjects from 2014 and 2015. 1013 total unique subjects for entire data set. CSII, continuous subcutaneous insulin infusion; MDI, multiple daily injection; ICR, insulin to carbohydrate ratio; SSI, sliding-scale insulin; NPH, neutral protamine Hagedorn insulin. Patients who calculate rapid acting insulin dose based on carbohydrate intake were counted in the MDI/ICR group. Patients who used fixed doses of rapid acting insulin at meals were counted in the MDI/SSI group.

Characteristic	2014 (n = 769)	2015 (n = 774)	P-value
Male	52%	52%	0.94
Race/ethnicity			
African American	3%	3%	0.98
Asian	0.8%	1%	
Hispanic	15%	16%	
Non-Hispanic white	71%	71%	
Other	6%	5%	
Unknown	4%	4%	
Insurance			
Medicaid	26%	31%	0.19
Military	5%	5%	
Private	63%	59%	
Other	5%	5%	
Insulin regimen			
CSII	53%	59%	0.0018
MDI/ICR	34%	34%	
MDI/SSI	12%	7%	
NPH	1.2%	0%	

Table 1 – HbA1c targets by year and professional organization.

	ADA 2005 [2]	ISPAD 2007 [3]	ADA 2014 [8]
<6 y	<8.5% (69.4 mmol/mol)	<7.5% (58.5 mmol/mol)	<7.5% (58.5 mmol/mol)
6–12 y	<8.0% (63.9 mmol/mol)	<7.5% (58.5 mmol/mol)	<7.5% (58.5 mmol/mol)
13–17 y	<7.5% (58.5 mmol/mol)	<7.5% (58.5 mmol/mol)	<7.5% (58.5 mmol/mol)
≥18 y	<7.0% (53 mmol/mol)	<7.0% (53 mmol/mol)	<7.0% (53 mmol/mol)

ADA, American Diabetes Association; ISPAD, International Society for Pediatric and Adolescent Diabetes.