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

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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=.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=.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.

Keywords

Pediatrics; Type 1 Diabetes; HbA1c

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

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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, 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 2014, but not statistically different (Table 3). A similar pattern was seen in each of the age categories, though only reaching statistical significance in the 13–25 year old group.

None of the comparisons in the least-squares means of HbA1c by year and age group from the mixed model reached significance (Table 4). Two severe hypoglycemic events were recorded in 2014 (0.58 events per 100 patient years) and 7 in 2015 (2 events per 100 patient years). Logistic regression did not show an association between severe hypoglycemia and year ($p = .80$). Severe hypoglycemia flowsheet data fields were more complete in 2015 than in 2014 (50% vs 43% of total visits).

4. Discussion

Following the June 2014 guideline update by the ADA, our clinic adopted the new HbA1c targets as policy in July 2014. Retrospective clinic data shows lower median HbA1c in the cross sectional analysis and in <6 year old patients in the mixed model between 2014 and 2015, but this did not reach statistical significance. The differences between the mixed effects model and cross-sectional analysis could be due to greater visit frequency in patients with lower HbA1c or because the mixed model accounts for paired measures and patients' baseline HbA1c values.

Aside from the change in targets, many other factors could impact HbA1c trends. Over the study period, there was a shift towards more intensive insulin regimens and insulin pump use. Payer profile also changed, possibly affecting access to clinic encounters and diabetes technology and supplies. Although it was difficult to evaluate continuous glucose monitor (CGM) usage from available data fields, other analyses from our clinic have shown a steady increase in CGM starts over the past several years.

Patients <6 years of age account for only 3% of the population of our pediatric diabetes clinic, making it challenging to detect a differences in those with the largest change in HbA1c goal. Further, the <6 years age group had lower median HbA1c in 2014, giving them less room for improvement than the older group who had higher median HbA1c and wider distribution in HbA1c values. It may be necessary to study larger populations over longer periods to more clearly establish whether pediatric HbA1c levels are decreasing and whether any decrease is temporally associated with the new HbA1c targets.

Previous HbA1c targets were higher for young children due to concerns that they are less able to communicate symptoms of hypoglycemia (2), and the potential for more profound effects on the developing brain (10). Even using a broader definition and accounting for the fact that only 48% of all encounters had complete severe hypoglycemia data fields, this is much lower than the 17.5 events leading to loss of consciousness or seizure per 100 person-years in T1D Exchange patients 0–25 years of age (11). Our data are consistent with the fact that medical record reviews underreport severe hypoglycemia in children with type 1 diabetes (5). Nonetheless, it is reassuring to find no evidence of increase across any age group despite improved overall reporting.

Translating clinical guidelines into measurable outcomes is a pervasive, multi-layered challenge. At our center, providers universally accepted and adopted the changes, although, we did not collect data on their communication with patients about HbA1c targets. Patient and family knowledge and acceptance of recommendations were not assessed, however awareness of HbA1c targets in adolescents has been shown to be low (9). Therefore, we conclude that any immediate effects of the change in HbA1c goals in our population are subtle but deserve further study. Understanding effective communication, patient awareness, and acceptance of HbA1c targets may help clarify how recommended targets impact outcomes.

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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

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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

Table 2

Characteristics of Subjects from 2014 and 2015.

Characteristic	2014 (n=769)	2015 (n=774)	P-value
Male	52%	52%	.94
Race/ethnicity:			
African American	3%	3%	.98
Asian	0.8%	1%	
Hispanic	15%	16%	
Non-Hispanic white	71%	71%	
Other	6%	5%	
Unknown	4%	4%	
Insurance:			
Medicaid	26%	31%	.19
Military	5%	5%	
Private	63%	59%	
Other	5%	5%	
Insulin Regimen:			
CSII	53%	59%	.0018
MDI/ICR	34%	34%	
MDI/SSI	12%	7%	
NPH	1.2%	0%	

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.

Table 3

Median (25th, 75th percentile) HbA1c by age group and year. N= unique patients

Year	2014			2015		
Age Group	N	HbA1c	N	HbA1c	P-value	
<6 years	109	8.3% (7.7, 8.9) 67.2 mmol/mol (60.7, 73.8)	100	8.2% (7.5, 8.85) 66.1 mmol/mol (58.5, 73.2)	.20	
6–12 years	660	8.4% (7.8, 9.2) 68.3 mmol/mol (61.7, 77.0)	674	8.3% (7.7, 9.2) 67.2 mmol/mol (60.7, 77.0)	.29	
0–12 years	769	8.4% (7.7, 9.2) 68.3 mmol/mol (60.7, 77.0)	774	8.3% (7.7, 9.1) 67.2 mmol/mol (60.7, 76.0)	.17	

* Cross-sectional p-value for year from Kruskal-Wallis test

Table 4

HbA1c least-squares means from mixed-effects models, adjusted for insurance.

Year	2014	2015	
Age Group	N	HbA1c LS Mean	P-value
<6 years	109	8.43+/-0.10% (69 +/- 1.2 mmol/mol)	100 (67 +/- 1.4 mmol/mol) .18
6-12 years	660	8.63+/-0.05% (71 +/- 0.6 mmol/mol)	674 (71 +/- 0.6 mmol/mol) .80
0-12 years	769	8.59+/-0.04% (70 +/- 0.5 mmol/mol)	774 (70 +/- 0.5 mmol/mol) .90

Table 5

Severe hypoglycemia (SH) events by year and age category. N = ambulatory encounters

Year	2014		2015	
Age Group	N	SH	N	SH
<6 years	195	0	161	2
6–12 years	1172	2	1156	5