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The Utility of 1,5 Anhydroglucitol as a Reliable Indicator of Glycemic Control in Diabetes Mellitus

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Abstract

This study is a retrospective chart review examining the utility of serum 1,5 anhydroglucitol as a measure of glycemic control in diabetics in outpatient endocrinology clinic. It is hypothesized the addition of testing for 1,5 anhydroglucitol will lead to significant reduction in hemoglobin A1c levels and testing for this may cause earlier reductions in A1c levels, and therefore improved glycemic control.

Introduction

Within the field of internal medicine, serum hemoglobin A1c has become a household name as a routine test ordered in both inpatient and outpatient settings to assess glycemic control. This study, however, aims to examine the outpatient setting with the use of a newer, less commonly used (and perhaps less known) test at our facility, serum 1,5 anhydroglucitol, also trademarked as Glycomark.

What is serum 1,5 Anhydroglucitol or Glycomark? What is its Clinical Significance?

Traditionally when testing for serum hemoglobin A1c, we are aiming to observe a trend to gage glycemic control, and oftentimes there may be significant glycemic variability noted. Current research in the United States show 40% of diabetics, with what is considered moderate-well controlled hemoglobin A1c levels, have persistently high glucose patterns [1]. For instance, two patients with similar hemoglobin A1c levels of 7.2% can present in clinic with very different glucose monitoring logs. One of these patients may have higher and more frequent spikes in postprandial glucose, whereas the other patient may actually have well controlled glucose levels throughout the day. Without any additional further testing, clinicians will inevitably manage these two patients similarly simply because their hemoglobin A1c are the same.

Furthermore, there are noted limitations in testing for hemoglobin A1c as certain medications and medical conditions may either falsely elevate or decrease serum hemoglobin A1c levels. For example, it is known that iron deficiency anemia, severe hypertriglyceridemia and the use of opiates can falsely elevate hemoglobin A1c levels whereas hemolytic anemia, HIV and the use of dapsone can falsely lower hemoglobin A1c levels [2]. Testing for 1,5 anhydroglucitol is helpful because it would not be affected by such hemoglobinopathies and other medical conditions.

Serum 1,5 anhydroglucitol is a monosaccharide found in most foods, and is filtered via the glomerulus. Once serum glucose exceeds 180mg/dl and has met its renal threshold, the resulting glycosuria will decrease reabsorption of 1,5 anhydroglucitol and it becomes excreted in urine, resulting in decreased serum 1,5 anhydroglucitol levels. 1,5 anhydroglucitol testing is a great measure of post-prandial hyperglycemia of the preceding 1-2 weeks. Therefore, an indirect relationship exists - the lower the 1,5 anhydroglucitol level, the more severe the frequency and duration of post-

prandial hyperglycemia. Generally, a 1,5 anhydroglucitol level >10 microgram/dl is considered normal; this indicates well controlled glucose, with no significant hyperglycemia or postprandial hyperglycemia over past 2 weeks [3]. Conversely, a 1,5 anhydroglucitol level of < 10 microgram/dl indicates presence of post prandial hyperglycemia. The FDA has approved the use of 1,5 anhydroglucitol testing in 2003, however it has not been available at our facility until more recently.

Based on this information, we hypothesize that the addition of serum 1,5 anhydroglucitol testing will help lead to significant reductions in hemoglobin A1c levels and thus, improved glycemic control. Clinical studies published have also shown that the use of 1,5 anhydroglucitol may result in an earlier reduction of serum hemoglobin A1c levels [4]. This is significant to all healthcare providers, not just endocrinologists, as we know hyperglycemia is independently associated with diabetic-related complications, increasing patient mortality, morbidity and overall healthcare costs.

Methods

This study is a retrospective chart review of the outpatient endocrinology clinic at Coney Island Hospital, targeting our diabetic population during a 2-year period from 2017-2019, examining those who were tested or not tested for serum 1,5 anhydroglucitol. Serum hemoglobin A1c levels were recorded at baseline, 6-months and 1-year intervals for both groups. The control group who was not tested for serum 1,5 anhydroglucitol consisted of diabetic subjects who were matched for age, ethnicity, and sex. We arbitrarily set a reduction of hemoglobin A1c of at least 0.5%, at either the 6-month or 1-year mark, to be considered as significant in this study. We selected this target as it has been noted by the American Diabetic Association that for every 1% reduction in serum hemoglobin A1c, the risk of microvascular complications decreases by 37% and the risk of any other diabetes-related complication or death also decrease by 21% [5,6].

All diabetic patients over the age of 21 years, either type 1 or type 2 diabetes mellitus, regardless of treatment modality, were included in this study. All diabetics with history of CKD stage 4-5 or end-stage renal disease requiring hemodialysis, cirrhosis or those on home total parenteral nutrition or on sodium-glucose co-transporter 2 inhibitors were excluded from this study.

Results

Out of the 873 patients seen in endocrinology clinic over this 2-year time period for diabetes, about 45 patients were tested for serum 1,5 anhydroglucitol at least once. In the group of patients who were tested for 1,5 anhydroglucitol, baseline hemoglobin A1c was recorded at baseline visit, 6 months and 1-year intervals. At baseline, pretesting showed an average baseline hemoglobin A1c of 9.8% in type 1 DM and an average baseline hemoglobin A1c of 8.9% in type 2 DM. Remarkably, once testing for 1,5 anhydroglucitol started, serum hemoglobin A1c levels were noted to decline.

By 6 months, the average hemoglobin A1c for a type 1 diabetic was noted 8.9% and average hemoglobin A1c for type 2 DM was 8.2%, After 1 year of testing, we noted in type 2 diabetics, the average serum hemoglobin A1c further dropped to 7.8%. Unfortunately, there was insufficient data for type 1 diabetics at the 1-year mark due to lack of follow up. It was noted that 44% of the control group that were not tested for 1,5 anhydroglucitol were noted to achieve an overall average reduction in serum hemoglobin A1c of 2.5% by the 1-year mark, as compared to the group that was tested for 1,5 anhydroglucitol which was 2.27%. The average time elapsed for the group tested for 1,5 anhydroglucitol to reach a significant reduction in hemoglobin A1c was 6.4 months, compared to 7.5 months in the control group.

Statistical Analysis

It was noted the baseline characteristics for both the control group and the group tested for serum 1,5 anhydroglucitol levels were well-matched. The average age of the patient in the control group was noted to be 55.3 years (range of 23-80 years) and the average in the group tested for serum 1,5 anhydroglucitol was 54.4 years (range of 25-75 years). The proportion of male and female in both groups were noted to be constant. The number of type 1 diabetics and type 2 diabetics in both groups were also the same. Baseline hemoglobin A1c at initial endocrinology clinic visit was noted to be 9.1% in the control group and 9.2% in the group tested for 1,5 anhydroglucitol (Table 1).

At least 50% of the control subjects reached the target end-point of significant A1c reduction of at least 0.5% and it was noted 76% of the group tested for serum 1,5 anhydroglucitol were also able to reach this significant reduction (Table 2), however this data was unable to achieve statistical significance. Additionally, examining the distribution of data among type 1 and type 2 diabetics, there was no statistical difference noted between the two populations in either the control group or group tested for serum 1,5 anhydroglucitol for age, gender, or hemoglobin A1c levels at baseline, 6 months or 1 year (Table 3).

Group	N Obs	Variable	N	Mean	Minimum	Maximum
Controls	47	Age	45	55.3	23.0	80.0
		Gender	45	1.4	1.0	2.0
		Type 1 or 2 DM	45	1.9	1.0	2.0
		Baseline Hg A 1c	45	10.0	5.6	15.5
		Base# A 1c intial endoc#vst	44	9.1	5.6	15.5
		First 1 5 Anhydroglucitol level	0	-	-	-
		Hg A 1c 6 months post	44	8.4	5.4	14.3
		Hg A 1c 1 year post	39	8.1	5.4	14.0
		Occurrence 1,5 anhydroglucitol o	0	-	-	-
		Time elapsed for A 1c reduction	44	9.1	6.0	12.0
		Groupon	47	1.0	1.0	1.0
		Censored	44	0.5	0.0	1.0
Glycomark	45	Age	45	54.4	25	75.0
		Gender	45	1.4	1.0	2.0
		Type 1 or 2 DM	45	1.8	1.0	2.0
		Baseline Hg A 1c	45	10.4	5.5	15.5
		Base# A 1c intial endoc#vst	45	9.2	5.1	15.5
		First 1 5 Anhydroglucitol level	44	6.3	0.3	25.0
		Hg A 1c 6 months post	26	8.6	5.4	11.9
		Hg A 1c 1 year post	12	7.9	5.4	12.0
		Occurrence 1,5 anhydroglucitol o	45	1.1	1.0	3.0
		Time elapsed for A 1c reduction	26	6.9	2.0	12.0
		Groupon	45	0.0	0.0	0.0
		Censored	25	0.2	0.0	1.0

Table 1: Baseline Characteristics.

Fisher's Exact Test	
Cell (1,1) Frequency (F)	4
Left-sided Pr <= F	0.2608
Right-sided Pr >= F	0.9017
Table Probability (P)	0. 1625
Two-sided Pr - P	0.5216

Simple size=90; Frequency Missing=2.

Table of Group by A1c reduc#1/2 pct6mos-1yr			
Group	A1c reduc#1/2 pct6mos-1yr		
	N	Y	Total
Controls	22	22	44
	50.00	50.00	
	78.57	53.66	
Glycomark	6	19	25
	24.00	76.00	
	21.43	46.34	
Total	28	41	69
Frequency Missing		23	

Table 2: Fisher's Exact Test.

t-test output comparing two independent means				
Variable	**all**	**Glycomark n=45 mean(std dev)**	**Control n=47 mean(atd dev)**	**p-value**
TYPE 1 09 2 IM	1.88(0.3)	1.84(0.4)	1.91(0.3)	0.3399
BASELINE HG A1C	10.17(2.8)	10.36(2.5)	9.98(3.1)	0.5222
HG A1C 6 MONTHS POST	8.47(2)	8.62(1.8)	8.38(2.2)	0.6373
HG A1C 1 YEAR POST	8.06(1.8)	7.86(1.8)	8.12(1.8)	0.6629
AGE	54.84(12.2)	54.38(12.3)	55.31(12.3)	0.7195
GENDER	1.42(0.5)	1.42(0.5)	1.42(0.5)	1.0000

Table 3: T-test comparing two independent means.

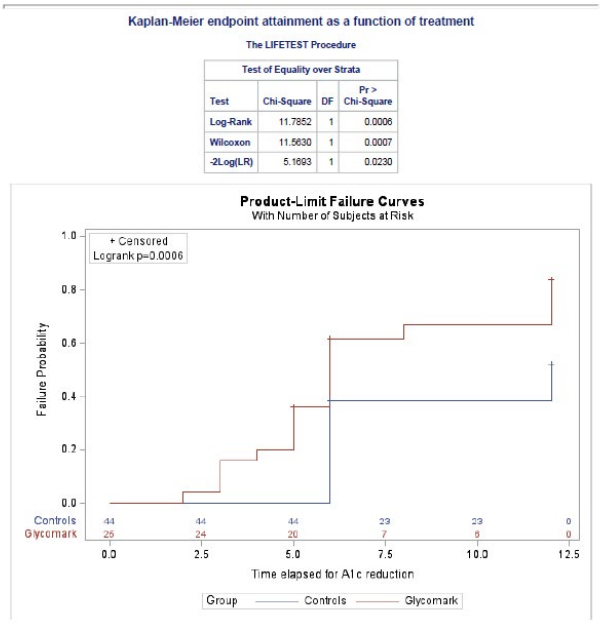

Figure 1: Kaplan Meier endpoint as function of treatment.

As seen in the Kaplan Meier survival curve, the time elapsed to reach a significant hemoglobin A1c reduction for the group tested for serum 1,5 anhydroglucitol was 6.4 months, earlier than the 7.5 months for the control group to achieve significant reduction. This was noted have statistical significance with p-value of 0.0006 (Figure 1).

Discussion

This study was conducted with the goal of applying testing for serum 1,5 anhydroglucitol in the primary clinics as a reliable indicator for glycemic control, in addition to routine hemoglobin A1c testing. As seen in the Kaplan Meier survival curve, there was a significant difference noted in the time elapsed to reach this significant hemoglobin A1c reduction for the group who was tested for serum 1,5 anhydroglucitol as this group was able to achieve a significant reduction earlier than the control group, with p-value of 0.0006 noted.

We acknowledge certain limitations in our study and find that it may be beneficial for further analysis to be conducted with longer follow up data as this was a retrospective chart review over a two-year period. The sample size in this study of patients who were tested for 1,5 anhydroglucitol is small and may be a reason statistical significance could not be reached. However, we can see that there was a steady decline in serum hemoglobin A1c levels for both type 1 and type 2 diabetics after being tested for Glycomark, also known as 1,5 anhydroglucitol. We can also see that that diabetics who were tested for 1,5 anhydroglucitol noted an earlier reduction of serum hemoglobin A1c than their counterparts who were not tested; clinicians can utilize this information to modify treatment options and subsequently have timely interventions for patients.

We believe that testing for 1,5 anhydroglucitol should not replace hemoglobin A1c testing, however it should be used in conjunction with hemoglobin A1c to help guide treatment strategies and is of clinical importance for all clinicians as a reliable indicator of glycemic control.

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