Journal of Clinical & Translational Endocrinology 20 (2020) 100224

Contents lists available at ScienceDirect

Journal of Clinical & Translational Endocrinology

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

Finding the clinical utility of 1,5-anhydroglucitol among primary care practitioners

John Peabody[a,b,c,*], David Paculdo[c], M. Czarina Acelajado[c,d], Trever Burgon[c], Jeffrey R. Dahlen[e]

[a] University of California, San Francisco, United States
[b] University of California, Los Angeles, United States
[c] QURE Healthcare, United States
[d] Athens Limestone Hospital, Athens, AL, United States
[e] Hikari Dx, Inc., San Diego, CA, United States

ARTICLE INFO

Keywords:
Diabetes management
Primary care
1,5 anhydroglucitol
Glycemic variability
Clinical utility

ABSTRACT

Background: HbA1c is widely used as the standard measure to track glycemic control in patients with diabetes and pre-diabetes but measures average levels of glycated hemoglobin over two to three months, with limited utility in the presence of recent and/or short-term fluctuations in glycemic control, which are correlated with worse patient outcomes.

Methods: We examined the clinical utility of 1-5-anhydroglucitol (1,5-AG) in six different, but common, case types of diabetes patients with short-term glycemic variability. We conducted a randomized controlled trial of simulated patients to examine the clinical practice patterns of primary care physicians before and after introducing 1,5-AG. The 145 participants were randomly assigned into standard care or standard care + 1,5-AG arms. Provider care was reviewed against explicit evidence-based care standards.

Results: At baseline, we saw no difference between the two study arms in clinical quality of care provided ($p = 0.997$). After introduction of 1,5-AG, standard care + 1,5-AG providers performed 3.2% better than controls ($p = 0.025$. In diagnosis and treatment, there was a slight, but nonsignificant trend toward better care (+1.1%, $p = 0.507$) for intervention providers. Upon disaggregation by case, almost all the improvement occurred in the medication-induced hyperglycemia patients (+8.1%, $p = 0.047$).

Conclusions: A nationally representative sample of primary care physicians demonstrated that of six different cases used in this study, 1,5-AG was found to be most effective increasing awareness of poor glucose control in medication-induced hyperglycemia. If 1,5-AG is used in this particular circumstance, the overall savings to the healthcare system is estimated to be $28 million.

Introduction

30.3 million (9.4%) of American adults has diabetes, and there are 1.5 million more Americans diagnosed every year. An estimated 7.2 million Americans with diabetes remain undiagnosed [1]. Healthcare spending for people with diabetes is approximately 2.3 times greater than spending without the disease, and about $9600 per year is spent on patients with diabetes.

To increase diagnostic and therapeutic accuracy and to lower costs, the American Diabetes Association and the European Association for the Study of Diabetes have jointly recommended more individualized diabetes evaluation and treatment to prevent unintended harm from poor glycemic control [2,3]. Following individualized glycemic control treatments rather than general recommendations would save almost $14,000 per patient per year [4].

Glycated hemoglobin, specifically hemoglobin A1c (HbA1c), is widely used to measure and track hyperglycemia in patients with pre-diabetes and diabetes. Lower diabetes-related medical care costs are associated with lower HbA1c levels [5]. HbA1c testing measures average levels of glycated hemoglobin over two to three months [6] and thus has limitations in the presence of recent and/or short-term fluctuations in glucose levels that also lead to vascular damage [7]. A recent abstract, for example, indicates that HbA1c underestimates the prevalence of poor glucose control, especially among different races and ethnicities [8].

HbA1c incompletely describes post-prandial and co-morbidity induced glycemic excursions [9,10]. Of equal or greater importance, patients with diabetes may be prescribed drug treatments that increase

* Corresponding author at: 450 Pacific Ave, Suite 200, San Francisco, CA 94133, United States.
E-mail address: jpeabody@qurehealthcare.com (J. Peabody).

https://doi.org/10.1016/j.jcte.2020.100224
Received 23 December 2019; Received in revised form 2 April 2020; Accepted 4 April 2020

insulin resistance and are missed with HbA1c testing [11,12]. HbA1c is also misleading in other conditions such as patients who have just received a blood transfusion or pregnant women. In particular, missing impaired insulin sensitivity due to drug use can lead to excess risk of hypoglycemia, diabetic ketoacidosis and coma [11].

One test, which has been widely available since it was approved for short-term glucose monitoring by the FDA in 2003 is 1-5-anhydroglucitol (1,5-AG). 1,5-AG is sensitive to changes in glycemic control for the prior one to two weeks and is used in diabetes disease management to uncover early changes in glycemic control and post-prandial glucose excursions. Low 1,5-AG (< 6.0 μg/mL) is predictive of an increased risk of coronary heart disease, stroke, heart failure, and death, even after adjusting for Hb1Ac [13].

Introducing another glucose measure beyond Hb1Ac to manage diabetes and recommend treatment could uncover the populations of patients with recent changes in their glycemic control and positively contribute to more individualized glycemic control for patients with diabetes otherwise missed by HbA1c. 1,5-AG testing does not require fasting and it reveals poor glycemic control in the preceding weeks and glycemic excursions not typically reported through Hb1Ac measurement. We report on the prospective GLUCAR (GLUcose Control using 1,5-Anhydroglucitol Randomized) trial on a group of simulated patients to see if we could experimentally determine whether using this diabetes diagnostic tool increases the clinical recognition and improves the treatment of type II diabetes mellitus with poor, short-term glycemic control.

Methods

The GLUCAR clinical trial of clinical care was conducted between November 2018 and February 2019. Using simulated patients, we examined how primary care physicians (PCPs) cared for patients with diabetes in the United States before and after introducing a new biomarker test for hyperglycemia that measures 1,5-AG. We collected two rounds of clinical data on diabetes diagnosis, disease stage categorization, and recognition of complications due to diabetes with and without the new biomarker test. To control for patient variability and focus on physician practice in this study, all participants cared for the same six Clinical Performance and Value (CPV) vignettes—a validated, online patient simulation platform [14,15]. In each round, physicians cared for three of the patient simulations, who present with short term changes in their glucose control from various causes: glycemic excursions due to either postprandial hyperglycemia requiring an increase in their hypoglycemic therapy (case #1) or post prandial hypoglycemia requiring a decrease in oral hypoglycemic agents (OHA, case #2) or their insulin (case #3), hyperglycemia following the initiation of steroid therapy (i.e., prednisone in case #4) or anemia treated with a transfusion (case #5), and gestational diabetes (case #6). Using these 6 simulated CPV cases, we determined whether use of the 1,5-AG test changed the quality of the overall care, diagnosis and/or treatment.

Ethics

This study was conducted in accordance with ethical standards, approved by the Advarra Institutional Review Board, Columbia, MD, and listed in clinicaltrials.gov (NCT03765164). We obtained informed consent from all study participants.

Physician selection

From a list of over 25,000 practicing PCPs, we randomly recruited a nationally representative (regional geography, age, gender, and practice size) sample of 156 physicians in the first round. From this group, 145 physicians completed the second round. To be eligible for participation, physicians had to be: (1) be board-certified in either internal or family medicine, (2) have between two and 40 years of post-residency or post-fellowship practice, (3) have an active panel of patients and see at least 40 patients per week, and (4) have at least 15% of their patients receiving diabetes care. If the physician met the eligibility criteria and completed a six-question questionnaire, the physician would be invited to participate. Participants were randomized into two groups, control and intervention, with a 1:1 ratio. The intervention was delivered approximately three weeks after the first round was completed. The intervention included review of the following five materials: (1) an on-demand, online video of the 1,5-AG test, (2) a test results interpretation guide, (3) example test results, (4) an example case study, and (5) a test brochure. We tracked participant review of all materials. Approximately two weeks after the intervention group received education materials, all providers received three more simulated patients with similar characteristics as those in the first round.

Clinical performance and value (CPV) cases

CPV vignettes are a well-known patient simulation platform that have been validated against standardized patients and known to reflect actual clinical care [14,16]. Over the past two decades, CPV patients have been used to evaluate and compare clinical practice of physicians and other clinical providers [17–19]. Vignette scores that improve 3–5% over time are known to be clinically significant, reflecting actual change in real patients [20]. The vignette is open-ended, and the CPVs are divided into five domains of care: (1) taking a history, (2) performing a physical, (3) ordering diagnostic workup, and (4) making a diagnosis with (5) a treatment plan and follow-up.

A team of physicians designed each case to resemble a typical patient with diabetes visiting their PCP to better understand how their short-term glycemic control affects diagnosis and treatment (diagnosis + treatment). Before starting on treatment, each vignette queried the PCP, asking if they felt that based upon the work up and their diagnosis if they felt that the patient was under good glycemic control. Each vignette had between 61 and 81 evidence-based criteria evaluated. Two independent physician scorers use explicit, pre-determined criteria with a third physician adjudicating in the case of a disagreement on any of the individual criteria to measure physician care. With these measurements, an overall score and a care score in three specific clinical domains: ordering diagnostic workup, making the diagnosis, and developing and outlining a treatment plan for these diabetes case types.

Analysis

The primary outcome was to determine whether use of the 1,5-AG demonstrated clinical utility and improved patient care through (a) better identification of the etiology of the short-term changes in glycemic control, (b) better treatment of the patient, and (c) appropriate changes in medication management in response to the glycemic excursions within the three case types noted above. We also wished to know whether providers correctly understood the level of glycemic control of their patients. For categorical outcome outcomes, we used Fisher's exact test and logistic regression for multivariate modeling. For analyses involving continuous outcomes, *t*-tests and linear regression modeling were performed. All analyses were performed in Stata 14.2.

Results

A total of 145 board-certified family or internal medicine primary care physicians met the eligibility criteria and completed both rounds of data collection (Table 1). At baseline the two groups had similar demographic characteristics. The modal practitioner was male, specialized in internal medicine, practiced in a suburban setting, was between the ages of 40 and 55, had 21.2 years of experience, and had just more than 30% of their patients with diabetes.

Prior to introducing the 1,5-AG test, there was no significant

Table 1
Physician characteristics.

	Control	Intervention	p-Value
N	73	72	–
Male	84.9%	75.0%	0.151
Internal Medicine	54.8%	50.0%	0.619
Age Group			
< 40	6.9%	4.2%	0.619
40–55	61.6%	58.3%	
> 55	31.5%	37.5%	
Region			
Midwest	27.4%	18.1%	0.345
Northeast	23.3%	18.1%	
South	30.1%	41.7%	
West	19.2%	22.2%	
Practice locale			
Urban	19.2%	33.3%	0.101
Suburban	61.6%	45.8%	
Rural	19.2%	22.2%	
Practice setting (providers could select more than one)			
ACO and/or HMO	19.2%	16.7%	0.829
Private practice, solo or group	91.8%	88.9%	0.587
Hospital/Int Delivery	8.2%	15.3%	0.207
Other	0.0%	0.0%	1.000
Employed by practice	69.9%	76.4%	0.455
Receive quality bonus	43.8%	54.2%	0.246
Years in practice	21.0 + 6.6	21.3 + 6.2	0.745
Active panel size	3027 + 1413	3069 + 1403	0.856
Patients with diabetes	30.7% + 15.0%	32.7% + 17.6%	0.454

difference in the way the two groups cared for the six simulated patients. Their overall quality scores, which reflected their adherence to evidence-based practice, was similar (50.9% for controls vs. 51.4% for intervention, p = 0.594) and, as has been reported elsewhere, there was wide variation in their practice as a group (Peabody, et al 2019). When we looked at their performance in more detail, diagnostic accuracy was similar in the two groups (80.1% for intervention vs 84.5% for controls, p = 0.259), as was their ability to diagnose the etiology of the poor glycemic control (35.2% vs. 36.5%, p = 0.842).

After introduction of the 1,5-AG test, the overall quality of care improved 2.7% in the intervention group versus controls (p = 0.070) (Table 2). In a multivariate regression model, which controlled for physician, practice, and patient characteristics, the overall quality score among the intervention providers was +3.2% higher (p = 0.025) (Table 3). Among all of the cases, we found that 1,5-AG was most helpful in patients started on prednisone (case #4), with intervention providers scoring +11.2% higher than controls (p = 0.001). When we aggregated two cases (#2 and #3) where the patient was experiencing hypoglycemia, 1,5-AG testing improved the overall quality score by 4.9% (p = 0.040). However, when we examined the changes in our primary outcomes (identification of etiology and appropriate changes in medication management), we found few significant differences. In case #3, where the patient had morning hypoglycemia, we found intervention providers improved in the difference-in-difference for these primary outcomes, but significantly only for etiology (etiology: +43.9%, p = 0.006; medication change: +13.1%, p = 0.347).

We then looked at the final primary outcome: whether care improved in the diagnosis + treatment domains with intervention. Across all cases, scores modestly improved but this was not statistically or clinically significant (+0.5%, p = 0.507). By case type, the only statistical (and clinical) improvement (+8.8%, p = 0.031) was seen in case #4 (prednisone induced hyperglycemia) indicating that, while it helped clarify care here, 1,5-AG test results did not more generally make a significant difference in the other cases of poor short-term glycemic control we investigated. In cases 2 and 3, where we saw significant improvements in overall quality scores, we found no significant improvements for either case (case 2: +8.9%, p = 0.079 and case 3: +0.4%, p = 0.912).

Based upon this, we examined whether use of the 1,5-AG results improved the accuracy of identifying the underlying etiology of the poor short-term glycemic control. At study outset, both control and intervention providers were similarly challenged in determining the underlying etiology (36.5% for control and 35.2% for intervention, p = 0.842). Post-intervention, both study arms improved and, in a

Table 2
CPV results for selected items.

	Control	Intervention	p-value	difference-in-difference p-value
Round 1	50.9% + 10.0%	51.4% + 11.1%	0.594	0.070
Round 2	48.9% + 10.8%	52.1% + 12.3%	0.003	
p-value	0.041	0.548		
Diagnosis-treatment performance				
Round 1	29.1% + 12.3%	31.7% + 13.4%	0.031	0.070
Round 2	31.9% + 12.2%	35.0% + 15.0%	0.018	
p-value	0.018	0.018		
Diagnosis of diabetes				
Round 1	84.5%	80.1%	0.259	0.889
Round 2	94.1%	91.7%	0.357	
p-value	0.002	0.001		
Diagnosis of etiology				
Round 1	36.5%	35.2%	0.842	0.483
Round 2	40.6%	44.0%	0.498	
p-value	0.432	0.076		
Glycemic control				
Round 1	44.8%	44.4%	1.000	0.001
Round 2	44.3%	24.1%	< 0.001	
p-value	1.000	< 0.001		
Primary medical treatment				
Round 1	57.5%	62.0%	0.379	0.798
Round 2	61.6%	64.4%	0.620	
p-value	0.436	0.690		
Unnecessary workup, #				
Round 1	0.8 + 1.1	1.0 + 1.3	0.220	0.053
Round 2	0.8 + 1.1	0.6 + 1.0	0.087	
p-value	0.897	0.003		
Unnecessary workup, $				
Round 1	$54 + $100	$78 + $156	0.056	0.003
Round 2	$60 + $116	$37 + $87	0.019	
p-value	0.554	< 0.001		

Table 3
The impact of 1,5-AG on overall and diagnosis + treatment scores.

	Total Score		Diagnosis + Treatment	
	Coefficient	p-value	Coef.	P > t
Male	−1.9	0.039	−2.2	0.047
Internal medicine	−3.9	0.000	−3.2	0.000
Age < 40	−6.0	0.001	−6.5	0.002
South region	2.8	0.000	1.3	0.162
Urban practice	3.5	0.000	2.7	0.008
ACO/HMO practice	4.4	0.000	4.2	0.000
Hospital practice	7.4	0.000	13.1	0.000
Male CPV patient	5.6	0.000	8.7	0.000
CPV patient age < 60	−3.3	0.007	0.7	0.647
Case Type				
Post-prandial excursion	Ref.	–	Ref.	–
Medication changes	0.4	0.753	−3.2	0.018
Co-morbidity	5.5	0.000	0.0	0.979
Round 2	−2.0	0.044	2.9	0.013
Intervention arm	−1.3	0.193	0.6	0.605
Round 2 * Intervention	3.2	0.025	1.1	0.507
Constant	48.4	0.000	26.0	0.000

Table 4
The impact of 1,5-AG on correctly identifying etiology and primary treatment.

	Etiology 95% C.I.			Primary Treatment 95% C.I.		
	O.R.	Lower	Upper	O.R.	Lower	Upper
Male	1.1	0.7	1.6	1.3	0.9	1.9
Internal medicine	0.9	0.7	1.3	0.9	0.6	1.2
Age < 40	0.6	0.3	1.2	0.6	0.3	1.2
South region	1.3	0.9	1.8	1.2	0.8	1.6
Urban practice	1.0	0.7	1.4	0.9	0.6	1.3
ACO/HMO practice	1.5	1.0	2.2	1.3	0.9	1.9
Hospital practice	1.8	0.8	4.1	3.7	1.4	9.5
Male CPV patient	1.0	0.7	1.5	3.1	2.1	4.4
CPV patient age < 60	0.1	0.0	0.2	0.3	0.2	0.5
Case Type						
Post-prandial excursion	Ref.	–	–	Ref.	–	–
Medication changes	2.0	1.3	3.2	0.9	0.6	1.5
Co-morbidity	36.7	16.8	80.1	2.9	1.6	5.3
Round 2	1.2	0.8	1.8	1.2	0.8	1.8
Intervention arm	0.9	0.6	1.4	1.1	0.7	1.7
Round 2 * Intervention	1.3	0.7	2.3	1.0	0.6	1.8
Constant	0.3	0.2	0.6	0.7	0.4	1.2

difference-in-difference calculation, we found that intervention providers improved +4.7%, but this did not prove significant (p = 0.483) (Table 2). In the multivariate logistic model, we also found no difference in the intervention group's ability to diagnose the etiology of the glycemic variability compared to control (O.R. 1.3, 95% C.I. 0.7–2.3) across all cases (Table 4). In case #3, however, we did we see a significant difference, with intervention providers using 1,5-AG more likely to ascertain the correct etiology compared to controls (O.R. 7.3, 95% C.I. 1.8–30.2). Similarly, we wanted to determine if testing with 1,5-AG led to correctly modifying the patient's hypoglycemic agents. Intervention providers did not perform better than control providers (O.R. 1.0, 95% C.I. 0.6–1.8) either overall or by individual case type, where we found no significant difference between the groups (Table 4).

Next, we ran another regression analysis, adding ordering of HbA1c as an explanatory variable to the model. Ordering HbA1c was associated with higher overall quality (+6.8%, p < 0.001) and diagnosis + treatment (+3.7%, p = 0.003), but it was not linked with an improvement in determining the etiology (O.R. 0.7, 95% C.I. 0.5–1.1) or correctly changing the patient's hypoglycemic medications (O.R. 1.3, 95% C.I. 0.9–2.0). Ordering HbA1c testing made directional positive but statistically insignificant improvements in the effectiveness of the 1,5-AG. Above and beyond HbA1c testing, those that ordered 1,5-AG testing had a higher overall score (+2.7%, p = 0.044), were better at diagnosis + treatment (+0.9%, p = 0.592), were more able to identify the etiology (O.R. 1.3, 95% C.I. 0.7–2.4), and correctly adjusted medications (O.R. 1.0, 95% C.I. 0.6–1.8).

Lastly, we went back to the survey and looked at the provider's perception of their patient's glycemic control collected at the end of each case. In the intervention group, those that had the 1,5-AG test results were more aware that their patients were poorly controlled, 75.9% in the 1,5-AG versus 55.7% in the control group. This is seen particularly in case #4 (the patient put on prednisone) (57.1% vs 20.0%, p = 0.003) and case #5 (s/p transfusion) (67.5% vs 21.2%, p = 0.001) and #6 (gestational diabetes) (67.5% vs. 32.5%, p = 0.003).

Discussion

Diabetes management is both highly variable and dependent on measuring HbA1c levels [21,22]. In certain patients, with short term or recent changes in their glycemic control, relying on a test that provides a 3-month average of glycemic control is unlikely to help when patients with wide swings in their glucose control, for example after eating or in patients with a recent change in their clinical status, such as the addition of a steroid, a transfusion, or pregnancy.

The GLUCAR study used six simulated patients to determine if testing with 1,5-AG would lead to better overall care, recognition of poor glycemic control or change in treatment. 1,5-AG, 510(k)-cleared by the FDA in 2003, is an attractive test for these patients. The test is sensitive to changes in glycemic control for the prior one to two weeks, uncovers early changes in glycemic control, and is predictive of an increased risk of coronary heart disease, stroke, heart failure, and death, even after adjusting for Hb1Ac [13].

In this prospective randomized controlled design, we found that 1,5-AG modestly improved the overall quality of care for all patients. The 3.2% (p = 0.025) improvement is clinically significant [17]. By case, providers found that 1,5-AG testing was most helpful in patients that were started on prednisone and to a lesser degree post-prandial hypoglycemia requiring a decrease in medications, but while these two cases met the statistical threshold of p < 0.05, this was not true for the other cases. 1,5-AG was also helpful in determining the etiology and improving the diagnosis and treatment in medication-induced hyperglycemia. Interestingly, providers that used 1,5-AG were significantly more likely to be aware that their patients had poor glycemic control. Another interesting but non-statistical finding is that providers that ordered a HbA1c and a 1,5-AG did better than controls on several outcome measures.

Diabetes management is multifactorial and we previously demonstrated that significant heterogeneity exists among physicians in how they manage diabetes [22]. We hypothesized that there would be a stronger impact from 1,5-AG testing for all of the cases with poor short-term glycemic control, but we found that the addition of a single blood test, did not resolve all the ambiguities of diabetes management. 1,5-AG has been previously described as having benefit in identifying hyperglycemic excursions that are not evident with HbA1c testing. Accordingly, we found that 1,5-AG testing was helpful in the case with (steroid) medication-induced hyperglycemia. Use of prednisone is clinically ubiquitous in the outpatient setting [23]. In the other cases of poor glycemic control, there was a positive trend but the effect was modest and failed to reach statistical significance. In cases with hypoglycemia (#2 and #3), 1,5 AG, based upon the results above, did not provide additional benefit. Other studies may be helpful to increase our understanding of the benefits of 1,5-AG testing. This would include evaluating other common medications that are associated with increased rates of hyperglycemia and glycosuria such as second-generation antipsychotics, fluoroquinolone antibiotics and benzodiazepines. Clinically, doctors are particularly concerned with post-prandial glycemic excursions [24]. These patients, as reflected in case #1, may need more hypoglycemic agents or they may need less, as reflected in case #2. Based upon our findings, we recommend confirmatory studies involving medication induced hyperglycemia and more providers to see if there is statistical and clinical effect on cases of post prandial hyperglycemia.

If true, the economic benefits from 1,5-AG testing in diabetes patients with medication changes are potentially significant. We know that in the United States there are 23.1 million people diagnosed with diabetes and an additional 7.2 million who are undiagnosed [1]. If we assume 1 in 20 of the known patients with diabetes and one-half of the patients with undiagnosed diabetes have some glycemic variability, then this means roughly 4.8 million people in the United States have poorly controlled glycemia. From other studies, we know that fair—as opposed to excellent—control costs approximately $292 more in healthcare costs annually [5]. If we can assume that 2% of this population has been prescribed a medication that increases insulin resistance and that the clinical outcomes of patients with glycemic variability are similar to patients whose glycemic control is fair (as opposed to excellent), this amounts to an added cost of approximately $28 million (=4,800,000 * 2% * $292) to the healthcare system.

This study demonstrated why there is widespread interest in measuring clinical utility using simulated patients [25]. Utility studies that solely rely on patient outcomes are expensive and subject to unobserved biases that will mislead payers [26]. Simulated patients control for patient variability, focus on whether provider practice has changes and control for unobserved heterogeneity [16]. Simply put, if the GLUCAR study design had been carried out using real patients instead of simulated patients, it would have cost millions of dollars to reach the same conclusion. Payers insensitive to these costs and unwilling to trust modeling and simulations risk thwarting diagnostic, drug and device advances while harming the innovators they seek to encourage [27].

This study has a number of important limitations. Due to the significant heterogeneity in diabetes management and multitude of treatment options available to physicians, it is possible that the study was underpowered, and a larger sample size might have revealed that the positive trends we saw were statistically significant. While the effect size of 3% was small, incrementally improving care in such an important and large group of patients would be helpful and 1,5-AG did improve overall care quality. We did not formally test if other tests of short-term glycemic control, such as fructosamine and glycated albumin, had a similar effect. While physicians could have ordered these tests within the context of the cases they evaluated, they did not. Our beneficial findings are potentially tempered by the timing of the test: detectable change in 1,5 AG could be encumbered by access to testing but they also might be enhanced by patient self-monitoring. Future research would, ideally include a sensitivity analysis to determine if the treatment changes associated with 1,5-AG testing were tempered or enhanced by self-monitoring of blood glucose and access to care after steroid treatment. Although efforts were made to match the demographics of practicing PCPs in the United States, our final participant population could have been systematically different from the population at large. Another shortcoming is that although we attempted to test a wide range of common patient presentations, there are other, untested presentations where the effect of 1,5-AG would be more pronounced.

HbA1c is a proven useful measure to determine long-term glycemic control. What is equally clear, is that HbA1c is unhelpful in patients with recent glycemic changes. This study shows that physicians struggle to recognize and treat these patients. The addition of 1,5-AG did not prove helpful in all of the patient types but it increased physician awareness of poor control and consistently helped in medication induced hyperglycemia due to steroid use.

Disclosures

CPV Technologies, LLC, owns the intellectual property used to prepare the cases and QURE, LLC collected the data. This study was funded by GlycoMark, Inc., New York, NY. Otherwise, there are no conflicts to disclose.

CRediT authorship contribution statement

John Peabody: Conceptualization, Formal analysis, Investigation, Methodology, Writing - original draft, Writing - review & editing. **David Paculdo:** Formal analysis, Methodology, Software, Validation, Writing - original draft, Writing - review & editing. **M. Czarina Acelajado:** Methodology, Resources, Writing - review & editing. **Trever Burgon:** Project administration, Supervision, Writing - original draft, Writing - review & editing. **Jeffrey R. Dahlen:** Conceptualization, Funding acquisition, Resources, Writing - review & editing.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcte.2020.100224.

References

[1] American Diabetes Association. Statistics about diabetes. Accessed Feb 2019. Available at: http://www.diabetes.org/diabetes-basics/statistics/.
[2] Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care 2012;35(6):1364–79. https://doi.org/10.2337/dc12-0413.
[3] Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position Statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2015;38(1):140–9. https://doi.org/10.2337/dc14-2441.
[4] Laiteerapong N, Cooper JM, Skandari MR, Clarke PM, Winn AN, Naylor RN, et al. Individualized glycemic control for U.S. adults with type 2 diabetes. A cost-effectiveness analysis. Ann Intern Med 2018;168:170–8. https://doi.org/10.7326/M17-0537.
[5] Esposti LD, Saragoni S, Buda S, Sturani A, Esposti ED. Glycemic control and diabetes-related health care costs in type 2 diabetes; retrospective analysis based on clinical and administrative databases. Clinicoecon Outcomes 2013;5:193–201. https://doi.org/10.2147/CEOR.S41846.
[6] WebMD. The Hemoglobin A1c test for diabetes. Accessed February 2019. Available at: https://www.webmd.com/diabetes/guide/glycated-hemoglobin-test-hba1c.
[7] Selvin E, Rawlings AM, Grams M, Klein R, Steffes M, Coresh J. Association of 1,5-anhydroglucitol with diabetes and microvascular conditions. Clin Chem 2014;60(11):1409–18. https://doi.org/10.1373/clinchem.2014.229427.
[8] Chang Villacreses M, Feng W, Karnchanasorn R, Samoa R, Chiu KC. Underestimation of the Prevalence of diabetes and overestimation of the prevalence of glucose tolerance by using hemoglobin A1c Criteria. Presented at ENDO 2019 of the Endocrine Society; March 23–26, 2019; New Orleans, LA. Poster #SAT-125.
[9] Suh S, Kim JH. Glycemic variability: how do we measure it and why is it important? Diabetes Metab J 2015;39(4):273–82.
[10] Tay J, Thompson CH, Brinkworth GD. Glycemic variability: assessing glycemia differently and the implications for dietary management of diabetes. Annu Rev Nutr 2015; l:389-424.
[11] Rehman A, Setter SM, Vue MH. Drug-induced glucose alterations part 2: drug-induced hyperglycemia. Diabetes Spectrum 2011;24(4):234–8.
[12] Vue MH, Setter SM. Drug-induced glucose alterations part 1: drug-induced hypoglycemia. Diabetes Spectrum 2011;24(3):171–7.
[13] Selvin E, Rawlings AM, Lutsey P, Maruthur N, Pankow J, Steffes M, et al. Association of 1,5-anhydroglucitol with cardiovascular disease and mortality. Diabetes 2016;65(1):201–8. https://doi.org/10.2337/db15-0607.
[14] Peabody J, Luck J, Glassman P, Dresselhaus TR, Lee M. Comparison of vignettes, standardized patients, and chart abstraction: a prospective validation study of 3 methods for measuring quality. JAMA 2000;283(13):1715–22.
[15] Peabody J, Luck J, Glassman P, Jain S, Hansen J, Spell M, et al. Measuring the quality of physician practice by using clinical vignettes: a prospective validation study. Ann Intern Med 2004;141(10):771–80.
[16] Dresselhaus TR, Peabody JW, Lee M, Wang MM, Luck J. Measuring compliance with preventive care guidelines: standardized patients, clinical vignettes, and the medical record. J Gen Intern Med 2000;15(11):782–8.
[17] Burgon TB, Cox-Chapman J, Czarnecki C, et al. Engaging primary care providers to reduce unwanted clinical variation and support ACO cost and quality goals: a unique provider-payer collaboration. Popul Health Manage 2018;0;0 doi:10.1089.pop.2018.0111.
[18] Luck J, Peabody JW, Dresselhaus TR, Lee M, Glassman P. How well does chart abstraction measure quality? A prospective comparison of standardized patients with the medical record. Am J Med 2000;108(8):642–9.
[19] Bergmann S, Tran M, Robison K, et al. Standardising hospitalist practice in sepsis and COPD care. BMJ Qual Saf 2019; pii: bmjqs-2018-008829.
[20] Quimbo S, Wagner N, Florentino J, Solon O, Peabody JW. Do health reforms to improve quality have long-term effects? Results of a follow-up on a randomized policy experiment in the Philippines. Health Econ 2016;25(2):165–77.
[21] Parrinello CM, Selvin E. Beyond HbA1c and glucose: the role of nontraditional glycemic markers in diabetes diagnosis, prognosis, and management. Curr Diab Rep 2014;14(11):548.
[22] Peabody JW, de Belen E, Dahlen JR, Acelajado MC, Tran MT, Paculdo DR. Variation in diabetes management: A national assessment of primary care providers. J Diabetes Sci Technol 2019. https://doi.org/10.1177/1932296819861662.
[23] Overman RA, Yeh JY, Deal CL. Prevalence of oral glucocorticoid usages in the United States: a general population perspective. Arthritis Care Res (Hoboken) 2013;65(2):294–8.
[24] American Diabetes Association. Postpranidal blood glucose. Diabetes Care 2001;24(4):775–8.
[25] Peabody JW, Strand V, Shimkhada R, Lee R, Chernoff D. Impact of rheumatoid arthritis disease activity test on clinical practice. PLoS ONE 2013;8(5):e63215.
[26] Peabody J, Martin M, DeMaria L, et al. Clinical utility of a comprehensive, whole genome CMA testing platform in pediatrics: a prospective randomized controlled trial of simulated patients in physician practices. PLoS ONE 2016;11(12):e0169064.
[27] Peabody JW, Shimkhada R, Tong KT, Zubiller MB. New thinking on clinical utility: hard lessons for molecular diagnostics. Am J Manage Care 2014;20(9):750–6.