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The use of predialysis glucose as long term glycemic marker in hemodialysis patients

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ABSTRACT

Aim: The major cause of chronic renal disease (CRD) is diabetes mellitus (DM). Although there are some other long term glycemic markers available, HbA1c remains the gold standart in CRD. In this study we aimed to explore the relation between average predialysis glucose and HbA1c levels.

Material and Method: 101 diabetic hemodialysis patients from two centers were included in this study. Last 2 and 3 months' average predialysis glucose levels were obtained. After 3 months, HbA1c levels were also studied.

Results: A significant and strong correlation between HbA1c and both 2 and 3 months' average predialysis glucose levels were found ($p<0.001$ and $R=0.700$, $p<0.001$ and $R=0.727$, The average of last 2 and respectively). Median of estimated glucose levels [146 (85-269) mg/dl] was lower than both median average of 3 months' predialysis glucose [172.6 (80-396) mg/dl] and median average of 2 months' predialysis glucose [180.5 (73-407) mg/dl] levels. Hb levels were not statistically different after grouping for HbA1c ≥7% and HbA1c <7%.

Conclusion: 3 months' predialysis glucose levels are strongly correlated with HbA1c levels. Although there are long term glycemic markers available, average predialysis glucose is an easy, cheap and reachable method for glycemic control.

Keywords: Predialysis glucose, HbA1c, long term glycemic marker, chronic renal disease, hemodialysis

INTRODUCTION

Chronic renal disease (CRD) is frequent in general population. 8-18% of adult population are estimated to have CRD (1). The major cause of CRD is diabetes mellitus (DM) and 20-40% of patients with DM developes CRD (2,3). 30-50% of end stage renal disease is considered to be secondary to DM (4). Glycemic control is crucial, for it predicts the morbidity and mortality of patients with diabetic renal disease (5). Glycated hemoglobin, known as hemoglobin A1c (HbA1c), is the most commonly used long term glycemic marker, which reflects the mean blood glucose during the preceeding 8-12 weeks (6). HbA1c is used for decades to assess the glycemic control in diabetic patients as a gold standard (7). Though, some limitations seems to affect the usage of HbA1c in individuals with CRD. Anemia, which is frequent in CRD, may alter HbA1c values. Anemia is mainly due to inadequate production of erythropoietin in CRD. Erythropoietin deficiency along with or without iron and vitamin B12 deficiency lead to increased circulating aged red blood cells, resulting in increased HbA1c levels due to long term exposure of glucose (8,9). Besides, acidosis due to CRD results in increased glycation (10). On the other hand, anemia treatment with iron and erythropoiesis stimulating agents leads to circulating immature red blood cells, which in turn causes decreased levels of HbA1c values (11). Although continuous glucose monitoring (CGM) as well as some other biomarkers of long term glycemic control like fructosamine (FA), glycated albumin (GA) and 1,5-anhydroglucitol (1,5-AG) are available, HbA1c is still widely used because of its low cost, best studied nature and availibility at all around the world. Indeed, Kidney Disease Improving Global Outcome (KDIGO) and American Diabetes Association (ADA) guidelines are recommending to use HbA1c for long term glycemic control (12,13). Despite the well documented relationship between fasting plasma glucose and HbA1c values in non-CRD diabetic individuals, it seems to be altered as renal disease progresses (14).

In this study we aimed to explore the relation between predialysis glucose and HbA1c values in hemodialysis patients.

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MATERIAL AND METHOD

This study was approved by KTO Karatay University Faculty of Medicine, Non-Pharmaceutical and Medical Device Researchs Ethics Committee Presidency (Date: 08.06.2021, Decision No: E-41901325-050.99-10015-006). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study was performed in two hemodialysis center. 101 diabetic patients who were on hemodialysis at least for 3 months were included in this study. Patients who were under 18 years old, who undergone major surgery, who had active hemorrhage or had blood transfusion in last 3 months were excluded. Patient characteristics like age, gender, dialysis vintage were noted. Weight and height of every patient were obtained to calculate body mass index as kg/m2. Serum glucose, creatinine, blood urea nitrogen, calcium, phosphorus, potassium, sodium, albumin, C-reactive protein (CRP), parathormone (PTH), ferritin, bicarbonate, uric acid, triglyceride (TG), cholesterol and complete blood cell count samples were obtained predialysis and were measured using automated and standardized methods. Serum glucose levels were obtained from routine monthly laboratory tests as spot glucose which was not related with previous meal. Last 3 months' serum glucose levels were used to calculate last 3 and 2 months' average predialysis glucose. HbA1c was measured at the end of 3 months. Glucose measurements were done by Roche COBAS 8000 c 702 module and HbA1c measurements by Arkray ADAMS HA-8180V system. Estimated average glucose was calculated by eAG= 28.7 x HbA1c- 46.7 formula (15).

The statistical analysis were done by SPSS (Statistical Package for the Social Sciences, SPSS Inc, Chicago, IL, USA.) for Windows version 22. After Kolmogorow-Smirnov normality test, correlation was done by Pearson correlation for parametric and Spearman correlation for non-parametric variables. Mann-Whitney U test was performed for non-parametric variables. A p value of <0.05 was considered statistically significant.

RESULTS

101 diabetic hemodialysis patients with a mean age of 62.79±12.40 were studied. 51 (%50.50) were men. Patient characteristics are shown in **Table 1**. Median HbA1c was 6.7% (4.6-11.0), median of estimated glucose levels according to HbA1c was 146 (85-269) mg/dl, median average of 3 months' predialysis glucose was 172.6 (80-396) mg/dl, median average of 2 months' predialysis glucose was 180.5 (73-407) mg/dl and median BMI was 27.31 (14.67-41.72) kg/m2. 2 and 3 months' average predialysis glucose levels were significantly positively correlated with estimated glucose according to HbA1c (p=0.000, R=0.700 and p=0.000, R=0.727 respectively) (**Table 2**). 2 and 3 months' average glucose levels were significantly positively correlated (p=0.000, R=0.946). HbA1c levels were significantly positively correlated with BMI (p=0.025, R=0.222), CRP (p=0.016, R=0.240) and TG levels (p=0.047, R=0.198). There were no difference between gender and in terms of HbA1c, 2 and 3 months' average glucose levels. After grouping HbA1c for ≥7% and <7%, there were no difference in terms of Hb levels [11.5 (8.1-13.9) and 11.25 (8.1-14.4) respectively, p=0.445].

Table 1. Patient characterisitics

Parameter	Mean values
Age (years)	62.97±12.40
Dialysis vintage (months)	50.71±1.38
Body mass index (kg/m²)	27.46±5.49
Hemoglobin (g/dl)	11.17±1.38
Albumin (g/dl)	3.82±0.39
Ferritin (µg/l)	609.15±455.04
Calcium (mg/dl)	8.44±0.62
Phosphorus (mg/dl)	4.97±1.29
Parathormone (µg/l)	390.12±358.14
C reactive protein (mg/l)	13.00±19.41
Triglyceride (mg/dl)	194.11±113.93

Table 2. Correlation of predialysis glucose with HbA1c.

Parameters	p and R value of correlation
2 months' average glucose	p<0.0001, R=0.700
3 months' average glucose	p<0.0001, R=0.726

DISCUSSION

In this study, predialysis glucose levels were found to be significantly positively correlated with HbA1c in diabetic hemodialysis patients. Both 3 and 2 months' average predialysis glucose levels were compatible with HbA1c. Estimated glucose was found to be lower than measured average 2 and 3 months' average predialysis glucose levels.

There are new long term glycemic control markers. Especially CGM seems to be a promising method in dialysis population (16). But its cost and inavailibility limits the use of CGM. Although affected by many parameters, HbA1c is still widely used to monitor long term blood sugar control in diabetic hemodialysis patients.

Sayed et al. (17) obtained 54 spot capillary blood glucose readings during 3 months and they calculated the mean glucose value of each patient. They showed that measured and expected HbA1c were significantly different among hemodialysis patients with DM. However the number of participants was low, as only 45.

In an another study of George et al. (18), HbA1c levels were found to be significantly correlated with fasting

plasma glucose in stage 3-5 CRD patients. They claimed that the association between fasting glucose and HbA1c decreased as renal disease progressed. However, this study did not include hemodialysis patients or previously known diabetic patients.

Speeckaert et al. (11) reviewed different long term glycemic markers in dialysis patients with DM. HbA1c was compared with GA, FA, 1,5-AG and CGM. They recommended the use of HbA1c as long term glycemic marker in dialysis patients because of its availibility and the other long term markers were insufficient to prove superiority.

Similarly, in the review of Copur et al. (9), the use of CGM and HbA1c was found to be valid as long term glycemic control markers in CRD patients. The latter was more favoured because of its availibility and best studied nature.

In the meta-analysis of Wang et al. (19), the strength of CGM in diabetic patients on dialysis was investigated. They found a significant positive correlation between CGM and HbA1c.

Hayashi et al. (20) studied 97 hemodialysis patients with DM. They were enrolled to a 72 hours CGM. HbA1c and GA samples were obtained thereafter. They found a better relation between HbA1c and CGM, rather than GA. They also concluded that HbA1c were found to be underestimated comparing to average glucose levels.

Watanabe et al. (21), investigated the relation of serum glucose levels with HbA1c and GA on 71 peritoneal dialysis patients. They found that serum glucose levels of both diabetic and non-diabetic peritoneal dialysis patients were significantly correlated with HbA1c, but not correlated with GA.

CGM was done on 80 diabetic chronic kidney disease patients in the study of Presswala et al. (22). HbA1c was significantly correlated with continuous glucose monitoring. HbA1c was found to be a more reliable method compared to fructosamine in diabetic CRD patients.

In the glycemic indices in dialysis evaluation (GIDE) study, Williams et al. (23) investigated long term glycemic markers on 1758 diabetic end stage renal disease patients (1476 on hemodialysis, 282 on peritoneal dialysis). This was the largest study up to date exploring glycemic markers in diabetic dialysis population and showed a significant correlation of casual glucose and HbA1c levels ($p<0.0001$, $R=0.69$), both in diabetic hemodialysis and peritoneal dialysis patients. In this study HbA1c underestimated casual glucose levels. Our study is consistent with this study in terms of correlation of glucose with HbA1c levels and the underestimation of HbA1c.

The main limitation of our study is the relatively small sample size. We did not use fasting glucose because it is hard to obtain fasting especially in midday and evening diabetic hemodialysis groups. Similarly, in the large populated GIDE study casual glucose –defined as not related to last meal- was investigated along with other long term glycemic control markers. We also found that HbA1c underestimated average glucose levels, which is consistent with some other studies (20,23). This finding also may favour the use of predialysis glucose levels.

CONCLUSION

This study revealed that last 2 and 3 months' average predialysis glucose levels are strongly correlated with HbA1c in diabetic hemodialysis patients. Despite long term glycemic markers are available, average predialysis glucose is an easy, cheap, reliable and reachable method for glycemic control. This relation has to be confirmed by large populated studies.

ETHICAL DECLERATIONS

Ethics Committee Approval: This study was approved by KTO Karatay University Faculty of Medicine, Non-Pharmaceutical and Medical Device Research Ethics Committee Presidency (Date: 08.06.2021, Decision No: E-41901325-050.99-10015-006).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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