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ABOUT COVER

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EDITORIAL

Utilising continuous glucose monitoring for glycemic control in diabetic kidney disease

Vamsidhar Veeranki, Narayan Prasad

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Abstract

In this editorial, we comment on the article by Zhang *et al*. Chronic kidney disease (CKD) presents a significant challenge in managing glycemic control, especially in diabetic patients with diabetic kidney disease undergoing dialysis or kidney transplantation. Conventional markers like glycated haemoglobin (HbA1c) may not accurately reflect glycemic fluctuations in these populations due to factors such as anaemia and kidney dysfunction. This comprehensive review discusses the limitations of HbA1c and explores alternative methods, such as continuous glucose monitoring (CGM) in CKD patients. CGM emerges as a promising technology offering real-time or retrospective glucose concentration measurements and overcoming the limitations of HbA1c. Key studies demonstrate the utility of CGM in different CKD settings, including hemodialysis and peritoneal dialysis patients, as well as kidney transplant recipients. Despite challenges like sensor accuracy fluctuation, CGM proves valuable in monitoring glycemic trends and mitigating the risk of hypo- and hyperglycemia, to which CKD patients are prone. The review also addresses the limitations of CGM in CKD patients, emphasizing the need for further research to optimize its utilization in clinical practice. Altogether, this review advocates for integrating CGM into managing glycemia in CKD patients, highlighting its superiority over traditional markers and urging clinicians to consider CGM a valuable tool in their armamentarium.

Key Words: Chronic kidney disease; Diabetic kidney disease; Glycemic control; Continuous glucose monitoring; Glycated hemoglobin; Glycemic variability

Core Tip: Continuous glucose monitoring (CGM) emerges as a transformative tool, offering real-time insights into glycemic variability among diabetic patients with chronic kidney disease (CKD), particularly during dialysis and post-transplantation phases. Innovations include CGM's ability to accurately detect hyper- and hypoglycemic events, aiding in timely therapeutic adjustments to mitigate risks. Studies demonstrate CGM's superiority over traditional markers like glycated haemoglobin in capturing acute glycemic fluctuations, particularly in dialysis patients, mainly due to the shorter life span of red blood cells, besides maintaining accuracy across all CKD stages, including those on peritoneal dialysis. CGM has substantive potential in individualized glycaemic management of CKD.

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INTRODUCTION

Chronic kidney disease (CKD) poses a significant challenge in managing glycemic control, particularly in diabetic patients who develop diabetic kidney disease (DKD). DKD is a prevalent complication of diabetes mellitus (DM), affecting 20%-25% of patients with type-2 DM[1,2]. DKD patients may experience frequent episodes of hypoglycemia with the progression of kidney disease. This is mainly due to impaired renal gluconeogenesis, defective renal clearance of insulin, elevated insulin resistance, and diminished β-cell function. With limitations of glycated haemoglobin (HbA1c), glycated albumin and fructosamine in CKD, the application of continuous glucose monitoring (CGM) in patients with diabetes is promising. In this comprehensive review, Zhang *et al*[3] have reviewed how glycemic control in these populations is crucial, yet conventional markers may not accurately reflect glycemic fluctuations.

LIMITATIONS OF CONVENTIONAL GLYCEMIC MARKERS

Although HbA1c is widely used as the primary method for monitoring blood sugar levels, its accuracy can be compromised by conditions such as anemia and renal dysfunction. Factors like reduced lifespan of red blood cells, anemia, blood transfusions, and the use of drugs that stimulate red blood cell production or iron supplements can falsely show lower HbA1c levels[4,5]. The risk of hypoglycemia and hyperglycemia is particularly heightened in patients in advanced stages of CKD and those undergoing dialysis. With the progression of renal decline and initiation of dialysis, glycemic variability (GV) can be further affected due to changes in glucose content in dialysates and the effects on insulin metabolism in failing kidney tubules. Monitoring glycemia is essential for effective management of DKD. Glycated albumin and fructosamine are suggested as alternatives for long-term blood sugar monitoring. These markers indicate blood sugar levels over a shorter period (2–4 weeks) compared to HbA1c, as they have a shorter lifespan in the bloodstream. Nonetheless, unlike direct blood glucose measurements, the glycated albumin and fructosamine assays can be affected by low albumin levels, which is often seen in nutritionally deprived CKD patients[6,7]. Hence, exploring alternative methods, such as CGM, is currently a necessity.

CGM AND ITS ADDED ADVANTAGE IN GLYCEMIC MANAGEMENT

CGM devices employ minimally invasive sensors that penetrate subcutaneous tissue to measure interstitial glucose. Interstitial glucose diffuses into the sensor's filament *via* capillary action, where it undergoes electrochemical reactions to determine its concentration. Real-time interstitial glucose readings are then transmitted to a mobile device for continuous monitoring. CGM offers a more reliable glycemic evaluation for patients with diabetes and CKD, including ESKD, by providing continuous, real-time glucose readings without frequent finger-pricking. CGM systems can be classified into professional, real-time (rt-CGM), and intermittently scanned (flash CGM) devices. The performance of CGM sensors in advanced CKD can be affected by factors like oxygen levels, uric acid, and exogenous substances, although CGM generally provides accurate monitoring. This makes CGM a valuable tool in managing diabetes in CKD patients, improving glycemic control and patient quality of life. Studies have shown that the correlation between HbA1c and mean sensor glucose decreases in advanced CKD stages, with HbA1c being less reliable as the CKD progresses. CGM-derived metrics, such as the glucose management index, have been proposed as alternatives for glycemic evaluation in CKD patients[8]. The 2020 Kidney Disease: Improving Global Outcomes guidelines suggest using glucose management indicator in advanced CKD or dialysis patients[9]. Time-in-range (TIR) metrics are also recommended for managing glycemia, though their validity and prognostic value in advanced CKD need further clinical trials.

GV and the role of CGM in the management of DM in progressive kidney disease

High GV is correlated with the pathogenesis and progression of diabetic-related complications, heightened risk of

hypoglycemia, and reduced patient quality of life[10,11]. GV is increasingly recognized as a pivotal parameter in glycemic management. CGM has become crucial in diabetes management because it continuously tracks glucose levels and offers a detailed picture of GV. Unlike traditional methods like self-monitoring of blood glucose (SMBG), which only provide snapshot measurements, CGM captures real-time data, enabling better management of hyperglycemia and hypoglycemia. GV is linked to diabetic complications, including microvascular issues like retinopathy, nephropathy, and neuropathy, as well as macrovascular complications like cardiovascular disease[12]. High GV increases the production of reactive oxygen species (ROS), activating pathogenic mechanisms such as the polyol pathway, advanced glycation end-products, protein kinase C, and the hexosamine pathway. This oxidative stress contributes to endothelial dysfunction and thereby increasing the risk of micro and macrovascular complications[13].

Long-term GV (variations over weeks to months), assessed by HbA1c and fasting/postprandial glucose levels, is associated with vascular complications and mortality. On the other hand, short-term GV (within-day and between-day glycemic fluctuations), measured by CGM indices like standard deviation, coefficient of variation, and TIR, is linked to diabetic retinopathy, kidney disease, peripheral neuropathy, and cardiovascular issues[14]. Various combinations of therapeutics, including dipeptidyl peptidase-4 inhibitors, sodium-glucose cotransporter-2 inhibitors, GLP-1 receptor agonists along with specific insulin preparations were found to have an improved GV and TIR across various studies[15-17]. However, whether this will benefit the end-organ damage is yet to be seen. CGM's detailed monitoring offers significant advantages over SMBG, highlighting the need for comprehensive glycemic control beyond HbA1c.

CGM in diabetic patients on various modalities of renal replacement therapy

In patients on hemodialysis, CGM has shown promise in improving glucose control and reducing the incidence of hypoglycemic events[18]. Despite challenges such as sensor accuracy fluctuation over dialysis sessions, CGM emerges as a valuable tool for clinicians to monitor glycemic trends and mitigate the risk of asymptomatic hypoglycemia in patients on hemodialysis. Similarly, in peritoneal dialysis patients, CGM emerges as a valuable adjunct in detecting and managing glucose variations induced by dialysate glucose absorption[19]. Notably, CGM accuracy remains unaffected by factors such as acidosis, urea levels, or volume overload, providing consistent monitoring across a wide range of glucose levels.

Nonetheless, there are certain limitations of CGM among patients with kidney disease. For instance, CGM sensors demonstrate variable accuracy, with mean absolute relative differences (MARD) values ranging from 11.3% to 36.1%, surpassing recommended thresholds[20]. Factors like inflammation post-sensor insertion, dialysis fluid loss, and interdialytic weight changes compromise CGM accuracy, especially in later dialysis sessions, weakening interstitial-capillary glucose correlation. Though MARD values are relatively stable in peritoneal dialysis patients, further research is needed in both cohorts to enhance CGM precision. The application of CGM in kidney transplant recipients is crucial, particularly its potential in managing perioperative and post-transplant hyperglycemia. Studies indicate that CGM offers valuable insights into glycemic control post-transplantation, aiding in the prevention of de novo post-transplant diabetes and complications related to pre-existing diabetes[21].

CONCLUSION

In conclusion, this article advocates for integrating CGM into the management of glycemia in CKD patients, emphasising its superiority over traditional markers in capturing dynamic glucose fluctuations and acute incidents of hypo- and hyperglycemia. However, challenges such as sensor accuracy, durability, and standardisation of application protocols persist. Future research should focus on addressing these challenges to optimise CGM utilisation in clinical practice. Furthermore, further research is essential to standardise and optimise CGM use in this population. Overall, this review serves as a comprehensive guide for clinicians navigating the complexities of glycemic management in CKD, urging them to consider CGM as a valuable tool in their armamentarium.

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