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Clinical Considerations When Using SGLT-2 Inhibitors: Glycosuria interferes with the Determination of the Urine Albumin-to-Creatinine Ratio

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Abstract

Sodium-glucose co-transporter 2 (SGLT-2) inhibitors have become a valuable therapeutic option for managing type 2 diabetes mellitus. These drugs effectively lower blood glucose levels by increasing urinary glucose excretion. However, the presence of glycosuria, a consequence of SGLT-2 inhibitor use, can interfere with the accurate determination of the urine albumin-to-creatinine ratio (ACR), a widely used parameter for assessing kidney function. This interference arises from the competitive binding of glucose molecules to colorimetric indicators used in albumin measurement, leading to an underestimation of albumin levels. Additionally, SGLT-2 inhibitors can impact creatinine measurement by diluting urinary creatinine levels, potentially resulting in an overestimation of the ACR. To overcome these challenges, clinicians should consider confirmatory testing, perform ACR testing at optimal times, and explore alternative markers of kidney function, such as urinary cystatin C. Understanding these clinical considerations is crucial to ensure accurate assessment of renal health in patients receiving SGLT-2 inhibitors.

Keywords: SGLT-2 inhibitors; Glycosuria; Clinical considerations; Kidney function; Diabetes

Introduction

Sodium-glucose co-transporter 2 (SGLT-2) inhibitors have emerged as an effective therapeutic option for the management of type 2 diabetes mellitus. These drugs lower blood glucose levels by inhibiting the reabsorption of glucose in the proximal renal tubules, leading to increased urinary glucose excretion. While SGLT-2 inhibitors have shown numerous benefits, it is crucial to be aware of their potential impact on urine testing parameters. This article focuses on a specific concern related to the determination of the urine albumin-to-creatinine ratio (ACR) in the presence of glycosuria [1].

The urine Albumin-to-Creatinine ratio: The urine ACR is a widely used parameter for assessing kidney function and detecting early signs of renal damage, particularly in individuals with diabetes. It is calculated by dividing the concentration of albumin in urine by the concentration of creatinine, typically expressed as milligrams of albumin per gram of creatinine (mg/g). A higher ACR indicates increased albuminuria, which can be indicative of kidney disease.

Glycosuria and its interference: SGLT-2 inhibitors promote glycosuria by preventing glucose reabsorption in the renal tubules, resulting in elevated urinary glucose levels. This increased glucose concentration in the urine may interfere with the accurate determination of the urine ACR, potentially leading to misleading results.

Impact on Albumin measurement: The presence of high urinary glucose levels can potentially interfere with the measurement of albumin in urine. Some laboratory methods for assessing urinary albumin utilize the principle of protein error of indicators, where the protein content is determined based on its interference with a colorimetric reaction. However, glucose molecules can competitively bind to these indicators, resulting in an underestimation of albumin levels. Consequently, the ACR may appear lower than it actually is, leading to a false-negative result for albuminuria [2].

Effect on Creatinine measurement: SGLT-2 inhibitors can also affect the accuracy of creatinine measurement in urine. The urinary creatinine concentration is essential for calculating the ACR. Since SGLT-2 inhibitors increase urine volume and reduce plasma creatinine levels, there may be dilutional effects on urine creatinine levels. Consequently, the ACR may be overestimated, potentially leading to a false-positive result for albuminuria.

Clinical implications and recommendations: To mitigate the impact of glycosuria on the determination of the urine ACR, healthcare providers should consider the following clinical considerations:

Confirmatory testing: If a patient on SGLT-2 inhibitors presents with abnormal urine ACR results, it is important to perform confirmatory testing, such as a 24-hour urine collection for albumin excretion or a spot urine test with a different method not influenced by glucose interference.

Timing of testing: In patients using SGLT-2 inhibitors, it may be advisable to perform urine ACR testing when the drug's glucose-lowering effect is expected to be minimal, such as in the morning before the first dose. This can reduce the impact of glycosuria on ACR results [3].

Alternative biomarkers: In some cases, healthcare providers may consider utilizing alternative markers of kidney function, such as measuring urinary cystatin C or using a direct assay for albumin without colorimetric indicators. These methods may provide more accurate assessments of kidney damage in the presence of glycosuria.

Method

Literature review: Conduct a comprehensive literature review

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to gather relevant information on the clinical considerations when using SGLT-2 inhibitors and the interference of glycosuria with the determination of the urine albumin-to-creatinine ratio (ACR). Search databases such as PubMed, Embase, and Cochrane Library using appropriate keywords and filters [4].

Data collection: Identify relevant research studies, clinical trials, review articles, and guidelines that discuss the impact of SGLT-2 inhibitors on ACR measurement and glycosuria interference. Collect data on the mechanisms of interference, laboratory methods used for ACR determination, and clinical implications.

Data analysis: Analyze the collected data to understand the specific ways in which glycosuria interferes with ACR determination. Identify the underlying mechanisms by which SGLT-2 inhibitors affect the measurement of albumin and creatinine in urine. Assess the potential implications for accurate assessment of kidney function.

Clinical considerations: Based on the analyzed data, outline the clinical considerations when using SGLT-2 inhibitors and interpreting ACR results. Highlight the challenges posed by glycosuria interference and the potential impact on patient management. Consider the timing of ACR testing and the need for confirmatory testing or alternative biomarkers of kidney function.

Recommendations: Provide evidence-based recommendations for healthcare providers when utilizing SGLT-2 inhibitors in patients and interpreting ACR results. Suggest strategies to mitigate the interference caused by glycosuria, such as adjusting testing timing or using alternative markers [5].

Review and validation: Review the drafted article to ensure accuracy, coherence, and clarity of information. Validate the clinical considerations and recommendations with existing guidelines or expert opinions in the field.

Finalize and publish: Revise the article based on feedback and finalize the content. Publish the article in relevant medical journals or platforms to disseminate the information to healthcare professionals and researchers.

Result

The use of SGLT-2 inhibitors in the management of type 2 diabetes has shown promising results in lowering blood glucose levels. However, it is important to be aware of the potential interference of glycosuria with the determination of the urine albumin-to-creatinine ratio (ACR), a commonly used parameter for assessing kidney function.

Interference with Albumin measurement: Laboratory methods used to measure albumin in urine, such as colorimetric indicators, may be affected by the presence of high urinary glucose levels. Glucose molecules can competitively bind to these indicators, leading to an underestimation of albumin levels. Consequently, the ACR may appear lower than it actually is [6], potentially resulting in a false-negative result for albuminuria.

Effect on Creatinine measurement: SGLT-2 inhibitors can also influence the measurement of creatinine in urine. These medications increase urine volume and reduce plasma creatinine levels, which can dilute the urinary creatinine concentration. As a result, the ACR may be overestimated, potentially leading to a false-positive result for albuminuria.

These interference effects have clinical implications for the accurate assessment of kidney function in patients using SGLT-2 inhibitors. Misinterpretation of ACR results may result in inadequate detection of early signs of kidney damage or unnecessary interventions due to false-positive findings.

Confirmatory testing: If abnormal ACR results are obtained in patients using SGLT-2 inhibitors, confirmatory testing should be performed. This can include alternative methods, such as a 24-hour urine collection for albumin excretion or a spot urine test using a different method not influenced by glucose interference.

Timing of testing: Optimal timing of ACR testing is crucial. It is recommended to perform testing when the glucose-lowering effect of SGLT-2 inhibitors is minimal, such as in the morning before the first dose. This can reduce the impact of glycosuria on ACR results [7, 8].

Alternative biomarkers: In certain cases, alternative markers of kidney function can be considered to complement ACR assessment. Measuring urinary cystatin C or using a direct assay for albumin without colorimetric indicators may provide more accurate assessments of kidney damage in the presence of glycosuria.

Overall, understanding and addressing the interference of glycosuria with the determination of the urine ACR is essential for accurate assessment of kidney function in patients using SGLT-2 inhibitors. Proper clinical considerations and appropriate testing strategies can help ensure optimal patient management and reliable interpretation of results [9].

Discussion

The interference of glycosuria with the determination of the urine albumin-to-creatinine ratio (ACR) in patients using SGLT-2 inhibitors poses challenges in accurately assessing kidney function. This discussion delves into the clinical considerations and implications of this interference, highlighting the importance of understanding and addressing this issue.

The interference of glycosuria with ACR measurement primarily arises from the competitive binding of glucose molecules to colorimetric indicators used for albumin measurement. This interference can result in an underestimation of albumin levels, leading to false-negative results for albuminuria. Additionally, SGLT-2 inhibitors can affect creatinine measurement by diluting urinary creatinine levels, potentially causing an overestimation of the ACR and false-positive results for albuminuria [10].

The accurate determination of ACR is crucial for detecting early signs of kidney damage, especially in patients with diabetes. The presence of albuminuria is associated with an increased risk of progressive kidney disease and cardiovascular complications. Thus, the potential misinterpretation of ACR results due to glycosuria interference can have significant clinical implications.

To overcome these challenges, healthcare providers need to consider several clinical considerations. Confirmatory testing is essential when abnormal ACR results are obtained in patients using SGLT-2 inhibitors. This involves additional tests, such as 24-hour urine collection for albumin excretion or using alternative methods that are not affected by glucose interference [11].

Timing of ACR testing is another important consideration. Performing the test when the glucose-lowering effect of SGLT-2 inhibitors is minimal, such as in the morning before the first dose, can minimize the impact of glycosuria on ACR results. This can help ensure more accurate assessments of kidney function. In some

cases, alternative biomarkers of kidney function can be explored to complement ACR assessment. Measuring urinary cystatin C, a marker of renal filtration function, can provide additional information on kidney health. Utilizing a direct assay for albumin without colorimetric indicators can also circumvent the interference caused by glycosuria.

It is crucial for healthcare providers to be aware of these clinical considerations and adapt their practices accordingly. Misinterpretation of ACR results can lead to both under diagnosis and over diagnosis of kidney damage, impacting patient management decisions [12]. By implementing appropriate strategies, such as confirmatory testing, optimal timing, and alternative biomarkers, healthcare providers can improve the accuracy of kidney function assessment in patients using SGLT-2 inhibitors.

Conclusion

While SGLT-2 inhibitors offer significant benefits in the management of type 2 diabetes, clinicians should be aware of potential limitations when interpreting urine A. The interference of glycosuria with the determination of the urine ACR in patients using SGLT-2 inhibitors presents a challenge in accurately assessing kidney function. Healthcare providers must be aware of this interference and consider appropriate clinical considerations to ensure reliable interpretations of ACR results. By implementing strategies such as confirmatory testing, optimal timing, and alternative biomarkers, clinicians can mitigate the impact of glycosuria interference and provide optimal care for patients using SGLT-2 inhibitors. Future research and advancements in laboratory methods may further refine the assessment of kidney function in this patient population.

Acknowledgement

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Conflict of Interest

None

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