INVESTIGATING THE RELATIONSHIP BETWEEN BLOOD KLOTHO LEVELS AND GLYCATED HEMOGLOBIN IN DIABETIC NEPHROPATHY PATIENTS

Botirova Nigina Akram qizi
Tashkent Medical Academy, Uzbekistan

Introduction

Diabetic nephropathy (DN) remains a significant complication of diabetes mellitus, characterized by progressive kidney damage due to prolonged hyperglycemia. Glycated hemoglobin (HbA1c) serves as a key marker for long-term glycemic control in diabetic patients, representing the average blood glucose levels over the preceding 2-3 months. Higher HbA1c levels are associated with an increased risk of diabetic complications, including nephropathy.

Recent research has highlighted Klotho, a protein with renoprotective properties, as a potential modulator of kidney health in DN. Klotho is primarily expressed in the kidneys and has anti-inflammatory, anti-fibrotic, and antioxidant effects, which may provide protection against the pathophysiological processes that damage renal function in diabetes. This study explores the relationship between blood Klotho levels and HbA1c in DN patients, aiming to determine how glycemic control correlates with Klotho concentrations and whether Klotho could serve as an indicator of kidney protection in these patients.

Key words: Klotho, glycated hemoglobin, diabetic nephropathy, glomerular filtration rate, kidney dysfunction.

Methods

This study involved patients diagnosed with diabetic nephropathy, who were divided into two groups based on their glycated hemoglobin levels. Group 1: Patients with target HbA1c (≤7%), representing better glycemic control. Group 2: Patients with elevated HbA1c (>7%), representing poor glycemic control.

Blood samples were collected from each group, and the following parameters were measured: Glycated hemoglobin (HbA1c): Measured using high-performance liquid chromatography (HPLC). Blood Klotho levels: Quantified using an enzyme-linked immunosorbent assay (ELISA). Glomerular filtration rate (GFR): Estimated using a combined creatinine-cystatin C formula to assess kidney function.

Results

In Group 1, characterized by target glycated hemoglobin levels, the mean HbA1c was 6.04 ± 0.6%, whereas in Group 2, with high glycated hemoglobin levels, it was significantly higher at 10.6 ± 1.81%. Correspondingly, blood klotho levels were higher

in Group 1 (345 ± 32.4 pg/ml) compared to Group 2 (277 ± 22.9 pg/ml). Interestingly, the glomerular filtration rate (GFR) measured by creatinine-cystatin C was slightly lower in Group 1 (66.48 ± 6.3 ml/min/1.73 m2) compared to Group 2 (70.2 ± 6.45 ml/min/1.73 m2), although not statistically significant.

Discussion

The results of this study suggest a potential inverse relationship between blood Klotho[4] levels and HbA1c in patients with diabetic nephropathy. Patients in Group 1, who had target HbA1c levels, exhibited significantly higher Klotho concentrations compared to those in Group 2, who had markedly elevated HbA1c levels. This finding implies that better glycemic control may be associated with higher circulating Klotho levels[6,7], which could, in turn, offer protection against kidney damage[1]. The exact mechanisms underlying the Klotho-HbA1c relationship remain unclear but may involve Klotho's role in mitigating the harmful effects of hyperglycemia[9]. Hyperglycemia is known to increase oxidative stress[3], inflammation, and fibrosis in the kidneys, all of which are processes that Klotho has been shown to counteract[2]. Therefore, lower Klotho levels[5] in patients with poor glycemic control may reflect a diminished capacity to protect the kidneys from hyperglycemia-induced damage. Interestingly, while Group 2 exhibited lower Klotho levels, their GFR was slightly higher than that of Group 1. This could be due to the early compensatory hyperfiltration that occurs in diabetic nephropathy, where GFR can initially increase before declining in the later stages of kidney disease. Therefore, the lack of significant difference in GFR between the groups may be explained by the varying stages of nephropathy among the patients. Further investigations are needed to fully understand the interplay between Klotho, glycemic control, and renal function, as well as to explore whether increasing Klotho levels could have therapeutic benefits in DN patients.

Conclusion

This study provides preliminary evidence of a relationship between blood Klotho levels and glycated hemoglobin in patients with diabetic nephropathy. The findings suggest that better glycemic control, as indicated by target HbA1c levels, is associated with higher circulating Klotho concentrations. This raises the possibility that Klotho may play a protective role in the progression of diabetic nephropathy, potentially by modulating glucose metabolism and reducing kidney damage.

Future studies should focus on elucidating the molecular mechanisms behind this association and determining whether Klotho could be a therapeutic target in the management of DN. Additionally, longitudinal studies are needed to assess changes in Klotho levels over time and their relationship with glycemic control and renal outcomes in diabetic patients.

References:

1. Kuro-o, M. (2012). Klotho and aging. Biochimica et Biophysica Acta (BBA) - General Subjects, 1822(3), 402-410.
2. Semba, R. D., Cappola, A. R., Sun, K., Bandinelli, S., Dalal, M., & Ferrucci, L. (2011). Plasma Klotho and cardiovascular disease in adults. Journal of the American Geriatrics Society, 59(9), 1596-1601.
3. Navarro-González, J. F., Mora-Fernández, C., Muros de Fuentes, M., & García-Pérez, J. (2011). Inflammatory molecules and pathways in the pathogenesis of diabetic nephropathy. Nature Reviews Nephrology, 7(6), 327-340.
4. Botirova N. A. DIAGNOSTIC SIGNIFICANCE OF KLOTHO AND CYSTATIN C IN THE EARLY STAGE OF CHRONIC KIDNEY DISEASE IN TYPE 2 DIABETES MELLITEUS //Proceedings of International Conference on Scientific Research in Natural and Social Sciences. – 2024. – Т. 3. – №. 2. – С. 111-113.
5. Botirova N. A., Mirahmedova H. T. SIGNIFICANCE OF STANDARD AND NEWLY STUDIED BIOMARKERS IN THE DIAGNOSIS OF ADVANCED CHRONIC KIDNEY DISEASE AGAINST THE BACKGROUND OF DIABETIC NEPHROPATHY IN TYPE 2 DIABETES //Western European Journal of Medicine and Medical Science. – 2023. – Т. 1. – №. 3. – С. 5-10.
6. Botirova N. A. THE SIGNIFICANCE OF THE KLOTHO PROTEIN AT THE EARLY STAGE OF DIABETIC NEPHROPATHY //Proceedings of Scientific Conference on Multidisciplinary Studies. – 2024. – Т. 3. – №. 2. – С. 28-29.
7. Мирахмедова Х. Т., Ботирова Н. А. Кандли диабетнинг 2-типида ривожланган сурункали буйрак касаллигини эрта ташхислашда Клото хамда цистатин С нинг ахамияти: дис. – Ташкентская медицинская академия, Ташкент, Узбекистан, 2024.
8. Мирахмедова Х. Т., Ботирова Н. А. 2-тип кандли диабет билан огриган беморларда диабетик нефропатиянинг эрта боскичида клото омилининг ахамияти: дис. – Ташкентская медицинская академия, Ташкент, Узбекистан, 2024.
9. Мирахмедова, Хилола Тухтасиновна, and Ботирова Нигина. "Actual Problems of Diabetic Nephropathy, Risk Factors, Stages, Progression, Mechanism, Diagnosis and Management." (2022).