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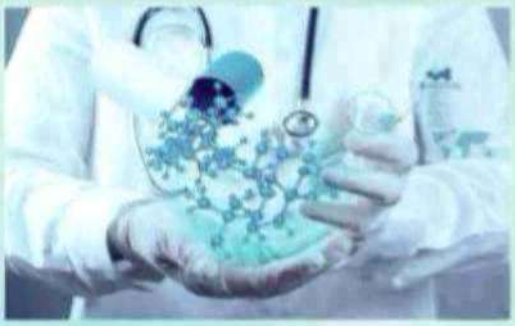

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ЭПИГЕНЕТИЧЕСКАЯ МОДИФИКАЦИЯ В ДИАБЕТИЧЕСКАЯ БОЛЕЗНЬ ПОЧЕК С ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ

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✓ ***Резюме***

Диабетическая болезнь почек (ДБП) является распространенной микроангиопатией у пациентов с диабетом и основная причина смерти у пациентов с диабетом. Основные проявления ДБП протеинурия и снижение почечной фильтрационной способности. Клубочковая фильтрация скорость и уровень альбумина в моче являются двумя наиболее важными признаками прогрессирование ДБП. Классическое лечение ДБП контролирует уровень глюкозы в крови и артериальное давление. Тем не менее, часто используемые клинические терапевтические стратегии и существующие биомаркеры только частично замедляют прогрессирование ДБП и примерно предсказать прогрессирование заболевания. Таким образом, новые терапевтические методы, цели и биомаркеры срочно необходимы для удовлетворения клинических требований. В в последние годы все большее внимание уделяется роли эпигенетических модификация в патогенезе ДБП. Эпигенетическая вариация в основном включает Метилирование ДНК, модификация гистонов и изменения в некодирующей РНК профиль экспрессии, который глубоко вовлечен в воспаление, связанное с ДБП, окислительный стресс, гемодинамика и активация ненормальной передачи сигналов пути. Поскольку ДБП обратим на определенных стадиях заболевания, полезно выявить аномальные эпигенетические модификации, такие как ранняя диагностика и лечение цели для предотвращения прогрессирования терминальной стадии почечной недостаточности (ТПН). Потому что текущее понимание эпигенетического механизма ДБП не всеобъемлющий, цель этого обзора состоит в том, чтобы обобщить роль эпигенетическая модификация в возникновении и развитии ДБП и оценить ценность эпигенетической терапии при ДБП.

Ключевые слова: эпигенетическая модификация, диабетическая болезнь почек, нарушение обмена веществ, биомаркер,некодирующая РНК.

EPIGENETIC MODIFICATION INTO DIABETIC KIDNEY DISEASE

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✓ ***Resume***

Diabetic kidney disease (DKD) is a common microangiopathy in diabetic patients and the leading cause of death in diabetic patients. The main manifestations of DKD proteinuria and a decrease in renal filtration capacity. Glomerular filtration rate and urinary albumin levels are the two most important features of DBP progression. Classic DBP treatment controls blood glucose and blood pressure. However, frequently used clinical therapeutic strategies and existing biomarkers only partially slow the progression of DKD and roughly predict disease progression. Thus, new therapeutics, targets and biomarkers are urgently needed to meet clinical requirements. In recent years, increasing attention has

been paid to the role of epigenetic modification in the pathogenesis of DBP. Epigenetic variation mainly involves DNA methylation, histone modification, and changes in the non-coding RNA expression profile that is deeply involved in DBP-related inflammation, oxidative stress, hemodynamics, and activation of abnormal pathway signaling. Because DKD is reversible at certain stages of the disease, it is useful to identify abnormal epigenetic modifications, such as early diagnosis and treatment of the target to prevent progression to end-stage renal disease (ESRD). Because the current understanding of the epigenetic mechanism of DBP is not comprehensive, the aim of this review is to summarize the role of epigenetic modification in the onset and development of DBP and to assess the value of epigenetic therapy in DKD.

Keywords: epigenetic modification, diabetic kidney disease, metabolic disorder, biomarker, non-coding RNA.

SURUNKALI YURAK YETISHMOVCHILIGI BILAN KECHADIGAN DIABETIK BUYRAK KASALLIGIDA EPIGENETIK MODIFIKATSIYA

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✓ ***Rezyume***

Diabetik buyrak kasalligi (DBK) diabetga chalingan bemorlarda keng tarqalgan mikroangiopatiya va diabetga chalingan bemorlarda o'limning asosiy sababidir. Proteinuriya DBRning asosiy ko'rinishlari va buyrak filtrlash qobiliyatining pasayishi. Klyukochkali filtrlash tezligi va siydikdagi albumin darajasi DBK rivojlanishining ikkita eng muhim belgisidir. DBPning klassik davolanishi qondagi glyukoza darajasi va qon bosimini nazorat qiladi. Shunga qaramay, tez-tez ishlatiladigan klinik terapevtik strategiyalar va mavjud biomarkerlar DBKning rivojlanishini qisman sekinlashtiradi va kasallikning rivojlanishini taxmin qiladi. Shunday qilib, klinik talablarni qondirish uchun yangi terapevtik usullar, maqsadlar va biomarkyerlar zudlik bilan zarur. Keyingi yillarda DBP patogenezida epigenetik modifikatsiyaning roli tobora ortib bormoqda. Epigenetik variatsiya asosan DNKni metillash, gistonlarni modifikatsiyalash va kodlanmagan RNKdagi o'zgarishlarni o'z ichiga oladi. Kasallikning ma'lum bosqichlarida DBBni qayta ko'rib chiqishimiz sababli, buyrak yetishmovchiligining terminal bosqichi (BAT) rivojlanishining oldini olish uchun maqsadni erta tashxis qilish va davolash kabi anormal epigenetik modifikatsiyalarni aniqlash foydalidir. Chunki DBPning epigenetik mexanizmini joriy tushunish keng qamrovli emas, ushbu sharhning maqsadi DBP paydo bo'lishi va rivojlanishida epigenetik modifikatsiyaning rolini umumlashtirish va DBPda epigenetik terapiyaning qiymatini baholashdan iborat.

Kalit so'zlar: epigenetik modifikatsiya, diabetik buyrak kasalligi, moddalar almashinuvining buzilishi, biomarker, kodlanmagan RNK.

Relevance

Diabetic kidney disease (DKD) is a common complication of diabetes and a leading cause of end-stage renal disease (ESRD), which significantly impacts patients' quality of life (1-4). The main pathological hallmarks of DKD include glomerular sclerosis, podocyte detachment, epithelial-mesenchymal transition/endothelial-mesenchymal transition/macrophage-myofibroblast transition, excessive extracellular matrix (ECM), and renal tubular fibrosis. These pathological changes affect glomerular and tubular function, leading to progressive proteinuria and decreased glomerular filtration capacity. A long-term hyperglycemic environment in diabetics causes metabolic disturbances, oxidative stress, and hemodynamic changes. Although these symptoms are caused by genetic mutations, they are more closely associated with epigenetic variations [5]. For example, studies have shown that even after a long period of strict glycemic control, diabetic patients may still develop complications due to early exposure to high glucose [4,6,7]. This metabolic memory phenomenon has been shown to be associated with DNA methylation and histone acetylation at the promoter, suggesting that epigenetic modifications are involved in the pathological process of diabetes and affect patients' condition over a long period of time

[9,16]. Therefore, a deeper understanding of epigenetic modifications in DKD may help to better understand the pathogenesis of the disease and provide potential prognostic and therapeutic targets for the treatment of DKD. In the current study, we conducted a comprehensive analysis and implementation of DKD-related epigenetic mechanisms and epigenetic therapy based on a search of published literature from PubMed (https://pubmed.ncbi.nlm.nih.gov) and Web of Science (http://www.webofknowledge.com/databases). Our goal is to encourage more clinicians and researchers to pay attention to the function of epigenetic modifications in the occurrence and development of DKD and to conduct laboratory, preclinical and clinical studies to develop epigenetic drugs and therapeutic strategies for DKD [15].

Since the direct cause of DKD in patients with diabetes is high blood glucose levels, lowering blood glucose levels is a priority for controlling the progression of DKD. Some hypoglycemic drugs also have a therapeutic effect on renal dysfunction. For example, SGLT2 inhibitors (e.g., empagliflozin) not only reduce tubular glucose reabsorption but also improve renal filtration capacity and delay the progression of kidney disease by reducing glomerular pressure and albuminuria. Overactivation of the renin-angiotensin-aldosterone system (RAAS) can cause glomerular hypertension, which in turn contributes to bulbar arteriolar constriction, endothelial cell damage, and albuminuria. Therefore, the use of antihypertensive drugs can significantly prevent renal dysfunction while maintaining normal blood pressure [13]. RAAS inhibitors are widely used drugs for the treatment of DKD and have been shown to be effective in all stages of DKD.

Potential Epigenetic Therapy for DKD Currently, epigenetic drug research for DKD remains largely at the experimental animal stage, and histone acetylation inhibitors are a hotspot of research. We summarized the potential epigenetic therapies for DKD. HDACIs have been extensively studied in tumors and are approved for the treatment of cutaneous T-cell lymphoma and multiple myeloma. HDACIs also exert a protective effect against diabetic kidney injury [11, 14]. For example, HDAC2 expression is increased in diabetic rats, and administration of trichostatin A (TSA) can reduce ECM-related protein and mRNA expression and prevent it. TSA also inhibits the activity of class II HDAC, which plays a similar role in blocking EMT. Xu et al. found that HDAC5 expression was increased in the renal tubules of diabetic mice. After TSA administration, HDAC5 expression was reduced and ECM accumulation was alleviated. Valproate (VPA), sodium butyrate (NaB), and vorinostat are all HDACs that inhibit class I and II HDACs. VPA is a branched-chain short-chain fatty acid that can alleviate renal tubular injury in STZ-induced diabetic rats, reduce autophagy and stress, reduce proteinuria, and prevent renal fibrosis. NaB is another branched-chain short-chain fatty acid that can reduce inflammation and oxidative damage and alleviate albuminuria in diabetic rats. Vorinostat can alleviate oxidative stress in STZ-induced diabetic rats and reduce renal tubular cell proliferation and glomerular matrix formation [8,12].

Although HDACIs hold great potential for the treatment of DKD, their drawbacks, such as adverse effects and poor tolerance, should not be ignored. For life-sustaining diseases such as cancer, side effects such as nausea, vomiting, and liver toxicity are acceptable. However, whether HDACIs are a good choice for chronic diseases such as DKD should be carefully considered. Furthermore, the specificity of HDACIs is poor. Because class I, II, and IV HDACs all rely on zinc for enzymatic reactions, and most HDACIs target the zinc domain, HDACIs have a broad spectrum of effects (commonly referred to as pan-HDACIs).

Conclusions and Prospects: Epigenetic modifications are common in diseases, and some epigenetic variations are highly specific to a particular disease or a specific stage of the disease, providing potential therapeutic targets for clinical treatment. Currently, many studies have confirmed the role of epigenetics in DKD. In this review, we summarized the literature to establish evidence for epigenetic changes associated with DKD. We found that epigenetic modifications are involved in the inhibition/activation of various pathogenic signaling pathways. Epigenetic variations influence multiple renal cellular functions, such as GR activity and glucose metabolism. In particular, epigenetic variations-induced EndMT/EMT processes are key to the genesis of DKD, which are the main events in renal fibrosis. Epigenetic modifications are a consequence of HG exposure and contribute to the progression of DKD. Because DKD is the result of multiple factors and their complex interactions, different epigenetic modifications may contribute to the same outcome through different signaling pathways and mechanisms. However, most existing epigenetic studies have focused on the effect of a single variant on changes in a signaling pathway to promote or mitigate the occurrence of DKD. Therefore, drugs or biomarkers designed for a single target are likely not accurate, and the combined use of multiple epigenetic drugs targeting different epigenetic alterations should be considered in the future treatment of DKD. However, most existing epigenetic studies have focused on the effect of a single variant on changes in the signaling pathway that promote or mitigate the onset of DKD processes. Therefore, drugs or biomarkers designed for a single target are likely inaccurate,

and the combined use of multiple epigenetic drugs targeting different epigenetic alterations should be considered in future DKD treatment. Furthermore, most of these studies were conducted in diabetic animal or cell models under hyperglycemic conditions, but we believe the human environment is more complex and that more influential factors and mechanisms must be involved in DKD than just animals and cells. Therefore, additional solid data from experimental and clinical trials on clinical samples and patients is eagerly awaited.

Conclusion

Epigenetic detection technology has rapidly advanced in recent years. With the widespread use of high-throughput sequencing technology in clinical settings, detection of epigenetic changes (primarily DNA methylation and noncoding RNA profiles) in kidney tissue or peripheral blood of DKD patients has become easier, faster, and less expensive. These sequencing results are crucial for accurate diagnosis and drug development for DKD.

Additionally, the CRISPR-Cas9 system is being tested as a new tool for editing specific epigenetic variations, which is a potential approach for the prevention and treatment of DKD.

LIST OF REFERENCES:

1. Retnakaran R, Cull CA, Thorne KI, Adler AI, Holman RR; UK Prospective Diabetes Study Group. Risk factors for renal dysfunction in type 2 diabetes: UK Prospective Diabetes Study 74. Diabetes. 2006;55(6):1832-1839. doi:10.2337/db05-1620
2. L'Heveder R, Nolan T. International Diabetes Federation. Diabetes Res Clin Pract. 2013;101(3):349-351. doi:10.1016/j.diabres.2013.08.003
3. Thomas MC, Brownlee M, Susztak K, Sharma K, Jandeleit-Dahm KA, Zoungas S, et al. Diabetic kidney disease. Nat Rev Dis Primers. 2015;1:15018. doi:10.1038/nrdp.2015.18
4. Thomas MC. Epigenetic mechanisms in diabetic kidney disease. Curr Diabetes Rep. 2016;16(3):31. doi:10.1007/s11892-016-0723-9
5. Simeone CA, Wilkerson JL, Poss AM, Banks JA, Varre JV, Guevara JL, et al. A dominant negative ADIPOQ mutation in a diabetic family with renal disease, hypoadiponectinemia, and hyperceramidemia. NPJ Genom Med. 2022;7(1):43. doi:10.1038/s41525-022-00314-z
6. Chalmers J, Cooper ME. UKPDS and the legacy effect. N Engl J Med. 2008;359(15):1618-1620. doi:10.1056/NEJMe0807625
7. Reddy MA, Zhang E, Natarajan R. Epigenetic mechanisms in diabetic complications and metabolic memory. Diabetologia. 2015;58(3):443-455. doi:10.1007/s00125-014-3462-y
8. Miao F, Chen Z, Genuth S, Paterson A, Zhang L, Wu X, et al. Evaluating the role of epigenetic histone modifications in the metabolic memory of type 1 diabetes. Diabetes. 2014;63(5):1748-1762. doi:10.2337/db13-1251
9. Chen Z, Miao F, Paterson AD, Lachin JM, Zhang L, Schones DE, et al. Epigenomic profiling reveals an association between persistence of DNA methylation and metabolic memory in the DCCT/EDIC type 1 diabetes cohort. Proc Natl Acad Sci USA. 2016;113(21):E3002-E3011. doi:10.1073/pnas.1603712113
10. Theofilis P, Vordoni A, Tsimihodimos V, Kalaitzidis RG. Metabolic dysfunction-associated fatty liver disease in newly diagnosed, treatment-naive hypertensive patients and its association with cardiorenal risk markers. High Blood Press Cardiovasc Prev. 2023;30(1):63-72. doi:10.1007/s40292-023-00558-5
11. Zhang X, Liu J, Shao S, Yang Y, Qi D, Wang C, et al. Sex differences in the prevalence of and risk factors for abnormal glucose regulation in adults aged 50 years or older with normal fasting plasma glucose levels. Front Endocrinol (Lausanne). 2020;11:531796. doi:10.3389/fendo.2020.531796
12. Stenvinkel P, Chertow GM, Devarajan P, Levin A, Andreoli SP, Bangalore S, et al. Chronic inflammation in chronic kidney disease progression: Role of Nrf2. Kidney Int Rep. 2021;6(7):1775-1787. doi:10.1016/j.ekir.2021.04.023
13. Chen Y, Zou H, Lu H, Xiang H, Chen S. Research progress of endothelial-mesenchymal transition in diabetic kidney disease. J Cell Mol Med. 2022;26(12):3313-3322. doi:10.1111/jcmm.17356
14. Duran-Salgado MB, Rubio-Guerra AF. Diabetic nephropathy and inflammation. World J Diabetes. 2014;5(3):393-398. doi:10.4239/wjd.v5.i3.393
15. Smith MJ, Simmons KM, Cambier JC. B cells in type 1 diabetes mellitus and diabetic kidney disease. Nat Rev Nephrol. 2017;13(11):712-720. doi:10.1038/nrneph.2017.138
16. Navarro-González JF, Mora-Fernández C. The role of inflammatory cytokines in diabetic nephropathy. J Am Soc Nephrol. 2008;19(3):433-442. doi:10.1681/asn.2007091048

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