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IMMUNE RESPONSE IN DIABETES

Abstract:

Diabetes mellitus (DM) is not only a metabolic disorder but also involves significant alterations in the immune system. Chronic inflammation, oxidative stress, and immune dysfunction contribute to increased susceptibility to infections and the development of diabetes-related complications. This paper explores the key immune responses in diabetes, including innate and adaptive immunity dysfunctions, chronic low-grade inflammation, and oxidative stress.

Keywords: diabetes, immune response, inflammation, oxidative stress, immune dysfunction.

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ИММУННЫЙ ОТВЕТ ПРИ ДИАБЕТЕ

Аннотация

Сахарный диабет (СД) — это не только метаболическое нарушение, но и значительные изменения в иммунной системе. Хроническое воспаление, окислительный стресс и дисфункция иммунитета способствуют повышенной восприимчивости к инфекциям и развитию осложнений, связанных с диабетом. В данной статье рассматриваются основные иммунные реакции при диабете,

включая нарушения врожденного и адаптивного иммунитета, хроническое вялотекущее воспаление и окислительный стресс.

Ключевые слова: диабет, иммунный ответ, воспаление, окислительный стресс, дисфункция иммунитета.

Introduction:
Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Beyond its metabolic effects, DM significantly affects the immune system, leading to increased susceptibility to infections and chronic complications. Understanding the immune response in diabetes is crucial for developing effective therapeutic strategies and improving patient outcomes.

Innate Immunity and Diabetes: Innate immunity serves as the first line of defense against pathogens. In diabetes, innate immune functions are often impaired. Studies show reduced phagocytic activity, dysfunctional neutrophils, and altered cytokine production. These changes lead to an increased risk of infections and delayed wound healing [1]. As a chronic condition, diabetes tends to increase the risk of several other diseases caused by macrovascular and microvascular damage, and it has negative impacts on several organs, such as the brain, kidney, heart, and eyes [2]. In addition, diabetic patients are more susceptible to infection. Several studies have reported the increased risk of lower respiratory tract infections such as pulmonary tuberculosis and pneumonia [3], urinary tract infections, and skin and soft tissue infections in people with diabetes. The outcome of infection treatment in patients who suffer from diabetes tends to be poor [4]. Infection in patients with diabetes increases the economic burden on the patient due to the high cost of care, the length of treatment, and related complications [4].

Adaptive Immunity and Diabetes: Adaptive immunity, involving T and B lymphocytes, is also disrupted in diabetes. Research indicates altered T-cell responses and impaired antibody production, which contribute to chronic inflammation and autoimmune processes, particularly in type 1 diabetes. In type 1 diabetes, the immune system mistakenly attacks pancreatic beta cells, leading to insulin deficiency. This autoimmune response is driven by the activation of autoreactive CD4+ and CD8+ T cells, along with dysregulated regulatory T cells (Tregs) that fail to suppress autoimmunity. B cells contribute to this process by producing autoantibodies against pancreatic islet cells, further amplifying the immune attack. In type 2 diabetes, while autoimmunity is less prominent, there is still evidence of disrupted adaptive immunity. Studies show increased activation of pro-inflammatory T cells and reduced numbers of anti-inflammatory Tregs, promoting a state of chronic low-grade inflammation. This imbalance in adaptive immune responses contributes to insulin resistance and metabolic dysfunction. Targeting adaptive immune pathways through

immunomodulatory therapies offers potential for improving outcomes in both forms of diabetes [5].

Chronic Inflammation: A hallmark of diabetes is chronic low-grade inflammation, characterized by elevated levels of pro-inflammatory cytokines like TNF-α, IL-6, and CRP. This persistent inflammation exacerbates insulin resistance and accelerates the development of vascular complications. Chronic inflammation also plays a critical role in the pathogenesis of both type 1 and type 2 diabetes. In type 1 diabetes, autoimmune destruction of pancreatic beta cells leads to sustained inflammation and loss of insulin production. In type 2 diabetes, obesity-induced inflammation contributes to insulin resistance and metabolic dysfunction. The involvement of inflammatory markers and pathways such as the NF-κB and JNK signaling pathways further emphasizes the importance of inflammation in the progression of diabetes. Targeting these inflammatory processes through pharmacological interventions or lifestyle modifications has shown promise in mitigating diabetes complications. This proinflammatory phenotype has been associated with accelerated vascular inflammation, leading to car diovascular morbidity and mortality, and may also play a role in the development of microvascular complications [6].

Oxidative Stress: Hyperglycemia in diabetes induces oxidative stress, leading to the excessive production of reactive oxygen species (ROS). This results in cellular and tissue damage, endothelial dysfunction, and the progression of diabetes-related complications. Oxidative stress not only damages pancreatic beta cells but also impairs insulin signaling pathways, contributing to insulin resistance. The imbalance between ROS production and antioxidant defenses results in oxidative damage to lipids, proteins, and DNA, further exacerbating inflammation and metabolic dysfunction. Hyperglycemia promotes mitochondrial dysfunction and induces the formation of reactive oxygen species (ROS) that cause oxidative stress in several tissues such as blood vessels and pancreatic beta cells. Accumulating damage to the mitochondria, as well as several macromolecules, including proteins, lipids, and nucleic acids by ROS promotes the process of aging. As a result, pancreatic β cells that require functional mitochondria to maintain insulin synthesis fail to generate high enough levels of insulin. In the absence of compensatory mechanisms, stress-responsive intracellular signaling molecules are activated and cellular damage occurs. Elevated intracellular levels of ROS and subsequent oxidative stress play an important role in the pro-atherosclerotic consequences of diabetes and the development vascular complications [7]. Antioxidant therapies, such as the use of vitamin E, vitamin C, and polyphenols, have been explored for their potential to reduce oxidative stress and improve metabolic outcomes in diabetic patients. Furthermore, lifestyle interventions like regular physical activity and a balanced diet rich in antioxidants play a significant role in managing oxidative stress and improving overall health [8].

Conclusion

Diabetes leads to immune system dysregulation, making individuals more vulnerable to infections and chronic inflammation. Both innate and adaptive immunity are affected, contributing to diabetes complications. Effective management of blood glucose, oxidative stress, and inflammation is essential to support immune function and prevent complications.

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