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ROLE OF PARATHORMONE IN THE DEVELOPMENT OF ATHEROSCLEROSIS IN THE CAROTID ARTERY

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Abstract:

Atherosclerosis of the carotid artery is a major risk factor for stroke and cardiovascular diseases. Parathormone (PTH), primarily known for its role in calcium and phosphate metabolism, has been increasingly implicated in vascular pathophysiology. This review explores the potential mechanisms by which PTH contributes to carotid atherosclerosis, including endothelial dysfunction, vascular calcification, oxidative stress, and inflammation. Understanding these pathways could provide new insights into the prevention and management of atherosclerotic diseases. This review examines the role of PTH in the pathogenesis of carotid atherosclerosis and its potential implications for cardiovascular risk management. PTH has pleiotropic effects on the cardiovascular system. Beyond its classical role in bone metabolism, it exerts direct effects on vascular smooth muscle cells (VSMCs), endothelial cells, and inflammatory pathways.

Key words: parathormon, bone metabolism, endothelial dysfunction, dyslipidemia, insulin resistance.

Atherosclerosis is a progressive disease characterized by lipid accumulation, inflammation, and vascular remodeling, leading to plaque formation in arteries. The carotid arteries, which supply blood to the brain, are particularly vulnerable to atherosclerotic changes, and their involvement significantly increases the risk of stroke. While traditional risk factors such as hypertension, diabetes, and hyperlipidemia are well-recognized contributors to atherosclerosis, emerging evidence suggests that hormonal imbalances, particularly involving parathormone (PTH), may also play a

significant role in vascular dysfunction and atherogenesis. PTH, secreted by the parathyroid glands, primarily regulates calcium and phosphate homeostasis in the body. However, studies have indicated that elevated PTH levels, commonly observed in conditions such as primary and secondary hyperparathyroidism, are associated with increased cardiovascular morbidity. This association raises important questions about the mechanisms through which PTH may influence vascular health. Research has shown that elevated PTH can contribute to atherosclerosis through several pathways.

Endothelial dysfunction (ECD) is a critical factor in the development of atherosclerosis and is significantly influenced by parathormone (PTH). Elevated levels of PTH can lead to changes in the endothelial barrier, making it more permeable. This increased permeability allows for the infiltration of lipoproteins and inflammatory cells into the vascular wall, which is a key step in the development of atherosclerotic plaques. PTH is associated with the upregulation of pro-inflammatory cytokines and adhesion molecules on endothelial cells. This inflammatory response can attract monocytes and other immune cells to the endothelium, further exacerbating inflammation and contributing to plaque formation [6]. PTH may disrupt the balance of vasodilatory and vasoconstrictive signals in the endothelium. This dysregulation can lead to impaired vasodilation, contributing to increased blood pressure and further endothelial injury. Elevated PTH levels can enhance oxidative stress within the vascular endothelium. Oxidative stress is known to damage endothelial cells and promote atherogenic processes, including lipid oxidation and inflammation [6]. The relationship between PTH and endothelial dysfunction highlights the importance of hormonal balance in maintaining vascular health. Elevated PTH levels can lead to significant endothelial impairment, promoting inflammatory processes that contribute to atherosclerosis and increasing cardiovascular risk. Understanding these mechanisms may provide new avenues for therapeutic interventions aimed at mitigating the effects of PTH on vascular health.

Elevated PTH levels have been associated with impaired endothelial function due to reduced nitric oxide (NO) bioavailability. PTH may decrease endothelial NO

synthesis, leading to vasoconstriction and increased arterial stiffness. Increased oxidative stress: PTH can induce oxidative stress by promoting reactive oxygen species (ROS) production, which further damages the endothelium and accelerates plaque formation [4]. PTH plays a complex role in vascular calcification, a hallmark of advanced atherosclerosis. It can both promote and inhibit calcification under different circumstances: induction of osteogenic differentiation in VSMCs: PTH can trigger VSMCs to transform into osteoblast-like cells, contributing to arterial calcification. Regulation of phosphate metabolism: high PTH levels lead to increased phosphate retention, which enhances vascular calcification. Chronic inflammation is a critical driver of atherosclerosis. PTH has been shown to modulate inflammatory responses through: Upregulation of pro-inflammatory cytokines: PTH can stimulate the production of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which promote plaque instability. Increased monocyte and macrophage infiltration: PTH enhances monocyte adhesion to endothelial cells, facilitating foam cell formation and plaque progression.

Parathormone (PTH) has been increasingly recognized for its role in inflammatory responses that can exacerbate atherosclerosis. Chronic inflammation is a critical factor in the development and progression of atherosclerotic plaques, and elevated levels of PTH may enhance this inflammatory environment through several mechanisms. Elevated PTH levels have been associated with increased production of pro-inflammatory cytokines, which play a significant role in the inflammatory processes that contribute to atherosclerosis. These cytokines can promote the recruitment of immune cells to the vascular endothelium, further driving inflammation and plaque development [7]. PTH may influence the activation and polarization of immune cells, particularly macrophages. This activation can lead to a shift towards a pro-inflammatory phenotype, which is known to exacerbate plaque instability and increase the risk of cardiovascular events [8]. In conditions such as primary hyperparathyroidism, elevated PTH levels are linked to chronic low-grade inflammation. This persistent inflammatory state can contribute to the progression of

atherosclerosis by maintaining an environment conducive to plaque formation and instability [7]. PTH can induce endothelial cell activation, leading to increased expression of adhesion molecules and further promoting the inflammatory response. This activation facilitates the adhesion and infiltration of leukocytes into the arterial wall, a key step in atherogenesis [8]. The link between elevated PTH levels and inflammation underscores the importance of considering hormonal factors in the context of cardiovascular health. By enhancing inflammatory responses, elevated PTH may contribute to the progression of atherosclerosis, highlighting the need for further research into targeted interventions that could mitigate these effects.

Parathormone (PTH) plays a significant role in influencing lipid metabolism, which can lead to dyslipidemia—a condition characterized by abnormal lipid levels in the blood. Dyslipidemia is a well-established risk factor for atherosclerosis, and alterations in lipid profiles can contribute to both the formation and stability of atherosclerotic plaques. Elevated PTH levels have been associated with changes in lipid metabolism, including increased levels of low-density lipoprotein (LDL) cholesterol and triglycerides. These alterations can promote the development of atherogenic dyslipidemia, which is characterized by high levels of triglycerides and low levels of high-density lipoprotein (HDL) cholesterol [1].

PTH may affect lipid metabolism through several mechanisms. PTH can stimulate lipogenesis, leading to higher triglyceride levels in the bloodstream. It may also impair the breakdown of fats, contributing to the accumulation of lipids in the vascular system [2]. PTH influences liver function, which is crucial for lipid metabolism. Dysregulation in hepatic lipid processing can lead to increased circulating lipid levels [2]. Changes in lipid profiles due to elevated PTH can enhance the formation of atherosclerotic plaques. High levels of LDL cholesterol are particularly atherogenic, as they can infiltrate the arterial wall and undergo modification, leading to inflammation and plaque instability [3]. Additionally, dyslipidemia can exacerbate endothelial dysfunction, further promoting atherosclerosis [2]. Understanding the role of PTH in lipid metabolism is essential for managing cardiovascular risk, especially in

patients with conditions associated with elevated PTH levels, such as primary and secondary hyperparathyroidism. Targeting lipid abnormalities in these patients may help mitigate the risk of atherosclerosis and related cardiovascular events [3].

PTH significantly influences lipid metabolism, leading to dyslipidemia, which is a critical factor in the development of atherosclerosis. The interplay between elevated PTH levels and lipid profile alterations underscores the importance of monitoring and managing lipid levels in patients with hormonal imbalances to reduce cardiovascular risk. Elevated PTH levels are associated with increased vascular calcification, which can further complicate atherosclerotic changes and lead to reduced arterial elasticity and increased stiffness. Given these mechanisms, it is evident that PTH may play a multifaceted role in the development of atherosclerosis, particularly in the carotid arteries. Understanding the relationship between PTH and vascular health could provide new insights into the management of cardiovascular risk, especially in patients with hormonal imbalances. Further research is needed to clarify these relationships and explore potential therapeutic interventions that target PTH-mediated pathways to mitigate cardiovascular risks associated with atherosclerosis.

Hyperparathyroidism has been linked to dyslipidemia and insulin resistance, both of which contribute to atherosclerosis. Elevated PTH levels are associated with: Higher levels of low-density lipoprotein (LDL) and triglycerides. Reduced high-density lipoprotein (HDL) [5]. Increased insulin resistance, which exacerbates endothelial dysfunction. Several epidemiological and clinical studies have explored the association between PTH levels and carotid atherosclerosis. Observational studies have reported a correlation between high PTH levels and increased carotid intima-media thickness (CIMT), a marker of early atherosclerosis. Patients with primary hyperparathyroidism often exhibit higher CIMT and greater plaque burden compared to healthy controls. Interventional studies suggest that parathyroidectomy in hyperparathyroid patients may reduce carotid atherosclerosis progression, supporting a causal relationship. Given the emerging role of PTH in atherosclerosis, targeting PTH-related pathways may offer new therapeutic opportunities: Vitamin D supplementation: Since vitamin D deficiency

is a common cause of secondary hyperparathyroidism, correcting vitamin D levels may mitigate PTH-induced vascular damage. Calcimimetics (e.g., cinacalcet): These drugs lower PTH levels and have shown potential in reducing vascular calcification in patients with chronic kidney disease. Parathyroidectomy: In selected cases, surgical removal of hyperactive parathyroid glands may improve vascular outcomes.

Conclusion

Parathormone (PTH) plays a significant role in the development of carotid atherosclerosis through multiple mechanisms. Elevated PTH levels can lead to impaired endothelial function, which is a critical factor in the initiation and progression of atherosclerosis. This dysfunction contributes to the inability of blood vessels to properly regulate blood flow and maintain vascular health. PTH is associated with increased vascular calcification, which can further exacerbate atherosclerotic changes in the carotid arteries. This calcification is often seen in patients with chronic kidney disease and hyperparathyroid states, where PTH levels are elevated. PTH has been linked to inflammatory processes that promote atherosclerosis. Chronic inflammation is a well-known contributor to the development of carotid plaques, and elevated PTH may enhance this inflammatory response. Lipid Metabolism Alterations: PTH influences lipid metabolism, leading to dyslipidemia, which is a significant risk factor for atherosclerosis. Changes in lipid profiles can contribute to the formation of atherosclerotic plaques in the carotid arteries. Elevated PTH levels, particularly in hyperparathyroid states, have been linked to increased carotid plaque burden and higher cardiovascular risk. This relationship highlights the importance of monitoring PTH levels in patients at risk for cardiovascular diseases. Further research is needed to clarify the causal relationships between PTH and vascular damage and to explore targeted interventions that may mitigate PTH-mediated vascular damage. Understanding these mechanisms could lead to improved management strategies for patients with elevated PTH levels and associated cardiovascular risks.

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ММ Асадуллаев, ХТ Мирахмедова, НА Ботирова – 2024

10. ЭНДОКРИННАЯ СИСТЕМА И АТЕРОМАТОЗНЫЕ СТАДИИ АТЕРОСКЛЕРОЗА

НА Ботирова, НМ Вахабова, ХТ Мирахмедова… - 2024

11. ЗНАЧЕНИЕ ИЗМЕНЕНИЙ НАРУЖНОЙ СОННОЙ АРТЕРИИ И ЩИТОВИДНОЙ ЖЕЛЕЗЫ У ПАЦИЕНТОВ С РИСКОМ ИШЕМИЧЕСКОГО ИНСУЛЬТА

ММ Асадуллаев, НА Ботирова, НМ Вахабова - 2024

12. ЎТКИР ИШЕМИК ИНСУЛТ ЎТКАЗГАН БЕМОРЛАРДА УЙҚУ АРТЕРИЯСИНИНГ ЎТКАЗУВЧАНЛИК ХУСУСИЯТЛАРИ

ММ Асадуллаев, ДР Жуманазаров, НА Ботирова - Modern education and development, 2025

13. АНАЛИЗ ПРОХОДИМОСТИ СОННОЙ АРТЕРИИ У ПАЦИЕНТОВ С ОСТРЫМ ИШЕМИЧЕСКИМ ИНСУЛЬТОМ: ИССЛЕДОВАНИЕ АТЕРОСКЛЕРОТИЧЕСКИХ ИЗМЕНЕНИЙ И ГЕМОДИНАМИЧЕСКИХ ПАРАМЕТРОВ

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