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Journal of Parathyroid Disease

Journal of Parathyroid Disease 2023,11, e11211

DOI:10.34172/jpd.2023.11211

Review

Association of parathyroid hormone with plasma magnesium in health and disease; a review

Maedeh Hamrah Siyani[1], Faraz Zandiyeh[2], Elahe Zaremoghadam[3], Sara Dehghan[4], Reyhaneh Sadeghian[4], Zahra Aboulfathiyarmohammadyar[5], Mina Alipoor[6*]

Abstract

Parathyroid hormone (PTH) is a hormone produced by the parathyroid glands that regulates calcium and phosphate metabolism in the body. Magnesium is an essential mineral that plays a role in many cellular processes, including nerve and muscle function, DNA synthesis, and bone health. This review aims to examine the association between PTH and magnesium in health and disease states. Several studies have shown that lower levels of magnesium in the blood are associated with higher levels of PTH. This association has been observed in both healthy individuals and those with chronic kidney disease, primary hyperparathyroidism, and vitamin D deficiency. The mechanism by which magnesium regulates PTH synthesis is not yet fully understood but appears to involve magnesium's role in the calcium-sensing receptor (CaSR) and cellular signaling pathways. In conclusion, the evidence suggests a clear and significant association between PTH and magnesium, with lower serum magnesium levels associated with elevated PTH levels. Further research is needed to understand clinical practice's underlying mechanisms and implications.

Keywords: Magnesium, Parathyroid hormone, Parathyroid glands, Calcium-sensing receptor, Hyperparathyroidism, Bone

Please cite this paper as: Hamrah Siyani M, Zandiyeh F, Zaremoghadam E, Dehghan S, Sadeghian R, Aboulfathiyarmohammadyar Z, Alipoor M. Association of parathyroid hormone with plasma magnesium in health and disease; a review. J Parathyr Dis. 2023;11:e11211. doi:10.34172/jpd.2023.11211.

Introduction

Parathyroid hormone (PTH) is produced by the parathyroid gland that regulates the body's calcium and phosphate levels. PTH acts on the kidneys, bones, and intestines, increasing calcium reabsorption and reducing phosphate reabsorption to maintain a stable serum calcium level (1,2). Magnesium is essential in many cellular processes, including nerve and muscle function, DNA synthesis, and bone health. The majority of magnesium in the body is found in bone tissue, but it also plays a vital role in calcium homeostasis (3,4). This review examines the association between PTH and magnesium in health and disease states.

Methods

A literature search using PubMed and Google Scholar was conducted using the search terms parathyroid hormone, "magnesium, hypomagnesemia, and hyperparathyroidism, parathyroid glands, calcium-sensing receptor, and bone. Articles published in English were considered eligible for inclusion if they investigated the relationship between PTH and magnesium in humans.

Results

Multiple studies have found an inverse association between serum magnesium levels and PTH levels, indicating that low magnesium levels are associated with elevated PTH levels (5,6). Studies have shown this association in healthy individuals, chronic kidney disease patients, primary hyperparathyroidism patients, and vitamin D deficiency. One study of postmenopausal women found that low magnesium levels were associated with both higher PTH levels and more significant bone loss. These findings suggest that hypomagnesemia may contribute to secondary hyperparathyroidism and increased bone resorption in some populations (6,7). The underlying mechanism by which magnesium regulates PTH synthesis is not yet fully understood. Still, it appears to arise from magnesium's role in the calcium-sensing receptor (CaSR) and cellular signaling pathways (3,8).

Received: 11 April 2023, Accepted: 9 July 2023, ePublished: 29 July 2023

[1]Department of Anesthesiology, Student Research Committee, Sabzevar University of Medical Sciences, Sabzevar, Iran. [2]Department of Emergency Medicine, Shohadaye Salamat Hospital, Iran University of Medical Sciences, Tehran, Iran. [3]Department of Internal Medicine, School of Medicine, Birjand University of Medical Sciences, Birjand, Iran. [4]Department of Nursing, Faculty of Nursing and Midwifery, Hormozgan University of Medical Sciences, Bandar Abbas, Iran. [5]Student Research Committee, School of Pharmacy, Eastern Mediterranean University of North Cyprus, Famagusta, Cyprus. [6]Department of Anesthesiology, School of Paramedical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

***Corresponding author:** Mina Alipour, Email: alipoormina22@yahoo.com

Implication for health policy/practice/research/medical education

The evidence supports an association between serum magnesium levels and PTH levels, with lower magnesium levels associated with elevated PTH levels in both health and disease states. The mechanisms that mediate these effects remain unclear, and further studies are required to understand them fully. Nonetheless, this association provides a potential avenue for interventions in patients with chronic hypomagnesemia, primary hyperparathyroidism, and possibly other conditions related to calcium homeostasis.

Discussion

Several theories exist regarding how magnesium regulates PTH secretion. One theory is that magnesium acts as an allosteric modulator of the CaSR on the parathyroid gland. The CaSR senses changes in the extracellular calcium concentration and adjusts PTH secretion accordingly (8,9). When extracellular calcium levels decrease, PTH secretion increases to restore levels to normal. Magnesium ions bind to the CaSR, modulating its sensitivity to extracellular calcium and altering PTH secretion. In vitro studies have shown that magnesium enhances the CaSR's responsiveness to calcium, reducing PTH secretion. Conversely, low magnesium levels impair CaSR functioning, potentially leading to excess PTH secretion (10,11).

Another potential mechanism for magnesium's effects on PTH synthesis is its role in cellular signaling pathways. Magnesium ions are required as cofactors for several enzymes, including adenylyl cyclase, generating the second messenger of PTH, cyclic AMP (cAMP). When levels of cAMP are high, PTH secretion is stimulated. Therefore, low magnesium levels may reduce cAMP formation, leading to fewer PTH secretions (8,12).

The exact mechanism of how magnesium regulates PTH secretion is still unclear and requires further study. It is possible that magnesium may regulate PTH synthesis by regulating intracellular calcium concentrations (8,13). Studies have shown that magnesium is required for calcium uptake and storage in bone, and osteoblasts and osteocytes express magnesium transporters. Magnesium deficiency may affect bone calcium resorption, leading to elevated PTH levels, which reinforce osteoclastic bone resorption leading to hyperparathyroidism and calcium leaching out of bone which may further reduce serum magnesium concentrations (14-16).

Clinical implications

The association between magnesium and PTH has important implications for clinical practice, given that hypomagnesemia is common in many patient populations and is also a feature in primary hyperparathyroidism (17,18). Hypomagnesemia may exacerbate secondary hyperparathyroidism in chronic kidney disease patients, leading to progression of bone mineral disease and cardiovascular complications. Measurement of magnesium levels among patients with chronic kidney disease and other populations at risk for hypomagnesemia may help identify patients at risk of hyperparathyroidism and bone loss and provide opportunities for early intervention (19,20). Hypomagnesemia has been associated with an increased risk of osteoporosis, fracture, and soft-tissue calcification in individuals with primary hyperparathyroidism. Therefore, magnesium supplementation may be beneficial in patients with chronic hypomagnesemia or primary hyperparathyroidism in parallel with other interventions, such as drugs that decrease elevated PTH levels (21).

Conclusion

Magnesium levels have a clear and significant association with PTH levels, with lower serum magnesium levels associated with elevated PTH levels. In some populations, chronic hypomagnesemia may contribute to secondary hyperparathyroidism and increased bone resorption. Further research is needed to understand the underlying mechanisms involved, especially in patients with chronic kidney disease or primary hyperparathyroidism. These findings have implications for clinical practice and may prompt the need to assess magnesium status in patients with diseases related to calcium homeostasis.

Limitations

It is essential to note some limitations regarding this review. Studies investigating the association between magnesium and PTH have been limited to smaller, observational studies, and the exact mechanisms involved remain unclear. The majority of these studies have focused on patients with chronic kidney disease, primary hyperparathyroidism, vitamin D deficiency, and older women, making it difficult to generalize the findings to other populations. More studies are needed to clarify these associations and identify more precise mechanisms involved.

Authors' contribution

Conceptualization: MH.
Validation: FZ.
Investigation: SD and EZ.
Resources: RS and EZ.
Data Curation: ZA and MA.
Visualization: FZ and SD.
Supervision: MA.
Funding acquisition: All authors.
Writing–original draft : SD, FZ, MH, and ZA.
Writing–review and editing: EZ, RS, and MA.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

None.

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