International Journal of Clinical Medicine, 2026, 17(10), 334-351
https://www.scirp.org/journal/ijcm
ISSN Online: 2158-2882
ISSN Print: 2158-284X

Recurrent Benign Paroxysmal Positional Vertigo: A Microcirculatory and Metabolic Hypothesis of Otoconial Degeneration Supported by Preliminary Clinical Observations

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How to cite this paper: Iannuzzi, L., Marrari, L.A. and Iannuzzi, S. (2026) Recurrent Benign Paroxysmal Positional Vertigo: A Microcirculatory and Metabolic Hypothesis of Otoconial Degeneration Supported by Preliminary Clinical Observations. *International Journal of Clinical Medicine*, **17**, 334-351.
https://doi.org/10.4236/ijcm.2026.1710023

Received: September 16, 2026
Accepted: October 25, 2026
Published: October 28, 2026

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Abstract

Background: Benign paroxysmal positional vertigo (BPPV) is the most common peripheral vestibular disorder, accounting for approximately 20% - 30% of patients presenting with dizziness in specialized clinics. Although canalith repositioning maneuvers achieve symptom resolution in most cases, recurrence remains a significant clinical challenge, affecting approximately 15% - 30% of patients within the first year and up to 50% during long-term follow-up. Current pathogenetic models primarily attribute recurrent BPPV to age-related degeneration of the otoconial membrane; however, they do not fully explain the strong association between recurrent disease and systemic vascular and metabolic disorders. **Objective:** To propose a novel pathophysiological hypothesis linking labyrinthine microcirculatory dysfunction, chronic tissue hypoxia, extracellular acidification, and degeneration of the otoconial membrane, and to describe preliminary clinical observations obtained following adjunctive oral alkalinizing mineral supplementation in patients with recurrent BPPV. **Methods:** A preliminary observational study was performed in approximately twenty patients with recurrent BPPV treated with standard canalith repositioning maneuvers followed by oral alkalinizing mineral supplementation (Alkimo HP®, one sachet twice daily). Clinical outcomes were evaluated according to recurrence of positional vertigo during follow-up and subjective improvement in balance and quality of life. Four representative clinical cases are presented. **Results:** During the observation period, all patients reported subjective clinical improvement after initiation of supplementation.

Several patients remained free of recurrent positional vertigo throughout follow-up, whereas recurrence was observed in some patients after treatment discontinuation. The representative clinical cases consistently demonstrated a reduction in recurrence frequency associated with improved postural stability and quality of life. **Conclusions:** Microvascular impairment may represent the common biological pathway linking many recognized risk factors for recurrent BPPV, including aging, hypertension, diabetes mellitus, hyperlipidemia, migraine, and chronic sleep disorders. We hypothesize that chronic labyrinthine hypoperfusion induces activation of hypoxia-responsive metabolic pathways, leading to extracellular acidification, alteration of the otoconial extracellular matrix, and increased susceptibility to otoconial detachment. Although preliminary clinical observations are encouraging, controlled prospective studies are necessary to validate both the proposed pathogenetic model and its therapeutic implications.

Keywords

Benign Paroxysmal Positional Vertigo, Otoconia, Microcirculation, Hypoxia, Extracellular Matrix, Alkimo HP®

1. Introduction

Benign paroxysmal positional vertigo (BPPV) represents the most common cause of peripheral vertigo and one of the most frequent vestibular disorders encountered in otolaryngological and neurological practice [1]. The lifetime prevalence has been estimated at approximately 2.4%, with a marked increase after the fifth decade of life and a higher incidence among women. Canalith repositioning maneuvers, including those described by Epley and Semont, achieve complete symptom resolution in most patients and currently constitute the gold standard treatment recommended by international guidelines [2] [3].

Nevertheless, recurrence remains a major unresolved clinical problem, with reported rates ranging from 15% - 30% during the first year to nearly 50% after prolonged follow-up [2] [4]. The currently accepted pathogenetic model is based on the detachment of calcium carbonate crystals (otoconia) from the utricular macula, followed by migration into one or more semicircular canals. Depending on whether these particles remain free within the endolymph (canalolithiasis) or become adherent to the cupula (cupulolithiasis), abnormal stimulation of vestibular hair cells generates the characteristic positional vertigo and nystagmus [5].

Although this mechanical theory adequately explains the immediate clinical manifestations of BPPV, it does not clarify why some individuals experience repeated recurrences despite technically successful repositioning maneuvers. The persistence or recurrence of otoconial detachment strongly suggests that the underlying pathological process involves chronic alterations of the utricular macula rather than merely mechanical displacement of otolithic debris. Electron micros-

copy studies performed on specimens obtained during posterior semicircular canal occlusion have demonstrated both intact and degenerating otoconia surrounded by amorphous gelatinous material, providing direct evidence of progressive degeneration of the otoconial membrane [5]. These findings indicate that recurrent BPPV should be regarded not simply as a disorder of displaced particles but as a disease affecting the biological integrity of the otolithic extracellular matrix.

Recurrent benign paroxysmal positional vertigo is a clinical condition characterized by recurring episodes of intense rotational vertigo of very short duration (less than one minute), triggered by specific head movements or changes in head position. Medical assessment involves the Dix-Hallpike maneuver, diagnostic imaging (contrast-enhanced MRI), and an evaluation of the symptoms and the circumstances under which they occur.

Over the past decade, numerous epidemiological studies have identified several independent predictors of recurrent BPPV, including advanced age, female sex, osteoporosis, vitamin D deficiency, hypertension, diabetes mellitus, hyperlipidemia, migraine, Ménière's disease, chronic insomnia, and cerebrovascular disease [3] [5] [6]. At first glance, these conditions appear unrelated; however, they share a common feature: each may impair systemic or local microvascular function.

This observation raises an important question: rather than representing independent risk factors, could these apparently diverse conditions contribute to a common pathophysiological pathway characterized by chronic labyrinthine hypoperfusion and progressive degeneration of the otoconial membrane?

The present article develops this hypothesis by integrating current knowledge regarding inner ear microcirculation, cellular adaptation to hypoxia, extracellular matrix biology, and metabolic regulation. We propose that recurrent BPPV represents the final clinical expression of chronic microcirculatory dysfunction leading to tissue hypoxia, activation of hypoxia-inducible pathways, extracellular acidification, and structural weakening of the otoconial membrane. Within this theoretical framework, the preliminary clinical observations obtained following oral alkalinizing mineral supplementation are presented not as evidence of therapeutic efficacy but as hypothesis-generating findings deserving further investigation.

2. Current Evidence on Risk Factors for Recurrent BPPV

Despite the high success rate of canalith repositioning maneuvers, recurrence remains a common clinical event. Recent systematic reviews and meta-analyses have confirmed that recurrence is influenced by multiple systemic conditions rather than by vestibular factors alone [6].

Advanced age is among the strongest predictors of recurrence. Degenerative changes affecting both the utricular neuroepithelium and the extracellular matrix progressively reduce the mechanical stability of the otoconial membrane, facilitating spontaneous detachment of otoconia. Age-related vascular alterations may further aggravate this process through chronic reduction of labyrinthine perfusion.

Hypertension has consistently emerged as another important risk factor [6].

Long-standing arterial hypertension induces endothelial dysfunction, arteriolar remodeling, and impairment of capillary blood flow. Because the inner ear is supplied by terminal arteries lacking significant collateral circulation, even modest reductions in microvascular perfusion may compromise metabolic homeostasis of the utricular macula [7].

Similarly, diabetes mellitus contributes to chronic microangiopathy through endothelial injury, oxidative stress, and thickening of capillary basement membranes. Histopathological studies have demonstrated diabetic alterations involving both cochlear and vestibular structures, supporting the concept that vestibular dysfunction may represent one manifestation of systemic microvascular disease.

Hyperlipidemia further contributes to vascular impairment by promoting endothelial dysfunction and progressive atherosclerosis [5]. Reduced blood flow may impair oxygen delivery and nutrient exchange within the metabolically active vestibular neuroepithelium.

Migraine has also been repeatedly associated with recurrent BPPV [5]. Although its precise mechanism remains uncertain, transient vasospasm, neurovascular inflammation, and endothelial dysfunction have all been proposed as possible contributors to repeated otolithic injury.

Vitamin D deficiency has attracted considerable attention because of its role in calcium metabolism and otoconial mineralization. Several randomized studies suggest that correction of vitamin D deficiency reduces BPPV recurrence in selected patients, although the exact biological mechanism remains incompletely understood [5].

More recently, chronic insomnia has emerged as an additional predictor of recurrence [8]. Sleep deprivation is associated with increased sympathetic activity, endothelial dysfunction, oxidative stress, and systemic inflammation, all of which may adversely affect inner ear microcirculation. Improvement of sleep quality through behavioral interventions has been associated with lower recurrence rates in preliminary studies.

Although these risk factors have traditionally been considered separately, their coexistence in many patients suggests the existence of a common pathogenic mechanism. The hypothesis proposed in this article is that chronic microvascular insufficiency represents the biological substrate through which these apparently diverse clinical conditions converge to promote progressive degeneration of the otoconial membrane.

3. Microcirculatory Dysfunction as the Common Biological Denominator

The inner ear possesses one of the most metabolically active microvascular systems in the human body. Its arterial supply derives almost exclusively from the labyrinthine artery, a terminal vessel that lacks functionally significant collateral circulation [9]. Consequently, vestibular tissues are particularly vulnerable to even transient reductions in blood flow.

Experimental studies have demonstrated that relatively mild ischemia rapidly alters ionic homeostasis, mitochondrial metabolism, and extracellular matrix turnover within the vestibular sensory organs. Chronic reductions in tissue perfusion may therefore produce cumulative structural damage long before irreversible cellular degeneration becomes clinically evident.

Interestingly, nearly all clinical conditions associated with recurrent BPPV—including hypertension, diabetes mellitus, hyperlipidemia, aging, migraine, chronic insomnia, smoking, and cerebrovascular disease—share the capacity to impair endothelial function and microvascular perfusion [5] [7] [8]. Rather than acting as isolated risk factors, these disorders may therefore converge on a common final pathway characterized by chronic labyrinthine hypoxia. This concept provides a coherent biological framework capable of integrating the diverse epidemiological observations reported over the past two decades.

4. Biology of the Otoconial Membrane

The otoconial membrane is a highly specialized extracellular matrix covering the sensory epithelium of the utricular and saccular maculae. Rather than representing a passive mechanical structure, it is a biologically active extracellular scaffold responsible for maintaining the spatial organization and mechanical stability of otoconia.

Otoconia are microscopic biomineralized particles composed predominantly of calcium carbonate ($CaCO_3$) deposited on an organic protein matrix [6]. Approximately 90% - 95% of their mineral content consists of calcite crystals, while the remaining fraction is composed of glycoproteins, proteoglycans, collagen, glycosaminoglycans, and other extracellular matrix components that regulate crystal nucleation, growth, and attachment.

Among the structural proteins, Otoconin-90 (OC90) is the major organic constituent of mammalian otoconia and plays a critical role in calcium carbonate biomineralization. Experimental studies have demonstrated that alterations in OC90 expression produce abnormal crystal morphology and reduced mechanical stability of otoconia. Another essential component is Otolin-1, a collagen-like glycoprotein that forms the scaffold connecting otoconia to the gelatinous membrane. Additional extracellular proteins—including keratan sulfate proteoglycans, collagen type IV, laminin, and fibrillar glycoproteins—contribute to maintaining the viscoelastic properties of the otoconial membrane.

The integrity of this extracellular matrix is fundamental for vestibular function. Under physiological conditions, continuous remodeling of extracellular matrix proteins is balanced by controlled synthesis, enzymatic degradation, calcium homeostasis, and local ionic regulation. Aging progressively disrupts this equilibrium, resulting in fragmentation of the gelatinous matrix, partial detachment of otoconia, and increased susceptibility to positional vertigo [6].

Electron microscopy studies have confirmed that patients undergoing surgery for intractable BPPV exhibit both intact and degenerating otoconia surrounded

by amorphous matrix material [6]. These observations strongly suggest that recurrent BPPV represents not only a mechanical disorder of displaced particles but also a degenerative disease affecting the extracellular matrix responsible for anchoring otoconia to the utricular macula.

Consequently, degeneration of the otoconial membrane should be viewed as a dynamic biological process rather than a purely age-related phenomenon. Identifying the mechanisms responsible for extracellular matrix instability may therefore provide new therapeutic targets beyond simple canalith repositioning.

5. Cellular Response to Hypoxia

Adequate oxygen delivery is essential for the metabolic homeostasis of the inner ear. Vestibular sensory organs possess one of the highest metabolic demands in the human body and rely almost exclusively on oxidative phosphorylation for ATP production. The labyrinthine artery is an end artery with virtually no collateral circulation [7]. Consequently, even modest reductions in blood flow may induce chronic tissue hypoxia, particularly in patients with systemic microvascular disease.

Under normoxic conditions, pyruvate generated through glycolysis enters mitochondria, where pyruvate dehydrogenase converts it into acetyl-CoA, allowing oxidative phosphorylation to generate approximately 30 - 32 ATP molecules per glucose molecule. When oxygen availability decreases, this metabolic pathway undergoes profound reprogramming. Reduced oxygen tension inhibits pyruvate dehydrogenase activity and stabilizes hypoxia-inducible factor-1 alpha, a transcription factor that orchestrates cellular adaptation to hypoxia [9] [10].

Factor-1 alpha induces the expression of multiple genes involved in anaerobic metabolism, including glucose transporters (GLUT-1), glycolytic enzymes, pyruvate dehydrogenase kinase (PDK), and lactate dehydrogenase A (LDH-A) [9] [11]. Pyruvate is consequently diverted away from mitochondrial oxidation toward conversion into lactate, allowing glycolysis to continue despite reduced oxygen availability.

Although this metabolic adaptation preserves short-term cellular survival, chronic activation of the HIF pathway has important biological consequences [9]. Progressive lactate accumulation contributes to local extracellular acidification, modifies the ionic composition of the extracellular environment, and influences multiple signaling pathways regulating inflammation, extracellular matrix remodeling, angiogenesis, and tissue repair [12].

Recent experimental evidence indicates that chronic hypoxia also alters extracellular matrix turnover through modulation of matrix metalloproteinases (MMPs), tissue inhibitors of metalloproteinases (TIMPs), collagen synthesis, and proteoglycan metabolism. Similar mechanisms have been implicated in degenerative diseases affecting cartilage, intervertebral discs, tendons, vascular walls, and other connective tissues.

Although direct evidence involving the otoconial membrane is currently una-

vailable, it is biologically plausible that chronic labyrinthine hypoxia may induce comparable extracellular matrix remodeling within the utricular macula. Progressive weakening of the gelatinous scaffold could reduce the mechanical anchorage of otoconia, thereby increasing their susceptibility to spontaneous detachment and migration into the semicircular canals. This hypothesis provides a coherent mechanistic link between systemic microvascular disorders and recurrent BPPV.

6. Proposed Pathophysiological Model of Recurrent BPPV

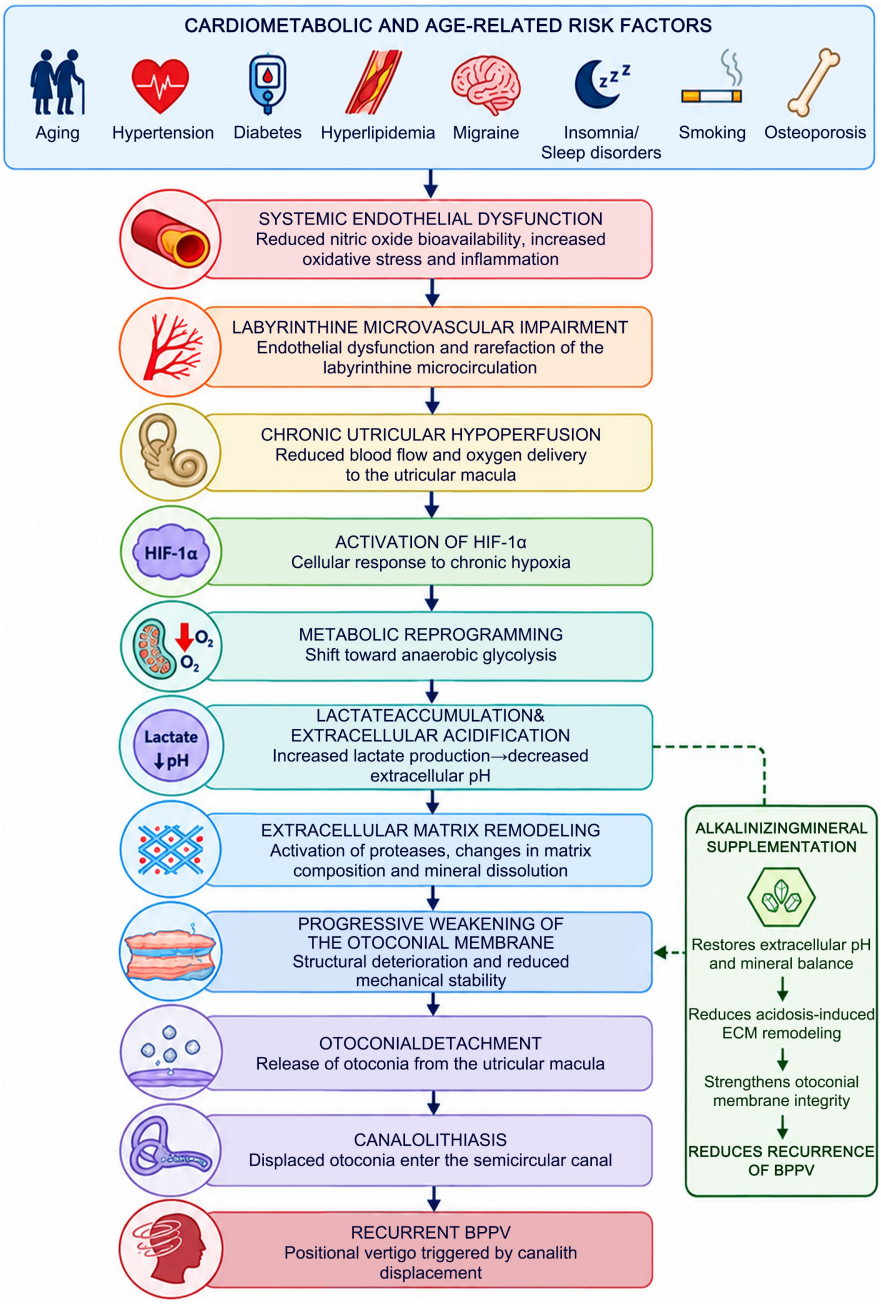


Figure 1. Proposed pathogenetic cascade linking systemic vascular risk factors to recurrent BPPV (figure created with AI).

The hypothesis proposed in the present study does not replace the canalolithiasis theory [1]; rather, it extends it by addressing the biological events that may precede otoconial detachment.

We propose that recurrent BPPV represents the final clinical manifestation of a chronic degenerative process affecting the otoconial extracellular matrix [5]. According to this model, several apparently unrelated systemic disorders—including aging, hypertension, diabetes mellitus, hyperlipidemia, migraine, chronic insomnia, smoking, osteoporosis, and other conditions associated with endothelial dysfunction—share the ability to impair labyrinthine microcirculation [5] [7] [8].

Progressive microvascular dysfunction may produce chronic low-grade hypoperfusion of the utricular macula. Because vestibular sensory organs possess limited metabolic reserve and are supplied by terminal arteries without significant collateral circulation, persistent reduction of oxygen delivery may induce repeated episodes of subclinical tissue hypoxia.

Activation of hypoxia-inducible factor-1 alpha (HIF-1α) constitutes the principal adaptive response to reduced oxygen availability [10]. While this mechanism preserves cellular viability through metabolic reprogramming toward anaerobic glycolysis, prolonged activation may also modify extracellular matrix homeostasis [9] [11].

Progressive remodeling of the gelatinous matrix could weaken the structural linkage between otoconia and the utricular macula. Mechanical stresses generated by normal head movements would then be sufficient to detach previously destabilized otoconia, allowing migration into the semicircular canals and producing recurrent episodes of positional vertigo [1]. Within this framework, canalolithiasis represents the terminal mechanical event of a much longer biological process characterized by chronic extracellular matrix degeneration (see **Figure 1**).

7. Integration with Current Literature

The proposed model should be regarded as an extension rather than an alternative to the current pathogenetic theory of BPPV. The classical canalolithiasis hypothesis, originally formulated by Hall, Ruby and McClure and subsequently refined by Parnes and colleagues, accurately explains the biomechanics responsible for positional nystagmus and the remarkable effectiveness of canalith repositioning maneuvers [2]. Nevertheless, it does not specifically address the biological mechanisms responsible for progressive weakening and repeated detachment of otoconia.

The present hypothesis integrates these observations into a single biological framework based on chronic labyrinthine microvascular dysfunction [7]. Rather than assuming independent mechanisms for each risk factor, it proposes that impaired oxygen delivery constitutes the common upstream event leading to progressive degeneration of the otoconial extracellular matrix [6] [9].

If confirmed experimentally, this hypothesis could have relevant clinical implications. Current management of recurrent BPPV focuses primarily on repeated

repositioning maneuvers after otoconial displacement has already occurred [2]. A better understanding of the biological mechanisms responsible for otoconial instability may eventually allow preventive strategies aimed at preserving extracellular matrix integrity before recurrent detachment develops, see Table 1.

Table 1. Methodological and conceptual comparison: classical vs. proposed model.

Feature	Classical Model	Proposed Model
Initial Event	Detachment of otoconia	Microcirculatory distress/tissue hypoperfusion
Primary Lesion	Mechanical	Biological/Metabolic
Mechanism	Canalithiasis	Hypoxia → HIF-1α activation → Matrix remodeling
Therapy	Canalith repositioning maneuvers	Repositioning maneuvers + potential preventive metabolic strategies (to be validated)
Objective	Clear otoconia from the semicircular canal	Preserve the structural stability of the otoconial membrane

8. Potential Role of Alkalinizing Mineral Supplementation in Recurrent BPPV

Benign paroxysmal positional vertigo (BPPV) is generally considered a mechanical disorder resulting from the detachment of otoconia from the utricular macula and their migration into the semicircular canals [3] [6]. Although canalith repositioning maneuvers effectively resolve individual episodes, they do not address the underlying biological mechanisms responsible for recurrent otoconial detachment. Consequently, recurrence rates remain substantial, particularly in older individuals and in patients with cardiovascular and metabolic comorbidities [3] [6].

Growing evidence suggests that recurrent BPPV may reflect chronic impairment of the utricular microenvironment rather than an isolated mechanical event. Aging, hypertension, diabetes mellitus, dyslipidemia, migraine, smoking, osteoporosis, and other vascular risk factors have all been associated with endothelial dysfunction and reduced labyrinthine microcirculation [2] [9]. Chronic hypoperfusion of the utricle may induce persistent tissue hypoxia characterized by activation of hypoxia-inducible factor-1α (HIF-1α), metabolic reprogramming toward anaerobic glycolysis, increased lactate production, and extracellular acidification [4] [5].

This acidic microenvironment may promote extracellular matrix remodeling through activation of matrix metalloproteinases, alteration of calcium homeostasis, and progressive weakening of the otoconial membrane, thereby facilitating repeated otoconial detachment and recurrent canalolithiasis [8] [9].

Within this pathophysiological framework, alkalinizing mineral supplementation may represent a biologically plausible adjunctive strategy aimed at restoring

extracellular acid-base balance and preserving the structural integrity of the utricular extracellular matrix.

9. Biological Rationale of the Mineral Salts

9.1. Potassium Bicarbonate

Potassium bicarbonate directly increases extracellular bicarbonate availability, enhancing systemic buffering capacity and reducing chronic low-grade metabolic acidosis [13]-[15]. By increasing extracellular pH, bicarbonate may reduce acid-induced extracellular matrix degradation and limit calcium carbonate dissolution. Clinical studies have demonstrated beneficial effects on bone mineral metabolism through reduction of urinary calcium excretion and bone resorption [13] [16]. Because otoconia consist predominantly of calcium carbonate crystals embedded within an organic extracellular matrix, preservation of calcium homeostasis may theoretically contribute to maintaining otoconial stability [17].

9.2. Magnesium Citrate

Magnesium citrate provides highly bioavailable magnesium, an essential cofactor for more than 300 enzymatic reactions involved in ATP synthesis, mitochondrial function, endothelial nitric oxide production, and calcium homeostasis [18]-[20]. Magnesium deficiency has been associated with oxidative stress, endothelial dysfunction, vascular inflammation, and impaired microvascular perfusion [21], conditions that could contribute to chronic utricular ischemia.

Magnesium also modulates intracellular calcium transport and extracellular matrix metabolism. Furthermore, the citrate moiety is metabolized through the tricarboxylic acid cycle, generating bicarbonate equivalents that contribute indirectly to systemic alkalinization [22].

9.3. Zinc Gluconate

Zinc is a mineral involved in numerous cellular processes and also contributes to the body's antioxidant defense systems. In particular, zinc plays a role in inner ear function and cellular antioxidant systems. An imbalance in zinc levels could theoretically increase the vulnerability of vestibular structures and otoconia [23].

9.4. Manganese Citrate

Manganese and selenium are trace elements involved in biological processes potentially relevant to inner ear physiology. Manganese, in particular, plays a role in the formation and maintenance of otoconia—the mineralized structures of the utricle and saccule whose displacement underlies BPPV. Experimental studies have shown that manganese deficiency can lead to alterations in otoconia and otolithic function. Manganese is also a functional component of manganese superoxide dismutase (Mn-SOD), one of the primary enzymatic defense systems against oxidative stress [24].

9.5. Sodium Selenite

Selenium, in turn, is essential for the activity of various selenoproteins, including glutathione peroxidase, involved in the control of reactive oxygen species. From a pathophysiological point of view, maintaining the integrity of the otoconial matrix and adequate control of oxidative stress could therefore contribute to the stability of the otolithic apparatus. These observations provide a biological rationale to study the association between trace elements, otocone metabolism and predisposition to BPPV relapses [24].

9.6. Potassium Citrate

Potassium citrate exerts its alkalinizing effect through hepatic metabolism of citrate to bicarbonate, thereby increasing systemic buffering capacity without directly administering bicarbonate [23]. Potassium citrate has been shown to reduce urinary calcium excretion, increase citrate availability, inhibit calcium crystal formation, and decrease bone resorption [14] [25] [26].

Since otoconia are biomineralized calcium carbonate structures, preservation of mineral homeostasis and correction of chronic acid load may theoretically contribute to maintaining their structural integrity and attachment to the otoconial membrane.

10. Clinical Case Series

To illustrate our preliminary observations, we report four representative cases of patients affected by recurrent BPPV who received oral alkalinizing mineral supplementation Alkimo HP (after repeated canalith repositioning maneuvers).

Alkimo HP is a mineral supplement produced by IMO SpA and supplied in sachets; it consists of potassium bicarbonate, magnesium citrate, and potassium citrate, along with bulking agents such as calcium phosphates and hydroxypropyl cellulose (E463), as well as zinc gluconate, manganese citrate, and sodium selenite. The recommended dosage for adults is two sachets per day, each to be dissolved in a glass of water and consumed by sipping slowly (one sachet two hours after lunch and one sachet two hours after dinner).

10.1. Case 1

A 48-year-old woman presented with recurrent posterior semicircular canal benign paroxysmal positional vertigo (BPPV). Her medical history was significant for Hashimoto thyroiditis, migraine, panic disorder, and hypercholesterolemia treated with rosuvastatin.

The first episode of posterior canal BPPV occurred in 2020 and resolved after a liberatory maneuver. A second recurrence developed in 2022 and was successfully treated with the Semont maneuver in the Emergency Department. Because of the recurrent episodes, a contrast-enhanced brain magnetic resonance imaging (MRI) performed in 2023 showed no pathological findings.

Further recurrences occurred on October 14, 2024, and April 30, 2025, the latter

successfully treated with the Epley maneuver. Laboratory investigations were performed to evaluate potential metabolic risk factors and included serum vitamin D, magnesium, and homocysteine levels. In an attempt to reduce recurrence frequency, adjunctive therapy with pentoxifylline (400 mg twice daily) was prescribed until January 2026, followed by flunarizine (5 mg once daily) until May 2026. Despite these treatments, the patient experienced additional recurrences on August 20, September 9, October 18, November 13, and December 6, 2025, and January 24, 2026, all successfully managed with canalith repositioning maneuvers.

Oral alkalinizing mineral supplementation was initiated in May 2026. During subsequent follow-up, no further BPPV episodes were reported. The patient also described a marked improvement in quality of life, with only occasional mild residual imbalance. From May 2026 to September 2026, she took the supplement for four consecutive months without experiencing any further clinical manifestations.

10.2. Case 2

A 69-year-old woman presented with recurrent benign paroxysmal positional vertigo (BPPV). Her medical history included arterial hypertension treated with angiotensin receptor blockers, hypercholesterolemia treated with rosuvastatin, and recurrent diverticular disease managed with rifaximin.

Over the course of several years, the patient experienced approximately ten episodes of BPPV, all successfully treated with canalith repositioning maneuvers. Despite the efficacy of these maneuvers, the patient continued to experience recurrent episodes.

Following the most recent recurrence, an oral alkalizing mineral supplement was introduced in January 2026 as an adjunctive therapy. At the last follow-up—conducted approximately two and four months after the start of treatment—the patient reported no further episodes of positional vertigo; she also noted improved postural stability and greater confidence in performing daily activities.

From January 2026, no episodes of BPPV occurred or were confirmed two months after the start of supplementation; at the subsequent visit in May 2026, the patient reported having experienced no episodes.

10.3. Case 3

A 56-year-old man presented with recurrent BPPV. His medical history included type 2 diabetes mellitus treated with metformin and semaglutide, arterial hypertension treated with olmesartan/hydrochlorothiazide, hypercholesterolemia treated with statins, and active cigarette smoking. His surgical history included varicocele repair and pilonidal sinus excision.

In August 2025, he developed sudden sensorineural hearing loss, which completely resolved following medical treatment. Brain MRI demonstrated small vascular gliotic lesions consistent with chronic microangiopathic changes.

The patient subsequently experienced an initial episode of vertigo that was treated symptomatically with sulpiride. He later developed recurrent posterior ca-

nal BPPV, with episodes occurring on October 1, 22, and 28, 2025. Each recurrence was successfully treated with canalith repositioning maneuvers performed by a vestibular specialist.

Oral alkalinizing mineral supplementation was initiated in November 2025. During follow-up, no further episodes of positional vertigo were observed, and the patient remained clinically stable without further acute episodes, as confirmed during an assessment in June 2026.

10.4. Case 4

A 79-year-old man presented with recurrent benign paroxysmal positional vertigo (BPPV). His medical history was significant for non-Hodgkin lymphoma undergoing chemotherapy and a prior SARS-CoV-2 infection in 2023.

The first episode of BPPV occurred in 2022 and resolved following a canalith repositioning maneuver. During 2025, the patient experienced two further recurrences, both successfully treated with liberatory maneuvers. Additional episodes occurred in March and April 2026, also responding to canalith repositioning treatment.

Following the last recurrence, oral supplementation with an alkalizing mineral supplement was initiated in May 2026. At the follow-up visit, the patient reported complete resolution of positional vertigo, accompanied by improved balance and a general subjective improvement in well-being. At the follow-up visit in September 2026, the patient reported complete resolution of positional vertigo, accompanied by improved balance and a general subjective improvement in well-being, with no acute episodes.

10.5. Summary of the Case Series

The observed cohort comprised 20 subjects with BPPV, however, only 4 patients underwent detailed screening and evaluation, as they returned to the clinic for follow-up. The remaining subjects were ineligible for assessment because the clinical information was insufficient to extrapolate data for real-world evidence.

The four patients presented heterogeneous clinical characteristics but shared recurrent BPPV despite repeated successful canalith repositioning maneuvers. Common comorbidities included vascular and metabolic disorders such as hypertension, diabetes mellitus, hypercholesterolemia, migraine, and chronic systemic diseases.

Following initiation of alkalinizing mineral supplementation, all patients experienced a period free from BPPV recurrence during the available follow-up. Although these observations are encouraging, the uncontrolled nature of this case series, the limited sample size, and the absence of standardized outcome measures preclude any definitive conclusion regarding treatment efficacy. These findings should therefore be considered strictly hypothesis-generating and warrant validation in prospective randomized controlled studies. All patients signed informed consent for the processing of anonymized clinical data. The study was conducted

in accordance with the principles of the Declaration of Helsinki.

11. Discussion

The present case series describes four patients with recurrent benign paroxysmal positional vertigo (BPPV) who remained free of further recurrences after the introduction of an oral alkalinizing mineral supplementation containing potassium bicarbonate, potassium citrate, and magnesium citrate. Although the observational nature of this report precludes any causal inference, the consistent clinical course observed in all patients raises the hypothesis that correction of the metabolic microenvironment of the inner ear may contribute to reducing otoconial instability in selected individuals.

BPPV is traditionally considered a purely mechanical disorder resulting from displacement of otoconia from the utricular macula into one of the semicircular canals. Canalith repositioning maneuvers effectively resolve the acute episode by relocating displaced otoconia back to the utricle; however, they do not address the biological mechanisms responsible for repeated otoconial detachment. Consequently, recurrence remains common, with reported rates ranging from approximately 15% within the first year to more than 50% after long-term follow-up.

Recent evidence indicates that recurrent BPPV should no longer be regarded solely as a mechanical disorder but rather as the clinical manifestation of chronic alterations affecting otoconial homeostasis. Large systematic reviews and meta-analyses consistently identify advanced age, hypertension, diabetes mellitus, hyperlipidemia, migraine, osteoporosis, thyroid disorders, and vitamin D deficiency among the principal risk factors for recurrence. Interestingly, most of these conditions share a common denominator: endothelial dysfunction and chronic microvascular impairment.

The vascular hypothesis of recurrent BPPV has gained increasing attention during the last decade. The inner ear is supplied by terminal arteries without significant collateral circulation, rendering the vestibular neuroepithelium particularly vulnerable to even subtle reductions in blood flow. Using extracranial Doppler ultrasonography, Neri and colleagues demonstrated that patients with recurrent BPPV frequently exhibit reduced vertebral artery flow and proposed that chronic labyrinthine hypoperfusion may induce degeneration of the utricular macula, thereby facilitating repeated otoconial detachment.

Our patients also presented several cardiovascular and metabolic comorbidities—including hypertension, diabetes mellitus, dyslipidemia, migraine, smoking, osteoporosis risk, and advanced age—that have all been independently associated with BPPV recurrence. Rather than acting as isolated risk factors, these conditions may represent different clinical manifestations of a common microvascular disorder affecting the inner ear.

Building upon this vascular hypothesis, we propose a complementary pathophysiological model centered on metabolic adaptation to chronic hypoperfusion. Persistent reduction of labyrinthine perfusion may expose the utricular neuroep-

ithelium to low-grade chronic hypoxia. In numerous tissues, hypoxia activates hypoxia-inducible factor-1α (HIF-1α), promoting a metabolic shift from oxidative phosphorylation toward anaerobic glycolysis with increased lactate production and extracellular acidification. Although this mechanism has not yet been directly demonstrated in the human utricle, it represents a well-established adaptive response in hypoxic tissues and may reasonably be extrapolated to the metabolically active vestibular sensory epithelium.

Progressive extracellular acidification may have several biological consequences relevant to otoconial stability. Acidic conditions favor extracellular matrix remodeling through activation of proteolytic enzymes, alteration of calcium homeostasis, and modifications of matrix protein interactions. Because otoconia consist of calcium carbonate crystals anchored to an organic extracellular matrix rich in otoconin-90, otolin-1, and other glycoproteins, disruption of this delicate microenvironment could progressively weaken the attachment of otoconia to the utricular macula. Experimental studies have shown that aging is associated with structural degeneration of otoconia and weakening of the interconnecting fibrillar network, supporting the concept that deterioration of the extracellular matrix plays a central role in recurrent BPPV.

An intriguing observation emerging from previous studies is that alterations in endolymphatic calcium concentration and pH have long been hypothesized to influence otoconial integrity. Otoconia exist in dynamic equilibrium with the surrounding endolymph, and their mineralization depends upon tightly regulated calcium and carbonate concentrations. Changes in local pH may modify calcium carbonate solubility and interfere with normal biomineralization processes. Although experimental confirmation in humans is currently lacking, this concept provides an attractive biological explanation linking systemic metabolic disturbances with recurrent otoconial instability.

Within this framework, the rationale for alkalinizing mineral supplementation becomes biologically plausible. Potassium bicarbonate directly increases systemic bicarbonate availability, improving extracellular buffering capacity and reducing chronic low-grade metabolic acidosis. Potassium citrate contributes to the same effect after hepatic metabolism of citrate into bicarbonate while simultaneously improving calcium balance and reducing urinary calcium loss. Magnesium citrate provides highly bioavailable magnesium, an essential cofactor involved in mitochondrial ATP production, endothelial nitric oxide synthesis, calcium transport, and antioxidant defense. Together, these compounds may improve endothelial function, optimize mineral homeostasis, reduce extracellular acid load, and preserve extracellular matrix integrity.

It is important to emphasize that our hypothesis does not imply that systemic alkalinization directly changes endolymph pH. The blood-labyrinth barrier and the tightly regulated ionic composition of endolymph make such a direct effect unlikely. Rather, we hypothesize that correction of chronic low-grade metabolic acidosis may improve the metabolic and vascular environment of the inner ear,

indirectly promoting preservation of the utricular extracellular matrix and otoconial attachment. This interpretation is consistent with current knowledge of endothelial biology and acid-base physiology while remaining appropriately cautious in the absence of direct experimental evidence.

Interestingly, all four patients in our series shared the common feature of repeated recurrences despite technically successful canalith repositioning maneuvers. After introduction of alkalinizing mineral supplementation, no additional episodes occurred during the available follow-up, and all patients reported subjective improvement in balance or quality of life. Although spontaneous remission cannot be excluded and placebo effects cannot be ruled out, the consistency of these observations suggests that modification of the metabolic milieu deserves further investigation.

The principal limitation of this study is the small sample size and the uncontrolled observational design, which preclude conclusions regarding efficacy. Follow-up duration differed among patients, and biochemical markers of systemic acid-base status, endothelial dysfunction, inflammatory activation, or oxidative stress were not serially assessed. Furthermore, no direct measurements of labyrinthine perfusion or utricular metabolism are currently feasible in routine clinical practice. Therefore, our findings should be regarded as hypothesis-generating rather than confirmatory.

Despite these limitations, this case series introduces a novel conceptual framework integrating several independent observations reported in the literature. Current evidence already supports the association between recurrent BPPV and vascular-metabolic disorders, age-related degeneration of otoconia, calcium metabolism abnormalities, and endothelial dysfunction. Our proposed model extends these observations by suggesting that chronic labyrinthine hypoperfusion may induce metabolic remodeling characterized by HIF-1α activation, increased anaerobic glycolysis, lactate accumulation, and extracellular acidification, ultimately promoting weakening of the otoconial membrane and recurrent otoconia detachment. Within this integrated model, alkalinizing mineral supplementation could represent a simple, inexpensive, and biologically plausible adjunctive strategy aimed at stabilizing the utricular microenvironment and reducing recurrence risk.

Future prospective randomized controlled studies incorporating serum biomarkers of acid-base homeostasis, endothelial function, vestibular function tests, and long-term recurrence rates will be necessary to validate this hypothesis and determine whether modulation of systemic metabolic homeostasis can influence the natural history of recurrent BPPV.

Provenance and Peer Review

All authors have read and approved the document.

Author Contributions

All authors contributed equally to this work.

Conflicts of Interest

Iannuzzi S. and Iannuzzi L. declare no conflicts of interest regarding the publication of this paper. Luigi Alberto Marrari is the medical director of IMO SpA.

References

[1] Kim, J. and Zee, D.S. (2014) Benign Paroxysmal Positional Vertigo. *New England Journal of Medicine*, **370**, 1138-1147. https://doi.org/10.1056/nejmcp1309481

[2] Bhattacharyya, N., Gubbels, S.P., Schwartz, S.R., Edlow, J.A., El-Kashlan, H., Fife, T., *et al.* (2017) Clinical Practice Guideline: Benign Paroxysmal Positional Vertigo (Update). *Otolaryngology—Head and Neck Surgery*, **156**, S1-S47. https://doi.org/10.1177/0194599816689667

[3] Casani, A.P. and Gufoni, M. (2023) Recurring Benign Paroxysmal Positional Vertigo after Successful Canalith Repositioning Manoeuvers. *Acta Otorhinolaryngologica Italica*, **43**, S61-S66. https://doi.org/10.14639/0392-100x-suppl.1-43-2023-08

[4] von Brevern, M., Bertholon, P., Brandt, T., Fife, T., Imai, T., Nuti, D., *et al.* (2015) Benign Paroxysmal Positional Vertigo: Diagnostic Criteria. *Journal of Vestibular Research*, **25**, 105-117. https://doi.org/10.3233/ves-150553

[5] Welling, D.B., Parnes, L.S., O'Brien, B., Bakaletz, L.O., Brackmann, D.E. and Hinojosa, R. (2009) Particulate Matter in the Posterior Semicircular Canal. *Laryngoscope*, **107**, 90-94. https://doi.org/10.1097/00005537-199701000-00018

[6] Wen, Y., Fan, Y. and Jian, B. (2025) Identifying Key Risk Factors for the Recurrence of Benign Paroxysmal Positional Vertigo Following Successful Canalith Repositioning Maneuvers: A Meta Analysis. *European Journal of Medical Research*, **30**, Article No. 262. https://doi.org/10.1186/s40001-025-02482-x

[7] Kao, W.T.K., Parnes, L.S. and Chole, R.A. (2017) Otoconia and Otolithic Membrane Fragments within the Posterior Semicircular Canal in Benign Paroxysmal Positional Vertigo. *The Laryngoscope*, **127**, 709-714. https://doi.org/10.1002/lary.26115

[8] Neri, G., Filograna Pignatelli, G.R., Pacella, A., Ortore, R. and Khasawneh, L. (2021) Recurring Paroxysmal Positional Vertigo: Evaluation of the Vascular Factor. *Acta Otorhinolaryngologica Italica*, **41**, 77-83. https://doi.org/10.14639/0392-100x-n0502

[9] Wang, P. (2025) Risk Factors for Recurrence in Benign Paroxysmal Positional Vertigo Patients and Construction of a Predictive Nomogram. *Medicine*, **104**, e44498. https://doi.org/10.1097/md.0000000000044498

[10] Semenza, G.L. (2012) Hypoxia-Inducible Factors in Physiology and Medicine. *Cell*, **148**, 399-408. https://doi.org/10.1016/j.cell.2012.01.021

[11] Lee, P., Chandel, N.S. and Simon, M.C. (2020) Cellular Adaption to Hypoxia through HIFs and Beyond. *Nature Reviews Molecular Cell Biology*, **21**, 268-283. https://doi.org/10.1038/s41580-020-0227-y

[12] Kaelin Jr., W.G. and Ratcliffe, P.J. (2018) Oxygen Sensing by Metazoans: The Central Role of the HIF Pathway. *Molecular Cell*, **30**, 393-402.

[13] Hansen, H.G. (1967) Reaktive veränderungen von leukocytenzahl und differentialblutbild. In: Weicker, H., *et al.*, Eds., *Erkrankungen der Stützgewebe Erkrankungen des Blutes und der Blutbildenden Organe*, Springer, 994-1006. https://doi.org/10.1007/978-3-642-94992-0_62

[14] Sebastian, A., Harris, S.T., Ottaway, J.H., Todd, K.M. and Morris, R.C. (1994) Improved Mineral Balance and Skeletal Metabolism in Postmenopausal Women Treated with Potassium Bicarbonate. *New England Journal of Medicine*, **330**, 1776-1781.

https://doi.org/10.1056/nejm199406233302502

[15] Jehle, S., Hulter, H.N. and Krapf, R. (2013) Effect of Potassium Citrate on Bone Density, Microarchitecture, and Fracture Risk in Healthy Older Adults without Osteoporosis: A Randomized Controlled Trial. *The Journal of Clinical Endocrinology & Metabolism*, **98**, 207-217. https://doi.org/10.1210/jc.2012-3099

[16] Frassetto, L., Morris, R.C. and Sebastian, A. (1997) Potassium Bicarbonate Reduces Urinary Nitrogen Excretion in Postmenopausal Women. *The Journal of Clinical Endocrinology & Metabolism*, **82**, 254-259. https://doi.org/10.1210/jcem.82.1.3663

[17] Frassetto, L., Morris, Jr., R.C., Sellmeyer, D.E., Todd, K. and Sebastian, A. (2001) Diet, Evolution and Aging—The Pathophysiologic Effects of the Post-Agricultural Inversion of the Potassium-to-Sodium and Base-to-Chloride Ratios in the Human Diet. *European Journal of Nutrition*, **40**, 200-213. https://doi.org/10.1007/s394-001-8347-4

[18] Lundberg, Y.W., Xu, Y., Thiessen, K.D. and Kramer, K.L. (2014) Mechanisms of Otoconia and Otolith Development. *Developmental Dynamics*, **244**, 239-253. https://doi.org/10.1002/dvdy.24195

[19] Gröber, U., Schmidt, J. and Kisters, K. (2015) Magnesium in Prevention and Therapy. *Nutrients*, **7**, 8199-8226. https://doi.org/10.3390/nu7095388

[20] de Baaij, J.H.F., Hoenderop, J.G.J. and Bindels, R.J.M. (2015) Magnesium in Man: Implications for Health and Disease. *Physiological Reviews*, **95**, 1-46. https://doi.org/10.1152/physrev.00012.2014

[21] Volpe, S.L. (2013) Magnesium in Disease Prevention and Overall Health. *Advances in Nutrition*, **4**, 378S-383S. https://doi.org/10.3945/an.112.003483

[22] Maier, J.A.M. (2012) Endothelial Cells and Magnesium: Implications in Atherosclerosis. *Clinical Science*, **122**, 397-407. https://doi.org/10.1042/cs20110506

[23] Hering-Smith, K.S. and Hamm, L.L. (2018) Acidosis and Citrate: Provocative Interactions. *Annals of Translational Medicine*, **6**, 374-374. https://doi.org/10.21037/atm.2018.07.37

[24] Günizi, H. and Savaş, H.B. (2023) An Evaluation of Trace Elements and Oxidative Stress in Patients with Benign Paroxysmal Positional Vertigo. *PLOS ONE*, **18**, e0277960. https://doi.org/10.1371/journal.pone.0277960

[25] Wang, J., Cao, C., Jiang, W., Sun, H., Jiang, T. and Hu, J. (2024) Circulating Levels of Micronutrients and the Risk of Benign Paroxysmal Positional Vertigo: A Mendelian Randomization Study. *Heliyon*, **10**, e38782. https://doi.org/10.1016/j.heliyon.2024.e38782

[26] Kraut, J.A. and Madias, N.E. (2017) Adverse Effects of the Metabolic Acidosis of Chronic Kidney Disease. *Advances in Chronic Kidney Disease*, **24**, 289-297. https://doi.org/10.1053/j.ackd.2017.06.005