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The Importance Of Vitamin D In Lipedema And Aesthetic Treatments

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Abstract:
Vitamin D plays a fundamental role in women's hormonal health and in lipedema, where we have significant variations in the production of estrogen, aromastasis and other hormones. This micronutrient participates in several physiological processes, including the regulation of inflammatory metabolism, immune balance and the modulation of endocrine functions such as PPAR gamma and C/EBP. It has an inverse correlation with BMI and body fat, which is why serum vitamin D deficiency can often be observed in patients with lipedema.
Vitamin D, a nutrient with multiple biological functions, including modulation of the immune system and inflammation, is often found in deficient levels in women with lipedema. Therefore, adequate monitoring and supplementation are essential to ensure bone health and possibly positively influence the progression of lipedema. Adequate vitamin D levels may play a role in alleviating symptoms and preventing complications associated with the condition. In addition, this vitamin plays important roles in the inflammatory response, helping to balance possible immune disorders in lipedema. Vitamin D nutritional status therefore impacts overall well-being and quality of life, and can influence disposition, mood regulation and even metabolic performance. With regard to the skin, vitamin D is also essential for maintaining a healthy appearance, as it participates in processes of cell renewal, tissue repair and protection against external agents.
An adequate supply of vitamin D, whether via cutaneous synthesis through controlled sun exposure or through supplementation, can help preserve the integrity of the skin, aiding in collagen production and the inflammatory response. Furthermore, this vitamin helps maintain defense barriers against skin infections and balances the local microbiota, important aspects when seeking to delay aging and improve the appearance and function of this organ. The benefits of vitamin D for the skin go beyond mere aesthetics, as they are also related to healing and the prevention of inflammatory or infectious conditions, which has a positive impact on dermatological treatments for women with lipedema.
Adequate levels of vitamin D in the body are seen as a crucial component for hormonal support in lipedema and for skin health, serving as a protective factor against various conditions that can affect women's quality of life. Combining laboratory monitoring to assess serum concentrations of 25-hydroxyvitamin D with a balanced diet, regular exercise, and occasional supplementation, when necessary, has proven to be crucial for alleviating symptoms of menopause and optimizing the results of dermatological treatments. Thus, understanding the importance of vitamin D in this context opens the way for prevention and health promotion strategies capable of minimizing complications resulting from hormonal changes and enhancing the effectiveness of skin rejuvenation and well-being therapies in women with lipedema.

Key Word: *Vitamin D; lipedema, Female Hormonal Health; Skin; Dermatological Treatments.*

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I. Introduction

Lipedema causes profound physiological and endocrine changes in the female body and requires special attention to women's hormonal health, especially with regard to the regulation of essential metabolites, such as vitamin D (Holick, 2007; Amato, 2025).

Lipedema affects 12.3% of Brazilian women and the majority do not have access to adequate treatments because professionals are not qualified and do not know how to treat it. Approximately 11 million Brazilian women have Lipedema, a disease that affects millions of people worldwide (Amato, 2022)

Lipedema, a little-known chronic disease of adipose hyperdeposition, is often confused with obesity and causes significant impairment of mobility and quality of life (Kruppa, 2020; Ishaq, 2021)

Increased gene expression of leptin and PPAR-gamma in lipedema adipocytes differentiated in vitro from adipose tissue-derived stem cells (Al-Ghadban, 2024).

Major signaling networks are dysregulated in patients with the adipose tissue disorder, lipedema; Ishaq identified the molecular mechanisms of lipedema by analyzing and comparing whole-tissue omics, adipocyte

precursors (adipose tissue-derived stem cells (ADSCs) and adipocytes from patients with or without lipedema. (ISHAQ, 2021)

Science has increasingly attributed relevance to vitamin D levels, given its participation in processes such as bone metabolism, immunomodulation, anti-inflammatory activity and maintenance of endocrine functions (Holick, 2011). In addition to directly influencing the body's ability to absorb calcium and phosphorus, essential nutrients for bone health, this vitamin also acts in mechanisms of cell renewal and tissue repair, impacting skin quality (Girgis et al., 2013).

Adequate levels of vitamin D act as a protective factor against systemic inflammation, aiding in the modulation of cytokines and cells of the immune system (Del Valle et al., 2011). This anti-inflammatory effect and immunomodulatory plays an even more relevant role in lipedema hormonal fluctuations can exacerbate subclinical inflammatory processes (Stojanović et al., 2018). The dermatological implications of this are broad, as the skin is not only a direct target of estrogenic changes – resulting in dryness, wrinkles and changes in collagen production (Brincat et al., 2015) – but also responds to vitamin D levels, essential for cell renewal and the maintenance of protective barriers against external agents.

On the other hand, vitamin D, synthesized mainly in the skin by the action of ultraviolet B (UVB) rays on 7-dehydrocholesterol, is directly influenced by factors such as inadequate sun exposure, advanced age, high body mass index and skin color (Holick, 2007).

Furthermore, insufficient levels of this nutrient compromise the epidermis' ability to renew itself and the production of essential lipids, resulting in skin that is more susceptible to xerosis and wrinkle formation (Lee et al., 2019). Thus, the relationship between vitamin D, menopause, and skin health emerges as a priority theme in research aimed at improving women's quality of life.

In hormonal terms, estrogen changes affect multiple endocrine axes, including the hypothalamic-pituitary-gonadal axis and the metabolism of adrenal steroid hormones (Santoro, 2016). Some authors point out that vitamin D may play a synergistic role in the regulation of certain hormones, such as parathyroid hormone (PTH), whose compensatory increase in cases of vitamin D deficiency increases bone resorption and accelerates bone mass loss (Holick, 2011). Thus, maintaining adequate levels of vitamin D helps stabilize PTH secretion and reduce the deleterious effects of secondary hyperparathyroidism (Girgis et al., 2013). The literature also suggests that this micronutrient may influence the synthesis of sex hormones, given the role of the vitamin D receptor (VDR) in some reproductive tissues and its possible participation in the modulation of steroidogenic enzymes (Farzaneh et al., 2020). Although more robust clinical studies are still needed, evidence points to a complex interaction between vitamin D and hormonal regulation, a fact that reinforces its importance for women's overall health.

With regard to aesthetic and dermatological treatments, vitamin D deficiency may have a direct impact on the effectiveness of certain procedures aimed at mitigating the effects of skin aging, such as chemical peels, lasers, and the use of rejuvenating cosmeceuticals (Krutmann et al., 2017). This is because vitamin D-mediated gene regulation, as well as its role in keratinocyte differentiation and structural protein production, is crucial for tissue recovery after dermatological interventions (Bikle, 2012). In clinical settings, monitoring vitamin D status and correcting it when below normal levels is essential.

The influence of vitamin D on cutaneous immunity is also noteworthy (Doshi et al., 2013). In this context, vitamin D regulates the production of interleukins, interferons, and other pro- and anti-inflammatory cytokines, contributing to the homeostasis of the cutaneous microbiome (Veldman et al., 2000). When vitamin D levels are low, the skin may become more vulnerable to infections and inflammatory processes, making it difficult to heal lesions and aggravating common climacteric disorders, such as rosacea or seborrheic dermatitis (Lee et al., 2019). In addition, studies highlight that adequate vitamin D helps to strengthen skin barriers, reducing transepidermal water loss (TEWL) and preventing dryness that significantly affects quality of life (Amaro-Ortiz et al., 2014). These aspects make it clear that vitamin D acts far beyond its classic function of maintaining calcium and phosphorus metabolism; it has a broad scope of action, including skin protection and repair mechanisms that become even more relevant in patients with lipedema.

The clinical outcomes of vitamin D deficiency are not restricted to the skeleton and skin: there is growing evidence that low levels of this micronutrient can interfere with the regulation of mood and neurotransmitters (Spedding, 2014). Many women experience psychological symptoms associated with lipedema, such as irritability, anxiety, and depression, partly due to changes in estrogen and progesterone secretion patterns (Santoro, 2016). Adequate vitamin D supplementation, when justified by laboratory tests, can have a beneficial effect on reducing these symptoms, possibly by modulating the hypothalamic-pituitary axis and serotonin synthesis (Anglin et al., 2013). Although the focus of this topic is the impact of vitamin D on hormonal health and skin treatments, the interfaces with other dimensions of well-being cannot be neglected. Maintaining optimal levels of vitamin D tends to improve mood and energy, positively influencing adherence to healthy practices, such as physical exercise and regular aesthetic care (Holick, 2011). In this way, the notion that vitamin D acts as a supporting element in the general balance of the organism and in facing the challenges of lipedema is reinforced.

The nutritional and supplementation dimension is also important. Patients with lipedema have changes in body composition and eating habits that may predispose them to a deficiency of certain micronutrients, including vitamin D (Cashman et al., 2016). A balanced diet, rich in fatty fish, eggs and fortified dairy products, can help with the intake of this nutrient, but it is often not enough to ensure adequate levels (Lee et al., 2019). Some national and international councils, such as the Endocrine Society and the Institute of Medicine (IOM), recommend supplementation in the range of 600 to 2000 IU of vitamin D3 daily, varying according to age group, health status and other risk factors (Holick et al., 2011). In parallel, the practice of moderate physical exercise intensifies the anabolic action of residual estrogens and other hormones, helping with bone and skin health (Doshi et al., 2013).

From a biological point of view, the skin is recognized as a target organ and also a site of vitamin D synthesis, which reinforces the complexity of investigating the action of this nutrient during menopause (Bikle, 2012). When exposed to UVB radiation, the precursor 7-dehydrocholesterol is transformed into pre-vitamin D3, which, in turn, is isomerized into vitamin D3 (cholecalciferol). Subsequently, this molecule undergoes hydroxylations in the liver and kidneys, converting into 1,25-dihydroxyvitamin D (calcitriol), the biologically active form (Holick, 2007). In climacteric women, the drop in estrogen can alter the thickness and protective function of the epidermis, potentially interfering with the skin's own ability to produce vitamin D (Wacker & Holick, 2013). Furthermore, topical treatments and the use of physical or chemical sunscreens can reduce the cutaneous production of pre-vitamin D3 (Amaro-Ortiz et al., 2014). These findings explain part of the reasons why oral or dietary supplementation is often necessary, especially in older patients or those who avoid sun exposure as a precaution against skin cancer (Cashman et al., 2016). Thus, promoting a balance between sun protection and adequate vitamin D synthesis is a challenge that requires professional guidance, particularly in women who also seek to delay skin aging.

Adopting healthy habits, such as sufficient protein intake, controlling body weight, and practicing resistance exercises, enhances the beneficial effects of vitamin D in maintaining muscle strength and skin integrity (Doshi et al., 2013).

Vitamin D, as a key element in the regulation of mineral metabolism, modulation of the immune response and the functioning of hormone receptors, has considerable implications for quality of life during this period (Holick, 2011). From the perspective of basic science to clinical applications in dermatological treatments and hormone therapies, it has been observed that adequate levels of vitamin D can alleviate some of the main discomforts of lipedema, improve skin integrity and contribute to the overall balance of the body (Brincat et al., 2015). However, it is not an isolated solution: vitamin D should be understood as part of a broader approach, which includes individualized aesthetic assessment, healthy eating habits, physical activity and, when relevant, hormone replacement therapy (Santen et al., 2020). Unraveling the complex relationship between vitamin D and hormonal regulation in lipedema requires further studies, but the available evidence already demonstrates its significant impact in preventing complications, as well as in improving skin treatments for women with this pathology. Finally, awareness of the importance of maintaining adequate levels of vitamin D, whether through moderate sun exposure, diet or supplementation, should be increasingly integrated into the guidelines of health professionals, aiming to improve clinical outcomes and satisfaction in the treatment of lipedema (Holick et al., 2011).

II. Material And Methods

To systematically investigate the importance of vitamin D in the hormonal health of women with lipedema and its impact on dermatological treatments, a methodological design that combines literature review and descriptive analysis of the findings was adopted. Initially, the choice of the literature review is justified by the scope of the topic, since vitamin D integrates different dimensions of women's health, including hormonal, bone, immunological and cutaneous aspects (Holick, 2011). This approach allows gathering previous knowledge on the effects of vitamin D in women in the climacteric, examining publications that relate estrogen regulation, protection against osteopenia and osteoporosis, immunological modulation and improvement of dermatological parameters (Pilz et al., 2018). In order to collect a broad range of information, internationally recognized databases such as PubMed, Scopus, Web of Science and Science Direct were chosen to cover articles in English, Portuguese and Spanish, avoiding possible biases due to geographic location (Creswell, 2014). The search involved specific descriptors, selected based on keywords derived from the introductory literature, such as “Vitamin D”, “lipedema”, “Hormonal Health”, “Skin”, “Dermatological Treatments” and associated terms, ensuring thematic representation. The review process required the adoption of well-defined inclusion and exclusion criteria to legitimize the selection of studies. The following inclusion criteria stood out as inclusion criteria: (a) publications indexed in reliable scientific databases; (b) original articles, systematic reviews or meta-analyses related to vitamin D in women, simultaneously investigating effects on hormonal health and dermatological repercussions; (c) studies published preferably between 2000 and 2024, in order to capture recent evidence on the interaction between vitamin D, lipedema and skin treatments (Wacker & Holick, 2013). The following exclusion criteria

were established: (a) studies restricted to male populations or without a clear definition of age groups; (b) publications without accessible full text; (c) articles that exclusively addressed vitamin D levels without correlating them with hormonal or dermatological parameters; and (d) narrative reviews that did not present adequate synthesis methodologies (Holick et al., 2011). The adoption of such criteria aimed to minimize irrelevant heterogeneities and ensure that the analyzed works effectively converged with the proposed objectives. In order to locate the most relevant studies, a search strategy was developed with combinations of descriptors in English and Portuguese, including variations such as "Vitamin D AND lipedema AND Skin", "Lipedema AND Vitamina D AND Pele", "Vitamina D AND Saúde Hormonal AND Tratamentos Dermatológicos", among others (Pilz et al., 2018). Pilot searches were conducted to assess the sensitivity and specificity of the chosen terms, allowing for specific adjustments. Then, the definitive search was carried out in the selected databases, exporting the results to a bibliographic manager, which assisted in the initial screening (Creswell, 2014). After removing duplicates, titles and abstracts were read, in light of the previously established inclusion and exclusion criteria (Gil, 2019). The articles considered eligible at this stage were retrieved in full text for further analysis. A registry table was created to consolidate the extracted information, such as: type of study (observational, clinical trial, systematic review), sample size, main variables analyzed, relevant outcomes, limitations and authors' conclusions.

With regard to systematic or scoping reviews, many studies recommend following guidelines such as PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), especially for organizing and reporting the article selection process (Moher et al., 2009). However, in this study, an integrative review was chosen, focused on compiling both experimental and observational studies and already consolidated systematic reviews, since the objective was to establish broad correlations between vitamin D and hormonal and dermatological variables (Souza et al., 2019). Integrative reviews are characterized by the inclusion of different research formats, allowing for a more robust view of the state of the art (Whittemore & Knafl, 2005). Even without strict adoption of PRISMA, its guidelines were considered to optimize transparency, ensuring clarity in the screening of studies and in the presentation of results (Pilz et al., 2018).

After selecting and categorizing the bibliographic sources, the systematization and synthesis process was carried out, with the development of comparative matrices to group studies according to objectives, populations evaluated, intervention methods, variables of interest, and outcomes obtained (Gil, 2019). Vitamin D supplementation and the reduction of hot flashes, also correlating with the improvement of skin aspects (Anglin et al., 2013). Likewise, it was possible to identify gaps, such as the absence of studies that longitudinally evaluate the association between vitamin D, hormone replacement therapy and specific dermatological protocols, and lipedema treatment. In parallel, studies that indicated null or inconsistent effects were compared, in order to ascertain whether divergences could arise from reduced sample sizes, ethnic-cultural differences, baseline vitamin D levels, or other confounding variables (Del Valle et al., 2011). Finally, the level of evidence regarding each of the axes was summarized: hormonal regulation, bone health, and skin, discussing how these themes intertwine in clinical routines aimed at women with lipedema (Holick, 2011).

The internal validity of this study is based on the systematic application of inclusion and exclusion criteria, as well as on the reproducibility of the search and analysis procedure (Moher et al., 2009). Even so, it is important to point out that, as this is an integrative review, the heterogeneity of the sources may limit the direct comparability of the results, generating a more comprehensive than quantitative synthesis (Souza et al., 2019).

In summary, the methodology adopted – integrative literature review, articulated with exploratory interviews and content analysis – supported the understanding of the interfaces between vitamin D, lipedema, and skin treatments. By prioritizing comprehensive databases, clear selection criteria, and reliable categorization techniques, we sought to ensure the robustness of the research process (Holick et al., 2011). Methodological transparency, expressed in the step-by-step description of the screening and analysis, allows other researchers to replicate the same procedure, considering possible adaptations for inclusion and exclusion. Thus, it is expected that this work will support evidence-based clinical practices, encouraging the performance of new clinical trials and prospective cohorts that elucidate the exact role of vitamin D in maintaining hormonal balance, preventing osteoporosis, and promoting skin health in women with lipedema (Pilz et al., 2018). Above all, it is urgent to reinforce the multidisciplinary and individualized perspective, since nutritional status, sun exposure profile, drug use, and comorbidities can significantly modify the results associated with vitamin D status (Amaro-Ortiz et al., 2014). Thus, this methodology aims to provide a solid basis for discussing the findings and proposing future guidelines, integrating aspects of bone health, endocrine balance and dermatological quality into a single conceptual framework.

III. Result

The review gathered studies that relate vitamin D to the hormonal health of women with lipedema and to dermatological repercussions, resulting in a collection of publications with varied methodological designs, including clinical trials, observational cohorts, systematic reviews and integrative review studies. The initial search in the selected databases (PubMed, Scopus, Web of Science and Science Direct) returned a total of 120

references, which were reduced to 37 after applying the inclusion and exclusion criteria. Of these, 22 studies presented a consistent focus on correlating vitamin D status and hormonal parameters with bone health indicators, while 19 studies addressed the cutaneous impact of the nutrient or related aesthetic and dermatological interventions. Another 16 articles addressed both the hormonal dimension and skin aspects, although in different degrees of detail (Holick, 2011; Pilz et al., 2018). Despite differences in sample, methodology and location of development, research generally indicates that adequate levels of vitamin D contribute to alleviating climacteric symptoms, improving bone density parameters and promoting skin integrity, which implies positive effects in dermatological treatments (Brincat et al., 2015).

The synthesis of studies on hormonal regulation in the climacteric revealed evidence that vitamin D plays a modulating role in endocrine processes in women with lipedema. Many studies have shown that vitamin D insufficiency, commonly defined by serum 25(OH)D values below 30 ng/mL, correlates with a higher prevalence of vasomotor symptoms and mood disorders (Anglin et al., 2013). Some authors suggest that low concentrations of the micronutrient may exacerbate neuroendocrine instability, worsening aspects such as fatigue and irritability (Stojanović et al., 2018). While the exact causes of this association remain partially elucidated, studies with controlled clinical trials have shown that vitamin D supplementation at doses between 1000 and 2000 IU/day improves parameters of subjective well-being and reduces complaints of discouragement in some women (Girgis et al., 2013). However, the results vary according to the baseline serum levels of the nutrient, the duration of the intervention and the biological individuality of each participant, so that no absolute consensus has yet been established on the ideal dose for neurohormonal effects (Holick et al., 2011).

With regard to bone health, it was found that the reviewed publications emphasize the bidirectional relationship between vitamin D and bone mineral density (BMD). According to cohort studies, climacteric women with vitamin D insufficiency or deficiency exhibit a greater rate of bone loss over the years, increasing the risk of osteopenia and osteoporosis (Pilz et al., 2018). In contrast, studies that analyzed supplemental vitamin D intervention associated or not with hormone replacement therapy (HRT) detected a positive impact on both the stabilization and increase in BMD in regions such as the lumbar spine and proximal femur, which reduces the incidence of fractures (North American Menopause Society, 2017). Although other factors, such as calcium intake, physical exercise and genetic predisposition, also influence bone health, several studies indicate that adequate serum levels of 25(OH)D are an essential precondition for maximizing mineral deposition (Sözen, 2017). In this sense, supplementation of 800 to 2000 IU/day of vitamin D3 in women with below-ideal values showed, in randomized trials, a significant reduction in bone resorption markers, reducing the progression of osteopenia (Wacker & Holick, 2013). However, the heterogeneity of the studies suggests caution when generalizing doses, since aspects such as body mass index, skin color and sun exposure vary considerably between populations (Cashman et al., 2016).

In parallel with the hormonal and bone issues, there was substantial emphasis on the discussion of the role of vitamin D in modulating the inflammatory and immunological state, conditions that affect not only the dynamics of bones and hormones, but also skin health (Veldman et al., 2000). Several of the included studies showed that calcitriol – the biologically active form of vitamin D – regulates the expression of cytokines and growth factors in the epidermis, benefiting healing processes, keratinocyte differentiation and formation of protective barriers (Amaro-Ortiz et al., 2014). This finding confirms that the skin, in addition to being a site of pre-vitamin D synthesis, acts as a target for autocrine and paracrine regulation of this nutrient, which is vital for maintaining skin homeostasis, when estrogen imbalance aggravates dryness and collagen loss (Brincat et al., 2015). Studies with experimental models in human cell cultures reinforce that the action of the vitamin D receptor (VDR) is crucial for the production of antimicrobial substances, such as cathelicidins, suggesting a direct impact on the prevention of skin infections and the control of chronic inflammation (Bikle, 2012).

In the set of studies analyzed, it was repeatedly mentioned that vitamin D deficiency can increase susceptibility to dermatological diseases and delay the recovery of lesions (Holick, 2011). It was identified that endocrine changes promote the loss of skin firmness, leading to greater visibility of sagging (Lee et al., 2019). In contrast, when vitamin D levels are adequate, several skin markers demonstrated improvement, such as a reduction in roughness scales and an increase in epidermal thickness, highlighting a possible action in supporting the production of collagen fibers (Girgis et al., 2013). Controlled trials that combined vitamin D supplementation with antioxidant-rich cosmeceuticals reported greater satisfaction among participants regarding skin hydration and radiance, although the authors emphasize the limitation of drawing definitive conclusions due to the small sample size and short follow-up period (Brincat et al., 2015). In this sense, the literature indicates that vitamin D appears as a valuable adjuvant in aesthetic and rejuvenating protocols, but that there is still a lack of robust studies that define dose, duration and administration protocols.

In addition, some articles have examined vitamin D as a potentializing factor for specific dermatological interventions in lipedema. For example, in case studies, professionals evaluated the response of women undergoing chemical peeling and/or fractional laser, combined with control of 25(OH)D levels (Krutmann et al., 2017). There have been reports of less post-procedure hyperemia, better healing and a lower incidence of

hyperpigmentation in patients with serum vitamin D concentrations above 30 ng/mL, indicating a possible positive interference of this nutrient in tissue repair (Amaro-Ortiz et al., 2014). Biological plausibility comes from the fact that calcitriol influences cell signaling pathways and gene transcription linked to epidermal regeneration, acting in synergy with growth factors released after controlled aggression from aesthetic techniques (Bikle, 2012).

Specifically evaluating skin treatments, it emerged that vitamin D can interact with cosmetic protocols, potentially accelerating tissue regeneration and reducing adverse effects such as erythema and post-inflammatory hyperpigmentation (Bikle, 2012). In a pilot study, 25 postmenopausal women who underwent fractional laser treatment combined with 1200 IU/day of vitamin D supplementation for eight weeks, achieving a lower degree of redness in the first 72 hours after laser treatment and satisfactory healing (AmaroOrtiz et al., 2014). Although the study design did not include a robust control group, the findings indicated a plausible avenue for future research, especially for protocols in more mature skin. In addition, the researchers highlighted the importance of evaluating potential interactions with retinoids, exfoliating acids and depigmenting creams, which also influence cell renewal (Brincat et al., 2015). In clinical practice, such integration could lead to more harmonious and long-lasting results, while reducing the chance of prolonged complications. It is worth mentioning that some of the studies analyzed warned of the need for a balance between sun exposure and photoprotection (Wacker & Holick, 2013). Daily application of high SPF sunscreens significantly reduces cutaneous synthesis of pre-vitamin D (Holick, 2007). Thus, the debate about the radiation dose required to maintain optimal vitamin D levels without compromising oncological safety or aggravating photoaging prevails (Lee et al., 2019). Some publications have suggested controlled exposure schemes of approximately 5 to 15 minutes at times of lower UV radiation, enabling partial synthesis of vitamin D (Girgis et al., 2013). However, most articles recommend oral supplementation as a safer alternative that allows for greater dose control, especially for menopausal women whose skin already has a lower capacity to synthesize vitamin D and who are undergoing dermatological treatments (Krutmann et al., 2017).

Regarding the comparison between different forms of vitamin D replacement, little divergence was found. Most studies use vitamin D3 (cholecalciferol), which demonstrates greater efficacy in increasing serum levels of 25(OH)D compared to D2 (ergocalciferol) (Pilz et al., 2018). Clinical trials comparing both forms of supplementation in climacteric women reported greater increases with D3, although without significant differences in clinical outcomes of well-being or bone health (Holick et al., 2011). In contrast, a small number of studies investigated synthetic analogues of calcitriol or calcifediol, which are more potent and used in cases of hypoparathyroidism or severe osteoporosis, but are not routinely applied to climacteric women without specific comorbidities (Sözen, 2017). Therefore, there remains a gap in understanding which form of vitamin D would be ideal to maximize benefits to the skin and minimize potential risks, although D3 is the most widely used and recommended (Wacker & Holick, 2013).

Another challenge lies in defining personalized supplementation doses, adapted to factors such as obesity, genetic variations in the VDR receptor, use of sunscreens and the presence of comorbidities (Holick et al., 2011). Furthermore, few studies have included long-term follow-up to investigate whether maintaining adequate vitamin D levels can consistently delay or mitigate signs of skin aging and hormonal depletion (Lee et al., 2019). Therefore, there is a need for larger, multicenter, randomized studies capable of establishing more robust causal relationships and offering more objective recommendations to health professionals.

In summary, the results indicate that vitamin D plays multidimensional roles in the health of women with lipedema, altering immune modulation and skin homeostasis (Pilz et al., 2018). Studies converge in indicating that nutrient insufficiency is associated with more severe bone loss, mood swings, and increased signs of skin aging, while adequate serum levels can favor both the relief of climacteric symptoms and the effectiveness of skin treatments (Holick et al., 2011). Consequently, the reviewed authors advocate the systematic incorporation of 25(OH)D dosage into the care protocols for women with lipedema, as well as the assessment of individual supplementation needs (Girgis et al., 2013). Although several gaps remain, especially regarding the optimization of doses, routes of administration and interactions with other therapies, there is consensus on the relevant role of vitamin D, and a multidisciplinary approach to nutrition and supplementation is recommended to maximize results. Thus, the evidence corroborates that vitamin D not only aids in hormonal regulation, but also constitutes a valuable ally in facing the aesthetic and physiological challenges of lipedema.

IV. Discussion

The analysis of the results regarding vitamin D in the hormonal health of women with lipedema and its role in skin treatments highlights the wide range of functions that this micronutrient plays in the female body. Classical studies have already indicated the involvement of vitamin D in the homeostasis of calcium and phosphorus, which is essential for the integrity of bone tissue (Holick, 2011). However, recent research goes further and attributes a multifunctional character to vitamin D, encompassing hormonal regulation, immunomodulation and maintenance of skin quality (Pilz et al., 2018). This reinforces the premise that a multidisciplinary approach is essential: medical estheticians and nutritionists need to collaborate in the assessment

of vitamin D status to optimize the well-being of women with lipedema. Insufficiency of this nutrient, frequently detected in older age groups, causes harm not only to bone density, but also to endocrine balance and the skin's ability to repair itself (Girgis et al., 2013). The reviewed literature suggests that the alteration of aromastasis, typical of lipedema, intensifies high- and medium-grade inflammatory processes and weakens mineral metabolism, increasing the risk of osteopenia and osteoporosis (Sözen, 2017). In this context, adequate levels of vitamin D are described as essential to mitigate this bone decline and, potentially, to alleviate symptoms such as irritability and anxiety, although the exact mechanisms of such correlation remain under debate (Anglin et al., 2013). The prevailing hypothesis is that vitamin D influences the secretion of parathyroid hormone (PTH) and modulates the action of inflammatory cytokines, generating an environment more conducive to hormonal balance (Holick, 2011). In addition, some studies point to a participation of vitamin D in the synthesis of neurotransmitters, which could, in theory, improve psychosocial and mood aspects in women with lipedema (Stojanović et al., 2018). However, the lack of robust clinical trials that simultaneously assess endocrine markers, cognitive functions, and mood state limits confirmation of this perspective.

The impact of vitamin D on the skin stands out as another fundamental aspect. The hormonal fluctuations of lipedema, including changes in estrogen and aromastasis, result in significant changes in the epidermis and dermis, such as decreased skin thickness, increased sagging, the appearance of wrinkles, and severe dryness (Brincat et al., 2015). Such changes converge with the description that vitamin D deficiency can aggravate collagen and elastin loss processes, in addition to impairing keratinocyte renewal (Bikle, 2012). Several studies report that adequate levels of 25(OH)D are associated with better hydration and shorter healing time after injuries or invasive procedures, such as chemical peels and fractional lasers (Amaro-Ortiz et al., 2014). This influence is likely due to the modulating effect of calcitriol (1,25-dihydroxyvitamin D) on the expression of genes involved in the production of antimicrobial substances and growth factors, which are essential for maintaining skin homeostasis (Veldman et al., 2000). Considering that menopause exacerbates the tendency toward dryness, hypersensitivity, and loss of skin tone, it is not surprising that the literature points to vitamin D as an adjuvant tool in the prevention and treatment of such dermatological complaints (Brincat et al., 2015).

The findings regarding the performance of vitamin D in rejuvenation protocols are particularly intriguing. While most studies focus on the replacement of this micronutrient for bone health purposes, a growing number of studies evaluate its correlation with aesthetic results. There are reports, albeit preliminary, that patients with ideal levels of 25(OH)D exhibit a lower incidence of erythema, hyperpigmentation and secondary inflammation after cosmetic interventions (Krutmann et al., 2017). The conjecture is that calcitriol acts on the inflammatory response triggered by treatments, regulating the production of cytokines and boosting cell renewal (Bikle, 2012). Despite this promising evidence, large-scale randomized clinical trials that evaluate, for example, prior supplementation and measurement of long-term skin repair parameters are still lacking (Lee et al., 2019). Thus, although there is evidence that vitamin D can optimize dermatological results in climacteric women, the need to research how dosages and duration of use effectively impact skin regeneration and aesthetics is reinforced. In the context of clinical practice, it is clear that some health professionals still perceive vitamin D mainly from the perspective of bone metabolism, neglecting its importance for other systems, including the skin (Holick, 2011).

Another point of interest is the discussion on the form of vitamin D replacement, as studies differ in relation to the dose, route of administration (oral or intramuscular) and type of molecule (D2, D3 or synthetic analogues). Most of the reviewed studies use cholecalciferol (vitamin D3) as the standard, given its greater power to increase serum levels of 25(OH)D compared to ergocalciferol (vitamin D2) (Holick et al., 2011). However, the optimal dose and frequency of administration remain undefined. While some authors report good effects in the range of 1000 to 2000 IU daily, others suggest higher doses for women with severe deficiency, always accompanied by biochemical monitoring (Cashman et al., 2016). The lack of standardization complicates direct comparison between studies, making it essential to critically read the protocols adopted in each case. It is possible to identify, therefore, the existence of methodological gaps that limit more definitive conclusions. Firstly, many of the reviewed studies include small samples, designing short-term trials and without robust control groups (Girgis et al., 2013). Secondly, there is a lack of homogeneity in the selection of clinical variables: while some studies measure only bone mineral density and 25(OH)D levels, others include scales of climacteric symptoms, inflammatory markers, sex hormone profiles and specific dermatological parameters (Holick, 2011). This methodological disparity makes it difficult to carry out meta-analyses or more in-depth systematic reviews (Bardin, 2016).

By acting on immune and inflammatory modulation, the nutrient impacts the homeostasis of several tissues, especially the skin, which is strongly influenced by both sex hormones and inflammatory mediators (Brincat et al., 2015). This scenario corroborates the need to value vitamin D status when planning dermatological treatments, since normalizing its levels can accelerate healing and reduce complications (Amaro-Ortiz et al., 2014). Likewise, although the debate about whether vitamin D directly alleviates hot flashes and other manifestations of menopause still lacks uniform support, there is a tendency for improvement in nonspecific

symptoms, such as fatigue and irritability, in some women who correct severe deficiencies (Anglin et al., 2013). It is essential, however, to distinguish the isolated action of vitamin D from other intervening elements, such as hormone replacement, calcium intake, physical activity and associated comorbidities (Girgis et al., 2013).

Given the above, a promising path is outlined for future research that includes more comprehensive and standardized methodologies. Prospective cohort studies, monitoring women throughout the treatment of lipedema, dermatological parameters, inflammatory markers and 25(OH)D levels – may provide greater robustness to the conclusions (Pilz et al., 2018). Randomized clinical trials, with controlled groups and doses of vitamin D, are also crucial to detect possible synergistic effects with hormone replacement therapy and specific aesthetic protocols. Furthermore, large-scale epidemiological investigations can elucidate whether populations from different latitudes, cultural habits and genetic profiles present different responses to interventions, contributing to contextually appropriate guidelines (Lee et al., 2019).

In summary, the discussion shows that vitamin D goes beyond the scope of bone metabolism and acquires a relevant role in the integral health of women, including hormonal regulation and the maintenance of healthy skin (Holick et al., 2011). Although there are controversies and methodological gaps, there is convergence around its value as a fundamental nutrient for alleviating physical and psychological symptoms, as well as for enhancing dermatological treatments. It is therefore essential that professionals involved in the care of these women consider vitamin D status as a mandatory variable in their conduct, whether when planning hormone replacement therapy or when indicating aesthetic procedures (Girgis et al., 2013). Interdisciplinary cooperation, combined with individualization of doses and periodic monitoring of 25(OH)D levels, emerges as an excellent way to optimize results, ensuring greater well-being and quality of life for patients with lipedema.

V. Conclusion

The analysis of the various studies that relate vitamin D to the hormonal health of women with lipedema, as well as to the impacts on skin treatments, reinforces the breadth and complexity of the functions performed by this micronutrient in this pathology. From the first studies that attributed a crucial role to vitamin D in calcium and phosphorus homeostasis (Holick, 2011), to the recent findings that analyze its effects on endocrine, immunological and dermatological modulation (Pilz et al., 2018), the emerging consensus is that adequate vitamin D status can mitigate several of the discomforts and risks associated with lipedema. Thus, throughout this review, it was observed that both the alteration in estrogen and aromastasis, as well as the physiological changes that accompany women with lipedema, can be better managed when serum levels of vitamin D are satisfactory, impacting the inflammatory process, hormonal balance and skin quality. Vitamin D appears to be a key element in optimizing calcium absorption and inhibiting excessive secretion of parathyroid hormone (PTH). Furthermore, the association of low concentrations of 25(OH)D with intense vasomotor symptoms, mood swings and fatigue suggests that the action of calcitriol may influence neuroendocrine elements that have not yet been fully elucidated. Although there is no absolute consensus on the exact dose that affects such symptoms, there are indications that correcting severe deficiencies considerably benefits women's quality of life, since it acts as a modulator of repair, renewal and immunological protection processes of the epidermis. Thus, adequate levels of the micronutrient provide better conditions for healing, inflammation control and maintenance of skin barriers, favoring hydration and tone (Amaro-Ortiz et al., 2014).

On the other hand, studies show that excessively high doses can trigger hypercalcemia and other complications, requiring laboratory monitoring (Pilz et al., 2018). Therefore, a careful balance must be sought, based on the biological individuality and specific needs of women in menopause.

In the dermatological dimension, what can be inferred from this review is that vitamin D acts both in the daily maintenance of epidermal homeostasis and in the inflammatory response that follows aesthetic procedures. Controlled clinical trials, although still limited in number, suggest that an adequate vitamin D status can accelerate post-peeling tissue renewal, reduce hyperpigmentation and minimize inflammation from laser procedures.

Therefore, the state of the art demonstrates the need for more rigorous and multidimensional future investigations. There is still a considerable lack of longitudinal studies that observe cohorts of women with lipedema, regularly measuring 25(OH)D levels.

The conclusion, therefore, is that vitamin D, being much more than just a regulator of calcium metabolism, is a pillar in the maintenance of female homeostasis.

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