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RESEARCH ARTICLE

Exploring the Link Between Serum Magnesium Levels and Acne Vulgaris Severity

Serum Magnezyum Seviyeleri ve Akne Vulgaris Şiddeti Arasındaki İlişkinin İncelenmesi

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ABSTRACT

Objective: Acne vulgaris is a prevalent long-term inflammatory skin disorder that notably impacts the quality of life, especially in teenagers and young adults. Although the pathogenesis of acne is influenced by multiple factors, the contribution of micronutrients like magnesium is not yet fully elucidated. This study sought to explore the relationship between serum magnesium concentrations and the severity of acne as assessed by the Global Acne Grading System (GAGS).

Materials and Methods: A case-control study with a prospective design was carried out at a single center between March and August 2023, including 60 individuals diagnosed with acne vulgaris and 60 healthy controls matched by age and sex, all between 18 and 30 years old. The severity of acne was evaluated using the GAGS and classified as mild, moderate, or severe. Serum magnesium levels were determined through the Xylidyl Blue colorimetric assay. Data were analyzed using SPSS version 29. For continuous variables not normally distributed, the Kruskal–Wallis H test was employed, with statistical significance defined as $p < 0.05$.

Results: The study included 34 female and 26 male acne patients and 31 female and 29 male healthy controls. No statistically significant differences were observed in serum magnesium levels among acne severity groups or between patients and controls ($p > 0.05$). Although the moderate acne group had slightly higher mean magnesium levels compared to mild and severe groups, the differences were not statistically significant. Magnesium concentrations remained within normal limits across all groups.

Conclusion: Our results indicate that there is no significant association between serum magnesium levels and the severity of acne. While systemic magnesium seems to have a limited role in the pathogenesis of acne, topical magnesium preparations might provide therapeutic advantages due to their anti-inflammatory and antimicrobial properties. Further studies are necessary to better understand its efficacy.

Keywords: Acne vulgaris, acne severity, global acne grading system, magnesium

ÖZET

Amaç: Akne vulgaris, özellikle ergenler ve genç yetişkinlerde yaşam kalitesini önemli ölçüde etkileyen yaygın, uzun süreli bir inflamatuvar cilt hastalığıdır. Aknenin patogenezi çok sayıda faktörden etkilenmekle birlikte, magnezyum gibi mikrobesinlerin katkısı henüz tam olarak aydınlatılamamıştır. Bu çalışma, serum magnezyum konsantrasyonları ile Global Akne Derecelendirme Sistemi (GAGS) ile değerlendirilen akne şiddeti arasındaki ilişkiyi araştırmayı amaçlamıştır.

Gereç ve Yöntemler: Mart ve Ağustos 2023 tarihleri arasında tek bir merkezde prospektif tasarımlı bir vaka-kontrol çalışması yürütülmüştür. Çalışmaya, yaş ve cinsiyet açısından eşleştirilmiş, 18-30 yaş aralığında 60 akne vulgaris tanısı almış birey ve 60 sağlıklı kontrol dahil edilmiştir. Akne şiddeti, GAGS kullanılarak değerlendirilmiş ve hafif, orta veya şiddetli olarak sınıflandırılmıştır. Serum magnezyum seviyeleri, Xylidyl Blue kolorimetrik yöntemiyle belirlenmiştir. Veriler SPSS sürüm 29 kullanılarak analiz edilmiştir. Normal dağılım göstermeyen sürekli değişkenler için Kruskal-Wallis H testi kullanılmış ve istatistiksel anlamlılık $p <0.05$ olarak kabul edilmiştir.

Bulgular: Çalışmaya 34 kadın ve 26 erkek akne hastası ile 31 kadın ve 29 erkek sağlıklı kontrol dahil edilmiştir. Akne şiddet grupları arasında veya hasta ve kontroller arasında serum magnezyum seviyelerinde istatistiksel olarak anlamlı bir farklılık gözlemlenmemiştir ($p> 0.05$). Orta akne grubunda hafif ve şiddetli gruplara kıyasla ortalama magnezyum seviyeleri biraz daha yüksek olmasına rağmen, bu farklılıklar istatistiksel olarak anlamlı değildi. Tüm gruplarda magnezyum konsantrasyonları normal sınırlar içinde kalmıştır.

Sonuç: Sonuçlarımız, serum magnezyum seviyeleri ile akne şiddeti arasında anlamlı bir ilişki olmadığını göstermektedir. Sistemik magnezyumun akne patogenezinde sınırlı bir rolü var gibi görünse de topikal magnezyum preparatları anti-enflamatuar ve antimikrobiyal özellikleri nedeniyle terapötik avantajlar sağlayabilir. İleri çalışmalar, bu potansiyel tedavi yönteminin etkinliğini ve mekanizmasını daha iyi anlamak için gereklidir.

Anahtar Kelimeler: Akne vulgaris, akne şiddeti, global akne derecelendirme sistemi, magnezyum

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INTRODUCTION

Acne is a common skin condition that affects 9% of the world's population (1,2). Although more frequently observed in females, acne affects around 85% of adolescents during their lifetime and can persist into adulthood (3,4). Acne lesions are broadly divided into two categories: non-inflammatory types, such as open and closed comedones, and inflammatory types (5). These lesions mostly happen in areas with many sebaceous glands, like the face and chest (6). While the diagnosis of acne is typically straightforward, the polymorphic nature and distribution of lesions can complicate the assessment of disease severity. In most cases, laboratory investigations are not required. However, if there is a suspicion of underlying systemic or secondary causes, further evaluation may be warranted (7). Although the number and types of acne lesions may vary significantly among individuals, assessing clinical severity requires both a thorough physical examination and, ideally, photographic documentation of the lesions (8). Two primary parameters are considered in acne grading: the type of lesions and the extent of the affected skin surface area. The Global Acne Grading System (GAGS) is a widely used, standardized tool that evaluates acne severity based on lesion type and anatomical distribution, aided by textual descriptions and/or photographs (9). GAGS is favored in clinical practice due to its simplicity, reproducibility, and ability to account for lesion size, type, and degree of inflammation. It also enables clinicians to monitor disease progression by focusing on dominant lesion types. Based on this system, acne severity is categorized as mild, moderate, severe, or very severe (9,10).

Recent studies have investigated diet and micronutrients' impact on skin conditions (11–13). In the course of research, it has been demonstrated that the levels of zinc are lower in individuals with acne than in healthy controls. Furthermore, both oral and topical zinc formulations have been shown to be efficacious in the treatment of acne (14,15). Magnesium is an indispensable intracellular cation that fulfils a pivotal role in a multitude of biological processes, encompassing energy metabolism, oxidative phosphorylation, glycolysis, and macromolecule synthesis. Given its physiological importance, magnesium may have a potential role in acne pathogenesis. However, current literature examining the relationship between magnesium and acne remains scarce and inconclusive (16–22). The objective of the present study is to examine the relationship between serum magnesium levels and the severity of acne vulgaris.

MATERIALS AND METHODS

Patients and data collection

This prospective, single-center case-control study was carried out between March 1 and August 1, 2023. Participants were between 18 and 30 years of age and included patients with varying severities of acne vulgaris, as well as age- and sex-matched healthy controls who attended our dermatology outpatient clinic during the study period. All individuals provided written informed consent prior to participation. Inclusion criteria were as follows: patients aged 18–30 years with a clinical diagnosis of acne vulgaris and healthy controls with no history of acne or other chronic skin conditions. Exclusion criteria included: individuals younger than 18 or older than 30 years; those with other dermatologic disorders (e.g., rosacea, seborrheic dermatitis); systemic diseases such as diabetes or renal/liver failure; pregnant or breastfeeding women; and individuals who had recently used systemic/topical retinoids, corticosteroids, antibiotics, dietary supplements, or hormonal therapy. Patients with known metabolic or endocrine disorders were also excluded.

The severity of acne was evaluated using the Global Acne Grading System (GAGS). GAGS allocate a specific weighting factor to each anatomical site, taking into account surface area, lesion distribution, and the density of pilosebaceous units. The severity of lesions (comedones, papules, pustules, and nodules) is graded numerically and subsequently multiplied by a regional factor to derive a local score. The total GAGS score is obtained by summing these local scores. Based on their total scores, patients were classified into three categories: mild, moderate, and severe acne, with the 'severe' and 'very severe' groups merged for the purpose of analysis." Acne severity was assessed by a single dermatologist blinded to the magnesium levels.

For biochemical analysis, a 5 mL peripheral venous blood sample was obtained from each participant. These samples were allowed to clot at room temperature for a one-hour duration, subsequent to which they underwent centrifugation at 2500 revolutions per minute (rpm) for 10 minutes. The resulting serum was then aliquoted and stored at –20°C until further analysis. Serum magnesium levels were measured using the Xylidyl Blue colorimetric method on an Olympus AU2700 autoanalyzer, in accordance with the manufacturer's protocol.The study followed the 1964 Helsinki Declaration and its later amendments. Ethics committee approval was obtained (Decision No: 2022-16/139).

Statistical analysis

Statistical analyses were conducted utilizing IBM SPSS Statistics, version 29. Continuous variables are presented using the mean ± standard deviation and median [range], while categorical variables are reported as frequencies and percentages. For continuous variables exhibiting non-normal distributions across independent groups, comparisons were performed using the Kruskal–Wallis H test. The Shapiro–Wilk test was employed to assess the normality of continuous variables. Associations between categorical variables were evaluated using the Pearson's chi-squared test. Statistical significance was defined as a p-value of less than 0.05 ($p<0.05$). A post hoc power analysis was conducted using G*Power software (version 3.1). Based on an assumed medium effect size ($f = 0.30$), a significance level (α) of 0.05, and a desired power ($1-\beta$) of 0.80, the achieved sample size of 120 participants was determined to be adequate for detecting medium to large effect size differences.

RESULTS

One hundred twenty individuals, including 60 patients

with acne vulgaris (34 females, 26 males) and 60 age- and gender-matched healthy controls (31 females, 29 males), were enrolled in the study. Participants were aged 18 to 30, with an average age of 22.83 ± 3.08 years. The average age of the acne group was 21.55 ± 2.47 years, while that of the control group was 24.12 ± 3.11 years. The distribution of participants by gender is given in Table 1. No statistically significant association was observed between gender and the acne-control groups (p>0.05). Furthermore, both the acne and control groups exhibited a homogeneous distribution with respect to gender. Analysis of the data revealed that within the male sample, eight individuals presented with mild acne (30.8%), twelve with moderate acne (46.2%), and six with severe acne (23.1%). In the female sample, 12 individuals (35.3%) had mild acne, eight individuals (23.5%) had moderate acne, and 14 individuals (41.2%) had severe acne (Table 2). No statistically significant association was observed between gender and GAGS grades (p>0.05). Furthermore, GAGS grades demonstrated homogeneity across genders. A statistical analysis was performed to ascertain potential differences in magnesium levels between the case and control groups. The normality of the data distribution was assessed using the Shapiro-Wilk test. The results of this assessment indicated that the magnesium values within the control and mild acne groups did not conform to a normal distribution (p<0.05). The Kruskal-Wallis H test was employed for comparisons between independent groups with non-normally distributed data. The magnesium values ranged from 1.6 to 3.1; the results are provided in Table 3. Average magnesium levels vary among acne groups, with the moderate acne group (2.0650 ± 0.2412) having higher levels than the mild acne group (2.0100 ± 0.1334) and the severe acne group (1.9850 ± 0.2207). Magnesium levels were normal across all samples from the acne groups. Moreover, statistical analysis revealed no significant difference in magnesium values between individuals in the acne vulgaris and control groups (p>0.05) (Figure 1).

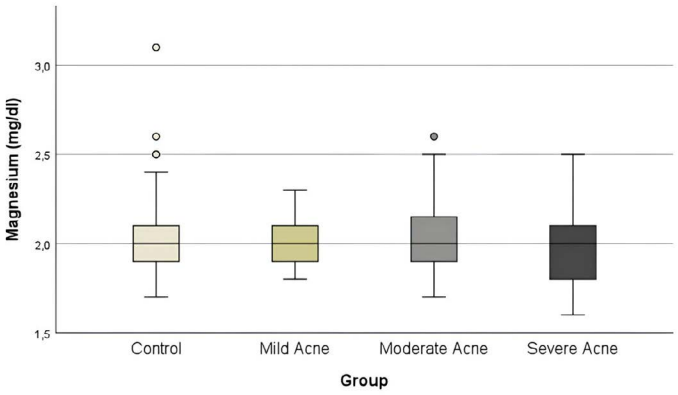

Figure 1. Box plot of serum concentration of Magnesium (mg/dl) in Healthy Control, Mild, Moderate and Severe acne patient groups.

Table 1. Gender of persons, Distribution of Findings, and Relationship with Status (Case-Control)

Gender	Status		Total n (%)	Chi-square Test
	Acne	Control		
Male	26 (47.3)	29 (52.7)	55 (45.8)	χ2=0.302 p=0.583
Female	34 (52.3)	31 (47.7)	65 (54.2)	

Table 2. Gender of persons, Distribution of Findings, and Relationship with GAGS

Gender	GAGS			Total n (%)	Chi-square Test
	Mild Acne	Moderate Acne	Severe Acne		
Male	8 (30.8)	12 (46.2)	6 (23.1)	26 (43.3)	χ2=3.801 p=0.150
Female	12 (35.3)	8 (23.5)	14 (41.2)	34 (56.7)	

GAGS: Global Acne Grading System

Table 3. Relationship between persons' magnesium levels and Status (Case-Control)

Magnesium Levels	GAGS	Mean±SD	Median [Min-Max]	Kruskal-Wallis H
	Control	2.0283±0.2478	2 [1.6-3.1]	χ2=0.926 p=0.819
	Mild Acne	2.0100± 0.1334	2 [1.8-2.3]	
	Moderate Acne	2.0650±0.2412	2 [1.7-2.6]	
	Severe Acne	1.9850±0.2207	2 [1.6-2.5]	

GAGS: Global Acne Grading System

DISCUSSION

Acne is a prevalent and intricate dermatological condition that impacts individuals across the globe. It has various causes and involves diverse factors contributing to its development. The pathological process in acne formation occurs due to some events related to the pilosebaceous unit following and affecting each other. This process involves excessive keratin production, increased sebum production, colonization by anaerobic bacteria, and an inflammatory response (23). Beyond these, emerging findings suggest that changes within the acne lesion are evident. The immune system plays a significant role, stimulated by factors such as Cutibacterium acnes phylotypes, antimicrobial peptides, sebaceous glands, matrix metalloproteinases, and other immune pathways (24). Contemporary investigations into acne pathogenesis underscore the crucial equilibrium among C. acnes phylotype members and the cutaneous microbiota. Emerging evidence posits that the proliferation of C. acnes is not the primary etiological factor in acne development. Rather, acne formation is attributed to a reduction in microbial diversity on the skin and the subsequent activation of innate immunity, culminating in a sustained inflammatory condition (25).

Trace elements, macro minerals, and vitamins are fundamental components playing vital roles in our body's biochemical processes and the immune system. Alterations in their normal homeostasis can harm various biological processes and lead to undesired complications (26,27). Macro minerals, particularly zinc, have been used since ancient times for their therapeutic effects on the skin (28). Zinc is vital for skin health, controlling inflammation, and renewing skin cells (29). Several studies have looked into the impact of zinc levels on acne vulgaris (15-30). Liu et al. found that applying zinc alone or with antibiotics like erythromycin and clindamycin positively affects acne (31).

Magnesium is essential for energy production, muscle contraction, maintaining heart rhythm, nerve transmission, and immune system function. It contributes to glutathione synthesis, DNA/RNA production, and bone development (32). Magnesium is thought to affect sebocytes and the inflammation process in acne pathogenesis. It enhances skin moisture and permeability, promotes skin cell growth for barrier repair, and decreases inflammation and epidermal differentiation. It is hypothesized that hypomagnesemia may elevate inflammatory markers and influence androgen hormones, particularly testosterone, through the stimulation of the hypothalamic-pituitary-gonadal (HPG) axis, consequently leading to increased testosterone secretion. Elevated testosterone levels can increase the activity of sebaceous glands, leading to higher sebum production and exacerbating acne formation (19).

We analyzed magnesium levels in patients with acne vulgaris compared to a healthy control group. The findings revealed no statistically significant difference in magnesium levels between the two groups across the various GAGS grades (p=0.819). Our study's findings are consistent with two previous studies (Saleh et al. and Salma et al., which also found no statistically significant difference in magnesium levels between different severities of acne vulgaris (p>0.05) (21,22). In contrast to the present investigation, Saleh et al. reported reduced magnesium levels in the severe acne group relative to the mild acne group. Tamara et al. found a direct link between acne severity and magnesium levels, but their cross-sectional design and observational nature raise concerns about the evidence (19). Chandrasekaran et al. discovered a distinct inflammatory reaction in the skin of people with magnesium deficiency (33).

Welch et al. investigated the antibacterial efficacy of topical mesoporous magnesium carbonate (MMC), employing Staphylococcus epidermidis as the model organism. This bacterium is frequently found in acne vulgaris lesions because it is common in human skin and develops antibiotic resistance. MMC has a potent antibacterial effect on bacteria, mainly attributed to the environmental change in alkalinity (34). Across two clinical investigations, Fabbrocini et al. administered liposomal magnesium in conjunction with folic acid and topical antibiotics, and a reduction in acne lesions was noted (35). Koshel and Chebotarev divided 252 patients with connective tissue dysplasia and acne into two groups in a separate study. They added magnesium-containing drugs to the regimen of the second group (126 individuals) and observed an improvement in acne severity (36). While magnesium has been shown to reduce acne in these studies, combining treatments in both studies limits their findings. It is challenging to attribute the healing of acne lesions solely to magnesium.

Muyan Li et al.'s investigation of 1137 women revealed significantly elevated copper concentrations (P<0.001) and reduced serum calcium levels (P<0.001) in individuals with polycystic ovary syndrome (PCOS) compared to controls. No significant differences were detected in serum zinc, magnesium, or iron levels between the groups. Within the PCOS cohort, higher magnesium levels were associated with the presence of acne (P=0.020), while lower magnesium levels correlated with hirsutism (P=0.037). This suggests a correlation between magnesium concentrations and acne and hirsutism in PCOS patients (37). Jaripur et al., in their study on 64 PCOS patients, divided them into two groups, one of which received daily oral magnesium oxide supplementation of 250 mg (for ten weeks). They reported no significant effect of this supplementation on acne severity (20).

Study limitations

Limitations of the present study include the relatively small sample size restricted to individuals aged 18–30 years, which may limit the generalizability of the findings. Furthermore, as this was a single-center study, the results may not fully represent populations with diverse geographic and sociodemographic characteristics. Finally, only serum magnesium levels were evaluated, whereas cellular or tissue magnesium measurements could provide a more comprehensive understanding of its role in acne pathogenesis.

CONCLUSIONS

In conclusion, our findings do not support a significant role for serum magnesium levels in acne severity. While oral magnesium shows limited benefit, topical magnesium formulations may have potential due to their anti-inflammatory and antibacterial effects. Further research is warranted to clarify these observations.

DECLARATIONS

Conflict of Interest: *The authors declare no conflict of interest with respect to the authorship and /or publication of this article.*

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