

Incidence of acne vulgaris in young adult users of protein-calorie supplements in the city of João Pessoa – PB*

Incidência de acne vulgar em adultos jovens usuários de suplementos protéico-calóricos na cidade de João Pessoa – PB

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Abstract: BACKGROUND: Based on personal observations of dermatologists, nutritionists and patients, a new problem emerges in the gyms: development and exacerbation of acne in users of whey protein, which is a protein derived from cow's milk. Whey Protein extract contains growth factors that may be related to acne. Its purity and composition are not fully known and there is no scientific research on its potential to cause acne. OBJECTIVES: Assess the relationship between the use of protein-calorie supplements and onset or exacerbation of acne vulgaris in young adults in the city of João Pessoa. Methods: Descriptive observational study conducted in gyms and in a dermatology clinic. Each participant was examined for acne on three occasions and followed for 60 days. RESULTS: 30 patients were examined. Onset or exacerbation of acneiform lesions were observed ($p < 0.0005$). The effect was more prominent in females and in individuals without current acne and no family history of acne. CONCLUSION: This study showed the onset of acne with the progressive use of protein-calorie supplementation, in a two-month period. It is suggested that this type of supplementation be discouraged.

Keywords: Acne vulgaris; Dietary supplements; Incidence

Resumo: FUNDAMENTOS: Na observação pessoal de dermatologistas, nutricionistas e dos próprios pacientes, um novo problema emerge nas academias de ginástica: desenvolvimento e exacerbação da acne em usuários de Whey Protein, proteínas derivadas do leite de vaca. Extratos de Whey Protein contêm fatores de crescimento que podem estar relacionados com a acne. Sua pureza e composição não são completamente conhecidas e não há investigações científicas sobre seu potencial causador de acne. Objetivo: Avaliar a relação entre o uso de suplementos protéico-calóricos e o aparecimento ou agravamento da acne vulgar em adultos jovens em João Pessoa – PB. MÉTODOS: Estudo observacional descritivo conduzido em academias de ginástica e em consultório de dermatologia. Cada participante foi examinado para acne em três ocasiões e acompanhado por 60 dias. RESULTADOS: Foram examinados 30 pacientes. Aparecimento ou exacerbação de lesões acneiformes foram observados ($p < 0,0005$), sendo o efeito mais proeminente no sexo feminino e em indivíduos sem acne atual e sem história familiar de acne. CONCLUSÃO: Este estudo demonstrou o aparecimento de lesões acneiformes com o uso progressivo de suplementos proteico calóricos, ao longo de dois meses. Sugere-se que o uso deste tipo de suplemento seja desestimulado. Palavras-chave: Acne vulgar; Incidência; Suplementos dietéticos

INTRODUCTION

Acne Vulgaris is a pathology that affects the pilosebaceous unit with multifactorial pathogenesis involving genetic factors, hormone influence, exacerbated sebum production, abnormal keratinization, inflammation and bacterial proliferation. It presents a polymorphous clinical picture, from minimal lesions (comedos) to severe deforming forms that cause serious disorders of a psychosocial order.¹

Acne etiology is still poorly defined and intensively studied. Although the majority of patients

report that acne is triggered by the intake of some food, the nutritional aspect of the disorder is controversial in the literature.^{2,3,4,5}

Whey Protein is a term that designates milk serum proteins, which may be associated with the potential acne trigger in this product and that are used as supplements by young people who are trying to increase muscle mass.^{6,7,8} Whey Protein extracts from cow's milk contain 6 growth factors that may be related to acne: TGF, IGF-I and -II, PDGF and FGF-1 and -2.⁹

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The amino acids that compose Whey Protein are mainly the branched chain amino acids (BCAAs), which also present bioactive peptides such as: Betalactoglobulin (BLG) - the major serum peptide, resistant to acids and enzymes present in the stomach, favoring intestinal absorption. It is the peptide with the highest content of BCAAs; Alpha-lactalbumin (aLA) - it has the highest tryptophane content among all of the protein food sources. It is easily and quickly digested, besides having antimicrobial activity that protects the organism against pathogenic bacteria; Bovine Serum Albumin (BSA) - rich in cystine, an important precursor of glutathione, fundamental to the antioxidant defense system; Immunoglobulins (Igs) - they enhance immunity and also have antioxidant activity; Glycomacropeptides (GMP) - they improve mineral absorption by the intestinal epithelium, assist in appetite regulation by stimulating the pancreas to release the CCK (Cholecystokinin) hormone, responsible for appetite suppression, acting as a prebiotic with an immunomodulating role. The potency and purity of protein supplements are unknown and there is not sufficient information about long-term effects; nevertheless, their use is popular to a degree that attracts the attention of specialists and scientific organizations.¹⁰

Based on personal observations of dermatologists, nutritionists and physical educators, the hypothesis of this investigation is that the use of protein-calorie supplements, such as the Whey Protein used in gyms, may trigger acneiform lesions. A thorough review of the literature revealed the scarcity of studies with the same hypothesis or that specifically discuss this theme, although several recent articles explore *tangential aspects* of diet related to acne, like the participation of milk in its etiology.

The objective of this study is to evaluate the relationship between the use of protein-calorie supplements and the onset or exacerbation of acne vulgaris in young adults of the city of João Pessoa.

MATERIAL AND METHODS

Study Model and Location

The investigation followed a prospective observational model for a case series. The study location comprised gyms and a dermatology clinic in the city of João Pessoa.

Population and Sample

The target population was composed of people who frequented gyms and patients of the dermatology clinic in João Pessoa. Sampling was of the non-probability convenience type, so that all of the young adults that met the eligibility criteria were included. The previously established minimum sample size was

30 participants. All participants agreed and signed the Informed and Free Consent Term approved by the Research Ethics Committee of Lauro Wanderley University Hospital (HULW).

Eligibility Criteria

Both male and female young adults in the 18 – 30 years old age group who mentioned having recently used protein-calorie supplements were included. Those with comprehension and/or verbal communication problems, as well as memory disorders or any other problem that might compromise the veracity of information obtained were excluded.

Instruments

The instrument used was a form containing a questionnaire with data for patient identification (name, date of birth, profession, gender, address, telephone), a table for lesion counting at every appointment, data on the protein-calorie supplement used by the participant (name, dosage, typology and application form), family history of acne, past acne episodes, use of acne medication and androgenic hormone dosage.

The classification followed the Leeds Acne Grading System revised by Cunliffe (modified), based on comedo, papule, pustule and scar counting, a validated instrument previously employed by SOBRAL FILHO (2010).

Data Collection Procedures

This was a prospective observational study, with no damaging or invasive procedures. The protein-calorie supplements were not supplied to the participants by the researchers nor was there any kind of incentive for their utilization, which was only referred by the participant.

Data collection was carried out by the investigators, who were a dermatologist and two 4th year medical students, duly trained to recognize acne lesions, between August/2011 and May/2012.

The students visited gyms and established contact with strength training instructors, who informed them which students used protein-calorie supplements. Those who accepted to participate in the investigation had a form filled out based on interview and facial skin examination.

The dermatologist orienting the investigation collected data by filling out the forms of patients from his clinic who started using protein-calorie supplements.

Each participant was examined on three occasions and followed for 60 days: the first examination occurred before use of protein-calorie supplements was started (the previous intention to use them was informed to the gym instructors, and not recommended by the investigators), the second one after 30 days of

use and the third after 60 days of use. Lesion count and classification were done during these appointments.

Variables

The variables age, gender, protein-calorie supplement used, presence of acne prior to supplement use, use of acne medications, degree of acne and counting of existing lesions before the use of supplements, family history of acne, presence of acne in the first month of supplement use, presence of acne in the second month of supplement use, degree of acne and counting of lesions in the second month of supplement use were recorded.

Ethical Aspects of Research

In accordance with the norms of Resolution 196/96 of the National Health Council/MS for Research Involving Human Beings, after evaluation of this project by the Research Ethics Committee of Lauro Wanderley University Hospital (CEP/HULW), the eligible individuals were invited to participate in the investigation.

Information regarding the study was supplied to the participants and their family members: objectives of the investigation, the reason why the young adult met the eligibility criteria, information regarding the protocol and procedures carried out, guarantee of confidentiality of information supplied and absence of risk, in case they participated in the investigation, in addition to communication of their right to withdraw from the investigation at any moment. Only those who signed the consent form were included.

Data Analysis

The Statistical Package for the Social Sciences (SPSS) version 20.0 was employed for data analysis. Descriptive analysis used central tendency and dispersion measures for quantitative variables and frequency distribution for qualitative variables.

In order to assess differences in lesion numbers at the three counts the multivariate model for repeated measures analysis was employed. Wilks test was used as model of multivariate comparison. The magnitude of the effect was demonstrated by means of the Partial Eta Squared (η^2 partial). The pairwise comparison method was used to assess differences in comparison of the evaluation occasions.

Mixed ANOVA was applied with the objective of evaluating the influence of secondary variables on the curve of total lesions, using the secondary variables (gender, family history of acne and supplement used) as intersubject factor and the evaluations in months 0, 1 and 2 as intrasubject factors. Levene test and Box M test were used to assess the variance homogeneity and covariance matrices, respectively,

with the objective of carrying out the mixed ANOVA.

The chi-square test was used for comparison between the acne degree and the evaluation occasion.

The level of significance adopted for inferential statistics was 5%.

RESULTS

Samples were obtained from 30 adults who were users of protein-calorie supplements. Participant ages varied between 18 and 45 years (mean 23 years); 11 were female (37%) and 19 were male (63%).

Prior history of acne was mentioned by 14 patients (46.7%). Nine patients (30%) had had previous acne treatments and only 4 (13.3%) were having treatment at the time of the interviews.

The acne lesions count was numerically ascending according to how long the supplement had been used (Graph 1). The multivariate model for repeated measures analysis demonstrated a significant increase in the comedos, papules and pustules count between the analyzed periods, but there was no significant difference in the total number of scars (Table 1). The pairwise comparison method showed a significant difference regarding comedo count between month 0 and month 1 ($p=0.003$), month 1 and month 2 ($p=0.003$) and month 0 and month 2 ($p=0.001$). The papules, pustules and total lesions followed the same pattern, so that the difference between the months presented statistical significance <0.0005 . As regards scar count, the difference between the periods analyzed was not significant: month 0 and month 1 ($p=0.084$); month 1 and month 2 ($p=0.163$) and month 0 and month 2 ($p=0.055$).

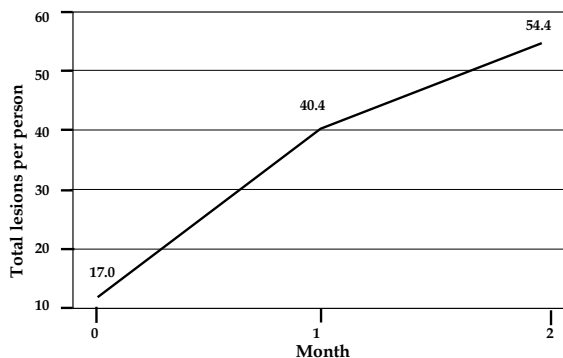
The degree of acne in the population studied was estimated before they began taking the supplements, then one month and two months after they started using them, by means of acneiform lesions count and application of the Leeds Acne Grading System revised by Cunliffe (Table 2). Comparison of distributions during the study months revealed significant statistical difference with tendency to acne degree increase according to time of exposure to the supplement ($p<0.0005$). While in month zero 93% of the studied population had up to Degree 1 of the grading system, this percentage was reduced to just 26.7% after two months of supplement use.

Regarding the secondary variables, it was demonstrated that the increase in total number of lesions during the period was not influenced by any other variable analyzed. The mixed ANOVA demonstrated that when the sample is divided by sex, there is no significant intersubject relationship [$F(1, 28) = 0.37$, $p = 0.55$, Partial Eta Squared = 0.01]. The same was found in the division of the sample by presence of family history of acne [$F(1, 28) = 0.007$, $p = 0.93$, Partial Eta Squared = 0.000]. Graph 2 and 3 illustrate

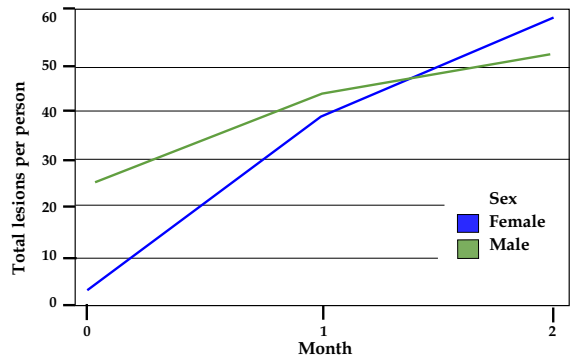
the evolution of total lesion count by division of sample by gender and family history of acne.

Whey Protein was the supplement most used by the participants – 22 of them. Other protein supplements (albumin, polyaminoacids, Leanbody, Mioplex, Oxyelit-plus) were used by the remaining 8 subjects, and the type of supplement (Whey protein *versus* another) did not have any influence on lesion count either, according to mixed ANOVA [F (1, 28) = 3.0, p = 0.09, Partial Eta Squared = 0.10].

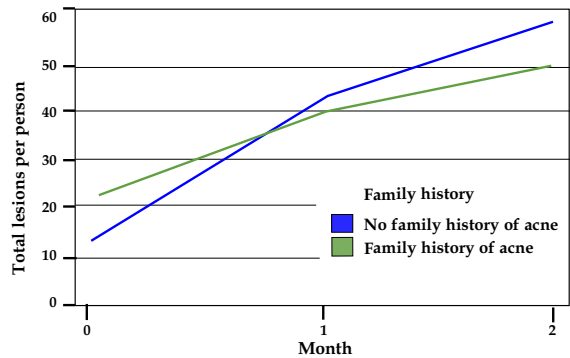
Only three patients affirmed being under some type of treatment for acne – one of them used topical tretinoin and two used benzoyl peroxide. Acne degree and the total quantity of lesions remained stable in these patients and did not affect the analysis of the sample as a whole.



GRAPH 1: Total number of acne lesions per person in the months after beginning protein-calorie supplement use in an adult population of the city of João Pessoa, in 2011



GRAPH 2: Total number of acne lesions per person by sex in the months after beginning protein-calorie supplement use in an adult population of the city of João Pessoa, in 2011



GRAPH 3: Total number of acne lesions per person by family history of acne in the months after beginning protein-calorie supplement use in an adult population of the city of João Pessoa, in 2011

TABLE 1: Multivariate model for repeated measures analysis of acne lesion count in months 0, 1 and 2 after the beginning of protein-calorie supplement use in an adult population of the city of João Pessoa, in 2011

Lesion	Month 0 MD ¹ (SD ²)	Month 1 MD (SD)	Month 2 MD (SD)	Wilks Lambda	F ³ (2, 28)	P ⁴	η ² partial ⁵
Comedos	11.7 (21.9)	16.6 (21.5)	19.7 (21.9)	0.64	7.86	0.002	0.36
Papules	1.87 (3.8)	10.2 (8.0)	15.8 (11.1)	0.43	18.42	<0.0005	0.57
Pustules	0.3 (0.8)	9.5 (11.0)	14.0 (14.9)	0.52	12.85	<0.0005	0.48
Scars	3.1 (5.5)	4.1 (5.8)	4.9 (6.9)	0.82	3.08	0.62	0.18
Total lesions	17.1 (25.6)	40.4 (28.0)	54.4 (34.8)	0.44	18.12	<0.0005	0.56

¹ Mean; ² Standard deviation; ³ Statistics F of Variance Analysis; ⁴ Statistical significance of multivariate model for repeated measures analysis; ⁵ Partial Eta Squared.

TABLE 2: Distribution of degree of acne according to Leeds Acne Grading System revised by Cunliffe in the months after beginning protein-calorie supplement use in an adult population of the city of João Pessoa, in 2011

Leeds Revised Grading System	Month 0		Month 1		Month 2	
	N	%	N	%	N	%
Degree 0	13	43.3%	0	0%	0	0%
Degree 1	15	50%	13	43.3%	8	26.7%
Degree 2	2	6.7%	14	46.7%	13	43.3%
Degree 3	0	0%	3	10%	9	30%
Total	30	100%	30	100%	30	100%

DISCUSSION

The research hypothesis was corroborated, as employment of protein-calorie supplements demonstrated significant association with the onset and exacerbation of acneiform lesions. Protein-calorie supplements, among them Whey Protein, have been indiscriminately used by both male and female young people, with no previous examination or follow-up. According to the personal observations of physicians, nutritionists and other health professionals, consumption of protein mixes containing casein and Whey Protein, which are proteins derived from cow's milk, could also be associated with the development of acneiform lesions.¹¹

An extensive review did not find specific studies about the relationship between acne and protein-calorie supplements; however, there is a large number of publications about the potential acne triggering effect of milk and relationship with its components, among them milk serum proteins (Whey Protein).

Seeking to bridge this knowledge gap, this investigation studied the relationship between supplements and acne, finding a strongly positive correlation ($p < 0.0005$). At the beginning of follow-up, only 56.7% of the sample presented acneiform lesions, with degrees that varied from I to II. After two months using the protein-calorie supplement, all of the patients presented acneiform lesions, 30% of them with degree III.

Milk is one of the most investigated factors as potential acne trigger.^{11,12} Milk derivatives paradoxically induce an increase in IGF-1 levels, especially if the milk serum protein content is high. IGF-1 promotes the growth and division of cutaneous cells, sebum production, efficacy of luteinizing hormone (LH) and estrogen production.^{11,13-17} Therefore, the acne mechanism developed through the use of protein supplements derived from milk may be related to the elevation of IGF-1, since IGF-1 seems to mediate comedogenic factors, such as androgens, growth hormone and glucocorticoids.^{13,14}

The frequent intake of carbohydrates of high glycemic content may expose adolescents to acute hyperinsulinemia that influences follicular epithelial growth, keratinization and sebaceous secretion.^{12,18} Hyperinsulinemia plays a role in circulating concentration of IGF-1 and the growth factor binding protein similar to insulin-3 (IGFBP-3), which act directly on the proliferation of keratinocytes and apoptosis. IGF-1 seems to mediate comedogenic factors, like androgens, growth hormone and glucocorticoids.^{13,14}

Hyperinsulinemia, which influences follicular epithelial growth, keratinization and sebaceous secretion by means of increased androgen levels, stimu-

lates sebum production.^{12,18} This mechanism might be involved in the development of acneiform eruptions in individuals using calorie supplements. However, this mechanism could only be confirmed through analytical studies of hormone dosages, including insulin and full androgenic profile of all participants.

The increase in quantity and degree of acneiform lesions was more pronounced during the first month of supplement use than during the second. Although there is no evidence in the literature supporting such finding, it is suspected that the impact of the supplement on acne rises to a peak during the first month, with gradual effect reduction over time.

There was significant difference in acne degree and response to supplements between the genders. Among those who did not use supplements, there were more acneiform lesions in men than in women, but these values were inverted after the first month of supplement intake and the difference became even more pronounced in the second month, showing that the effect of supplement use was greater in women than in men. A possible explanation would be the influence of androgenic hormones, whose increase is proportionally greater in women, after using Whey Protein, compared to men.

There was difference also in response to supplement use concerning family history of acne. Those who referred acne in the family presented more lesions before taking the supplements, a value that was inverted over the two months of use, suggesting that those without family predisposition would be more sensitive to the effects of supplements on acneiform lesions.

The acne degree and the total quantity of lesions remained stable in patients that had some kind of treatment for acne during the use of supplements. Even though in this study they corresponded only to a small proportion of the sample (10%) and did not affect the analysis as a whole, the prescription of acne treatment concomitantly with the beginning of supplement intake is suggested, in order to better analyze this possible protection factor.

Eventual methodological biases of this research should be considered. First of all, convenience sampling limits study validity by compromising the accuracy of findings. Secondly, there is posology variation in supplement utilization. As it was a non-controlled study, there was no pattern of supplement utilization, which may have limited association accuracy. Thirdly, the small proportion of the sample that considered other types of supplement limited the correlation between exacerbation of acne and type of supplement, which may also have limited association accuracy.

CONCLUSION

This study demonstrated the onset of acneiform lesions with progressive use of protein-calorie supplements over a two-month period. The association having been corroborated, it is suggested that larger studies be conducted, with the objective of evaluating the power of this association when other risk factors for acne exacerbation are considered in the same analysis, with the intention of eliminating possible confounding factors. It is also suggested that the use of this type of supplement be discouraged, given its significant effects in the aggravation of acneiform lesions. □

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