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COMPARISON OF ORAL ISOTRETINOIN VS ISOTRETINOIN WITH VITAMIN D3 (CHOLECALCIFEROL) IN THE TREATMENT OF ACNE VULGARIS

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ABSTRACT

Objective: To check the effect of oral Isotretinoin vs Isotretinoin with Vitamin D3 (Cholecalciferol) in the treatment of Acne Vulgaris

Material and Methods: This prospective cohort study was conducted in the outpatient dermatology clinic at Sandeman Provincial Hospital. Before initiating the study, a written informed consent was received from the participants after explaining the aim, value, and necessary steps in a simplified manner and the potential side effects of isotretinoin drugs.

Results: Acne vulgaris remains a prevalent dermatological concern, impacting individuals of all ages and genders worldwide, necessitating effective treatment modalities to address its multifactorial nature. This article presents a comparative analysis of treatment outcomes between oral isotretinoin monotherapy and a combination regimen comprising oral isotretinoin and vitamin D supplementation. Our findings illuminate the superior efficacy of the combination therapy, with the group receiving isotretinoin alongside vitamin D demonstrating marked improvement in clinical results. Drawing from a robust cohort study involving acne patients, we meticulously assess and contrast the efficacy of these treatment modalities. Our findings unveil a notable disparity in treatment response, with the group receiving combination therapy exhibiting significantly greater improvement in clinical outcomes compared to those undergoing isotretinoin monotherapy. Through this exploration, we advocate for a holistic approach to acne treatment, emphasizing the potential benefits of adjunctive vitamin D supplementation in enhancing therapeutic outcomes. This study provides valuable insights to optimize treatment strategies and improve patient care in the management of acne vulgaris.

Conclusion: In conclusion, combining oral isotretinoin with vitamin D supplementation demonstrates superior efficacy in treating acne vulgaris compared to isotretinoin monotherapy. The study underscores the importance of holistic approaches to acne management and highlights the potential benefits of adjunctive vitamin D therapy optimizing therapeutic outcomes for patients.

Keywords: Acne, Vulgaris, Isotretinoin, Vitamin, Balochistan

INTRODUCTION

Acne is one of the chronic inflammatory diseases for pilosebaceous units. It can be characterized by seborrhea, erythematous pustules and papules, and in more severe cases nodules, closed and open comedones formation, pseudocysts, and deep pustules (Barankin and Dekoven, 2002).

Acne Vulgaris (AV) affects both genders equally, and it usually starts in adolescence between 14 and 17 years of age in females and 16 and 19 years of age in males; however, its emergence may be delayed until 25 to 30 years of age (Zaenglein, 2018). The time at which AV fades varies (Aydemir, 2014). The pathogenesis of acne involves four primary factors: increased sebum production, increased follicular hyperkeratinization, colonization with cutibacterium acnes (formerly known as propionibacterium acnes), and an inflammatory process (Lone et al., 2012).

Topical therapies include antibiotics, azelaic acid, benzoyl peroxide, and retinoids. Systemic treatments include antibiotics, hormonal therapy, and isotretinoin. In latest years, combination therapy has become a vital part of acne treatment. There are different treatment modalities to acne vulgaris including systemic and topical drugs, depending on severity (Platsidaki and Dessinioti, 2018).

Isotretinoin (13-cis-retinoic acid) is a systemic nonaromatic retinoid that is highly effective in the treatment of nodulocystic and moderate-to-severe acne, and it affects all four underlying factors of AV pathogenesis. Therefore, isotretinoin is regarded as the most effective medication currently available for acne, and it is also an effective treatment for many other dermatological conditions (Fox et al., 2016). Isotretinoin is indicated mainly for severe cases of acne but can be used in moderate cases to minimize scarring. The recommended dose for isotretinoin treatment is 0.5–1 mg/kg daily, with a cumulative dose between 120 and 150 mg/kg (Ganceviciene and Zouboulis, 2010). Isotretinoin has many side effects, the most important of which are hepatotoxicity, psychological effects, social effects, teratogenicity, xerosis and hypertriglyceridemia (Leyden et al., 2014).

Vitamin D is a fat-soluble steroid hormone derived from dietary intake and synthesized through the skin via exposure to sunlight. Vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol) are manufactured through solar ultraviolet B radiation (UVB) (Zaenglein et al., 2016). Absorption of UVB radiation in the skin leads to the conversion of provitamin D to pre-vitamin D, followed by the production of vitamin D3 (Yesilova et al., 2012). Vitamin D has both anticomedogenic and antioxidant properties; it demonstrates a regulatory effect on the immune system, differentiation of sebocytes and keratinocytes. Therefore, its deficiency may contribute to the pathogenesis of acne (Wacker and Holick, 2013).

In this study, the effect of oral isotretinoin alone and combination of oral isotretinoin with vitamin D supplementation in acne vulgaris patients is explored. It is known that this is the first study in Balochistan province to address this issue.

METHODS

This prospective cohort study was conducted in the outpatient dermatology clinic at Sandeman Provincial Hospital, Quetta. The study was conducted in the cold weather seasons to minimize the effect of seasonal variation on vitamin D levels.

Before initiating the study, a written informed consent was received from the participants after explaining the aim, value, and necessary steps in a simplified manner and the potential side effects of isotretinoin drugs.

Data source

The severity of acne vulgaris was assessed by clinical examination according to: Tutakne (12) grading system for acne which classifies acne vulgaris into four grades as follows: Grade 1: Comedones, occasional papules, Grade 2: Papules, comedones, few pustules (1-3), Grade 3: Predominant

pustules >3, nodules, abscesses, Grade 4: Mainly cysts, abscesses, widespread scarring. All 100 subjects completed a data collection form to provide their demographics, family history of acne, sun exposure >2 hours/day, age of onset, duration of disease, site of acne (face, chest, or back), past medical history, and other relevant variables.

Inclusion criteria

Patients from 15 to 45 years of age with AV, irrespective of sex, and who did not opt for acne treatments for at least the previous four weeks and patients who were unresponsive to conventional topical therapies or systemic antibiotics (other than systemic isotretinoin) were included in this study.

Exclusion criteria

Pregnant and breastfeeding females, patients already taking vitamin D supplements and those who have taken vitamin D supplements in past 6 months were excluded from study.

RESULTS

In the study, two different treatment regimens were investigated: isotretinoin alone and isotretinoin with vitamin D. The isotretinoin alone group comprised 50 patients, with a frequency of 72%, indicating that 36 out of 50 patients in this group exhibited the variable under consideration. On the other hand, the isotretinoin with vitamin D group also consisted of 50 patients, but the frequency was higher at 96%, signifying that 48 out of 50 patients in this group manifested the specified variable. These frequencies provide insights into the prevalence or occurrence of the variable within each treatment group, offering valuable information for the study's analysis and interpretation as shown in Table-1.

Table-1: Overall Variable Percentage

Variables Percentage	No of Patients	Frequency
Isotretinoin Alone	50	36(72%)
Isotretinoin with Vitamin D	50	48(96%)

The table-2 presents a comparative analysis of the global clinical evolution among patients receiving two different treatment regimens: isotretinoin alone and isotretinoin with vitamin D. In the isotretinoin alone group, consisting of 50 patients, 60% demonstrated a completely cured clinical evolution, indicating a significant positive response to the treatment. Additionally, 12% of patients showed improvement in their clinical condition, while 28% remained unchanged.

On the other hand, the isotretinoin with vitamin D group, also comprising 50 patients, exhibited even more favorable outcomes. A remarkable 90% of patients in this group experienced a completely cured clinical evolution, suggesting a higher efficacy when vitamin D was included in the treatment. Furthermore, only 6% showed improvement, and another 4% remained unchanged. These findings highlight the potential synergistic effect of combining isotretinoin with vitamin D, leading to a higher percentage of patients with a completely cured clinical evolution compared to isotretinoin alone. Overall, the table provides valuable insights into the varying clinical responses associated with the different treatment regimens.

Table-2: The Global Clinical Evolution

Variables Percentage (Global Clinical Evolution)	Isotretinoin Alone	Isotretinoin with Vitamin D
Completely Cured	30(60%)	45(90%)
Improved	6(12%)	3(6%)
Unchanged	14(28%)	2(4%)
Total	50	50

The table-3 offers a detailed breakdown of the global clinical evolution based on gender within two distinct treatment groups: isotretinoin alone and isotretinoin with vitamin D. In the isotretinoin alone group, among male patients, 56% exhibited a completely curved clinical evolution, 4% showed improvement, and 40% remained unchanged. For female patients in the same group, 64% had a completely curved clinical evolution, 6% showed improvement, and 16% remained unchanged. This gender-specific analysis indicates a slightly higher proportion of females with a completely curved clinical evolution compared to males in the isotretinoin alone group.

Moving to the isotretinoin with vitamin D group, among males, 84% demonstrated a completely curved clinical evolution, 8% showed improvement, and 8% remained unchanged. For females in this group, 96% had a completely curved clinical evolution, 4% showed improvement, and none remained unchanged. Notably, the isotretinoin with vitamin D group shows a higher percentage of both male and female patients with a completely curved clinical evolution compared to the isotretinoin alone group. This gender-stratified analysis provides nuanced insights into the differential responses to the two treatment regimens.

Table-3: Gender wise effect of Drugs

Variables Percentage (Global Clinical Evolution)	Isotretinoin Alone		Isotretinoin with Vitamin D	
	Male	**Female**	**Male**	**Female**
Completely Cured	14(56%)	18(64%)	21(84%)	24(96%)
Improved	1(4%)	3(6%)	2(8%)	1(4%)
Unchanged	10(40%)	4(16%)	2(8%)	0
Total	**25**	**25**	**25**	**25**

The table-4 provides a comprehensive breakdown of the global clinical evolution among patients receiving two different treatment regimens: isotretinoin alone and isotretinoin with vitamin D, categorized by age groups. In the isotretinoin alone group, patients aged 10 to 25 years exhibited a 30% complete cure rate, with 8% showing improvement and 2% remaining unchanged. Within the 28 to 35 age group, the completely cured rate increased to 24%, with 4% improvement and 6% unchanged. The 36 to 45 age group showed 6% complete cure, 0% improvement, and 14% unchanged. The overall percentages for this group were 60% completely cured, 12% improved, and 28% unchanged.

Turning to the isotretinoin with vitamin D group, patients aged 10 to 25 years had a 28% complete cure rate, with 2% improvement and 0% unchanged. In the 28 to 35 age group, the completely cured rate increased to 42%, with 4% improvement and 0% unchanged. The 36 to 45 age group showed 20% complete cure, 0% improvement, and 4% unchanged. The overall percentages for this group were 90% completely cured, 6% improved, and 4% unchanged. This detailed analysis provides insights into the varying clinical outcomes based on age and treatment regimen, highlighting potential differences in treatment efficacy across different patient demographics.

Table-4: Age wise effect of Drugs

Variables Percentage (Global Clinical Evolution)	Isotretinoin Alone			Isotretinoin with Vitamin D		
	Completely Cured	Improved	Unchanged	Completely Cured	Improved	Unchanged
10-25 years	15(30%)	4(8%)	1(2%)	14(28%)	1(2%)	0
28-35 years	12(24%)	2(4%)	6(12%)	21(42%)	2(4%)	0
36-45 years	3(6%)	0	7(14%)	10(20%)	0	2(4%)
Total	**30**	**6**	**14**	**45**	**3**	**2**

After vitamin D supplementation, there was a significant improvement in acne grading where about 90% of acne patients treated with vitamin D supplementation reached stage zero of acne versus 60% among those treated with oral treatments only without supplementations (Table-5).

Table-5: Grades wise effect of Drugs

Acne Grades	Group-1 Isotretinoin	Group-2 Isotretinoin with Vitamin D
0	30 (60%)	45 (90%)
I	4 (8%)	2 (4%)
II	2 (4%)	1 (2%)
III	1 (2%)	1 (2%)
IV	13 (26%)	1 (2%)

DISCUSSION

Acne vulgaris is the formation of comedones, papules, pustules, nodules, and/or cysts as a result of obstruction and inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland). Acne develops on the face and upper trunk. It most often affects adolescents.

The observed differences in acne grades between the two groups were statistically significant. This suggests a substantial variation in treatment outcomes between isotretinoin alone and isotretinoin with vitamin D, with the latter demonstrating a notably higher proportion of patients achieving a complete resolution of acne. The detailed breakdown of acne grades in each group provides valuable insights into the effectiveness of the respective treatments across different severity levels, contributing to a nuanced understanding of the impact of vitamin D supplementation in conjunction with isotretinoin therapy.

CONCLUSION

In conclusion, the comparative analysis presented in this article sheds light on the effectiveness of combination therapy involving oral isotretinoin and vitamin D supplementation in the treatment of acne vulgaris. By meticulously assessing treatment outcomes in a robust cohort study, the study reveals a notable disparity in response between patients undergoing isotretinoin monotherapy and those receiving combination therapy. The group receiving the combination regimen exhibited significantly greater improvement in clinical outcomes, underscoring the potential benefits of addressing multiple factors implicated in acne pathogenesis. This underscores the importance of adopting a holistic approach to acne treatment, which acknowledges the multifactorial nature of the condition and seeks to optimize therapeutic outcomes. The findings advocate for the incorporation of adjunctive vitamin D supplementation alongside conventional acne therapies, providing valuable insights to clinicians in their efforts to improve patient care and management of acne vulgaris. Moving forward, further research into combination therapies and their mechanisms of action will be crucial in refining treatment strategies and enhancing outcomes for individuals affected by acne.

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