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Evaluation of Serum Cortisol Level in Chronic Superficial Dermatophytosis

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Introduction:

The epidemic-like scenario of superficial fungal infections in India has been complicated by the rampant use of systemic and topical potent steroids.In this study, we hypothesizethat the unjudicial use of topical corticosteroids can cause Hypothalamic pituitary axissuppression in chronic dermatophytosis patients.

Objectives: To estimate morning serum cortisol levels in chronic superficial dermatophytosis patients.

Materials and Methods: A totalof 208 individuals were enrolled in this study. In which, 104 (50%) patients had Chronic superficial dermatophytosis (case group) and 104 (50%) patients were healthy (control group). Their clinical details and laboratory investigations including KOH and serum cortisol, were recorded on a pre-designed proforma.

Results: The mean S. Cortisol level was 7.27±5.34 µg/ml in cases and 11.21±5.92 µg/ml in the control group. The mean S. Cortisol level was significantly lower in cases as than controls (p <0.001).

Conclusion: This study shows that patients with chronic superficial dermatophytosis have low serum cortisol compared to healthy controls.

Keywords: Hypothalamic Pitutary Axis; Superficial Dermatophytosis; Serum Cortisol Levels; Topical Corticosteroids

Introduction

Chronic dermatophytosis is defined as having a disease duration of more than six months and up to one year, with or without recurrence, despite treatment.[1] These cases have significantly increased over the past three to four years. Steroid modified tinea is a mycotic skin infection improperly altered by topical immunomodulators like calcineurin inhibitors and steroids, making it non-diagnostic. Since some high-potency topical steroids are readily available as over-the-counter (OTC) medicines and non-dermatologists can freely prescribe topical steroids without any fungal testing, the prevalence of this type of tinea appears to be asteadily increasing trend. Thedermatophytosis cases we observe in hospitals are merely the proverbial "tip of the iceberg" in terms of the widespread epidemic in the present study. We hypothesized that the Hypothalamic pituitary axis (HPA) might be suppressed in chronic dermatophytosis, similar to how it is suppressed in atopic dermatitissince corticosteroids are frequently abused in chronic dermatophytosis as well.

Study Objectives were:

To estimate morning serum cortisol levels in chronic superficial dermatophytosis patients.

To compare the serum cortisol level between patients with chronic dermatophytosis and the control group, who did not suffer from chronic dermatophytosis and had no history of taking topicalor systemic corticosteroids.

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Materials and Methods

This study was done in the dermatology department of a medical college located in the north central part of UttarPradesh. Period of the study was between January 2020 to June 2021 by convenientsampling.Sample size calculated as per a pilot study done 2 months earlier revealed a sample size of 104 with a 0.05 margin of error and 95% confidence interval. 104 study subjects were enrolled as cases alongwith another 104 age and sex-matched control,which consisted of apparently healthy non dermatophytic subjects as per inclusion and exclusion criteria.

The inclusion criteria of the study group were patients diagnosed with chronic dermatophytosis who attended the outpatient of teaching medical college in northern India willing to participate in the study, and were ready for further investigations after giving written informed consent. Patients having other skin disorders or any other chronic systemic skin disorders,pregnant,lactating females, and primary diagnosed adrenal,pituitary hypothalamic disorders were excluded.

KOH test was done for case confirmation. Patients wereasked to avoid strenuousphysical activity the daybefore a cortisol test and to lie down and relax for 30 minutes before the blood test. All samples were collected between 8 to 9 am to prevent any confounding due to the diurnal variation in cortisol levels.After collection of the venous blood, blood was allowed to clot by leaving it undisturbed at room temperature. This usually took 15–30 minutes. The clot was removed by centrifuging at 1,000–2,000 x g for 10 minutes in a refrigerated centrifuge. The resulting supernatant was designated serum (~ 2 ml). The serum was immediately separated from cells after the centrifugation and aliquot into another microfuge tube, labeled, and again stored at −200C centigrade. A separate tube was used for each test. The cortisol levels were measured using commercially available chemiluminescence system kits of the BeckmanCoulters Access 2 system (figure-1). Statistical analysis was performed by the SPSS program for Windows, trial version 21.0. The study was approved by the institutional ethical committee.

Figure1: Chemiluminescence system kit

Results

Table 1 and 2 provides the baseline description of cases and age and sex matched control with no significant difference between 2 groups(p=0.697 and 0.482). Figure 2 showsthat the mean serum cortisol level was significantly lower in the case group (7.27±5.34 µg/ml) compared to the control group (11.21±5.92 µg/ml). Table 3 shows the correlation of serum cortisol with different disease parameters in the case group.There was a significant correlation of serum cortisol level among patients who used corticosteroid,eitherparent eral,oral or topical.

	Cases (n=104)		Controls (n=104)			
Age group	n	%	n	%	Chi Sq.	ap-value
≤20 years	10	9.62	5	4.81		
21-30 years	45	43.27	51	49.04		
31-40 years	35	33.65	37	35.58		
41-50 years	13	12.50	10	9.62		
51-60 years	1	0.96	1	0.96	2.49	0.647
Mean ± SD	30.58±8.48		30.94±7.45			

aChi-square test

Table 1: Distribution of study population according to different age group

	Cases (n=104)		Controls (n=104)			
	n	%	n	%	Chi Sq.	1p-value
Male	62	59.62	55	52.88		
Female	42	40.38	49	47.12	0.70	0.402

1=Chi-square test

Table 2: Distribution of study population according to gender

Study Characteristic	mean Serum cortisol levels	Pearson's Coefficient	p-Value
Duration of Disease			
≤1 year duration of Disease >1 year duration of Disease	7.19 7.52	-0.027 0.027	0.784 0.784
Parenteral Corticosteroid Topical Corticosteroid Oral Corticosteroid	3.33 8.53 5.81	-0.391 0.391 0.220	<0.001* <0.001* 0.025*
Body surface Area involved			
≥5% Body surface Area <5% Body surface Area	7.59 5.96	0.121 -0.121	0.222 0.222
>5 No. lesion on body	6.39	-0.084	0.399
≤5 No. lesion on body	7.61	0.084	0.399

*=Significant (p<0.05)

Table:3 Correlation of S. Cortisol level with different parameters among cases

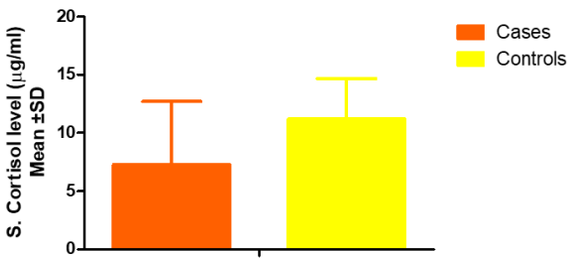

Figure2: Bar Chart shows the comparison of mean S. Cortisol level in between cases and controls group

Discussion

Topical corticosteroids are the cornerstone of anti-inflammatory therapy.However,topical corticosteroids are being used to treat other dermatological conditions and dermatophytosis also frequently[2]. Individuals with allergy illnesses have varied cortisol patterns in their natural environments and variable cortisol responses to stress. Acute stressors temporarily activate the HPA axis, but due to the phenomenon of adaptation, it returns to normal levels. Chronic stress increases the HPA axis's central tone and interferes with its ability to function normally. In several trials, both topical and systemic administration of corticosteroids resulted in HPA axis inhibition.[3] HPA axis evaluation can be done by estimating serum cortisol level and ACTH stimulation test. In our study, people aged 21-40 had a higher prevalence of superficial dermatophytosis (76.92%). In our study, the superficial dermatophytosis was more frequent in men, with a 1.48:1 male:female ratio. Male and female percentages were 59.62% and 40.38%, respectivelywhich corelated with the study done byThakran et al., (2021). According to the research, dermatophyte infections are61-67%, with a higher percentage of patients coming from lower socioeconomic categories.[4,5] Patients with dermatophytosis frequently self-administer oral or topical azoles and topical steroids individually or in combination.[6] According to recent studies, patients frequently (42%–81%) previously applied topical steroid-containing combination creams.[7]

In India, several FDC creams are effortlessly available as OTC, are cheaper, and give quick symptomatic relief due to the anti-inflammatory properties of steroids. These medicines are recommended by general practitioners, quacks, paramedics, pharmacists, friends, and family without adequate knowledge about diagnosing and managing dermatophytosis. On achieving some response, patients continue using these products indefinitely and repetitively in case of recurrence.Adverse effects of injudicious use of topical corticosteroids (TCs) may range from atrophy, hypopigmentation, striae, telangiectasia, hypertrichosis, and acneiform eruptions to more systemic severe side effects due to hypothalamic–pituitary–adrenal axis suppression. Neither the patient nor the pharmacist is aware of these hazards, resulting in an alarming rise in the number of patients approaching dermatologists with these side effects, which may sometimes be irreversible.[14]

A study reported that a few days of therapy of clobetasol propionate (0.05%) at a dose of 2 g/day is associated with decreased morning cortisol level[8], and use over 100 g/week can lead to signs and symptoms of Cushing's syndrome or adrenal insufficiency.[9,10] Approximately 48% of patients treated with highly potent topical steroids were found to have a transient and reversible reduction of HPA axis function but without any significant clinical symptoms.[11]

However, in the present study, theACTH stimulation test was not done due to financial constraints and the patients' refusal to administer ACTH.Therefore, serum cortisol estimation was done to evaluate the HPA axis.

In our study, the mean S. cortisol level was significantly lower (P=<0.001) in chronic superficial dermatophytosis patients (7.28±5.42 µg/ml) as compared to healthy controls (11.21±5.92 µg/ml). In asimilar study kaur etal., reported low serum cortisol levels as 1.29 ± 1.04 µg/dLin approximately 43% of patients, which was highly significant (P-value < 0.0001).[13] In the present study, topical, oral, and parenteral steroid medications all lowered the serum cortisol levels. As quoted in past studies among Indian patients,the normal range of serum cortisol levels is (7–25 µg/ml) ~ > 10 µg/ml3. The present study showed decreased S. cortisol levels irrespective of the type of steroid administration. The most significant factor contributing to the current outbreak of chronic and resistant dermatophytosis may be the abuse of topical steroids.

In the present study, the mean cortisol level in the exposed site was 8.20±4.51 µg/ml, 7.45±5.60 µg/ml in the non-exposed site, and 6.68±5.55 µg/ml in both exposed and non-exposed sites.This study assumed that, particularly under stressful circumstances, the failure to exert a proper HPA axis and provide a sufficient regulatory signal for the immunological target cell could raise the risk for abnormal immune functioning.[12] Moreover, evidence of mild suppression of the hypothalamic-pituitary-adrenal (HPA) axis was seen in chronic superficial dermatophytosis patients when the steroids were used, but recovery of function was rapid when the intensive treatment ceased.

Therefore, we can provide a physiological dose of corticosteroid (5mg prednisolone) for a short period with an antifungal treatment in steroid-abused chronic superficial dermatophytosis patients to overcome the steroid withdrawal symptoms.

Conclusion

This study clearly shows that abuse of steroids in any form (topical, oral, and parenteral/inhalational) leads to lower serum cortisol levels in chronic superficial dermatophytosis patients compared to the healthy control group. However, to ascertain HPA suppression, future studies should be planned with ACTH stimulation tests in addition toserum cortisol levels.

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