



ORIGINAL RESEARCH PAPER

Dermatology

ASSOCIATION OF PSORIASIS SEVERITY HYPOTHALAMIC PITUITARY ADRENAL AXIS FUNCTION

KEY WORDS: HPA axis, Psoriasis, PASI

Dr. Sunjanaa Dhepa R L*

Assistant Professor, Department of Dermatology venereology & leprosy, Vinayaka Missions Medical College & Hospitals, Karaikal- 609609
*Corresponding Author

Dr. Srivenkateswaran K

Professor, Department of Dermatology venereology & leprosy, Vinayaka Missions Medical College & Hospitals, Karaikal- 609609

Dr. Sivasubramanian V

Professor, Department of Dermatology venereology & leprosy, Vinayaka Missions Medical College & Hospitals, Karaikal- 609609

ABSTRACT

OBJECTIVE: Evaluation of role of cortisol and Adrenocorticotrophic hormone , a key component of the hypothalamic pituitary adrenal axis , in influencing the severity of psoriasis
METHODOLOGY: Prospective study was conducted involving 100 subjects for a duration of 1 year. Serum Adrenocorticotrophic hormone and cortisol was evaluated for all participants and the correlation with psoriasis severity was elicited.
RESULTS: Among the study subjects it was found that the mean comparison of cortisol was significantly lower (P value < 0.001) whereas in Adrenocorticotrophic hormone it was significantly higher(P value <0.001). A significant positive correlation was seen between PASI and Adrenocorticotrophic hormone whereas a significant negative correlation was seen between PASI and cortisol levels.
CONCLUSION: The daily stressors cause HPA axis dysfunction due to which the levels of Adrenocorticotrophic hormone is increased and the levels of Cortisol is decreased which relatively increases the severity of psoriasis.

I. INTRODUCTION

Psoriasis is a non-contagious disease and it is mostly associated with high levels of psychological distress and considerable life impact. In India , incidence of psoriasis among total skin patients ranged between 0.44 and 2.2%, with overall incidence of 1.02% [1]. Patients with psoriasis presented with an increased incidence of psychological disorders like depression[2]. In fact, most of the patients who presented with psoriasis had exacerbation episodes which are often preceded by major stressful life events[3]. The stress response is mainly due to the activation of both the HPA axis and the autonomic nervous system, since they both interact with the immune system. There is increasing evidence that the experience of stressful events is associated with the course of chronic inflammatory skin diseases such as psoriasis[4,5,6]. For example, external stressors stimulate the secretion of hormones such as cortisol, with peripheral and central HPA axis activity[7] that activate skin mast cells [8,9] which in turn alters the barrier function of skin and upregulate proinflammatory cytokines[10], which in turn might exacerbate the severity of psoriasis. The severity of psoriasis can be measured using Psoriasis Area and Severity Index (PASI) [11]. With this background the association between hypothalamic pituitary adrenal axis and the severity of psoriasis using Psoriasis Area Severity Index was thought to be elicited. This study would give better insight regarding the correlation between the changes elicited in serum cortisol and ACTH levels depending on the severity of psoriasis.

II. MATERIALS AND METHODS

This is a prospective study where 50 psoriasis patients who attended the Department of Dermatology, venereology and leprosy ,above 18 years of age and 50 age and gender matched healthy controls were recruited for the study after obtaining institutional ethical committee clearance and the purpose of the study was explained to the subjects in their own dialect and informed consent were obtained from them. Psoriatic patients below 18 years and suffering from adrenal gland dysfunction were excluded. With strict aseptic precautions, blood sample was drawn by venepuncture at 8.00 am and 2 ml of blood was collected in Ethylene Diamine Tetra Acetic Acid (EDTA) anticoagulant tube and was

subjected to investigations like serum cortisol and ACTH. Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. Pearson correlation or Spearman's correlation was done to find the correlation between two quantitative variables.P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

III. RESULTS

A total of 100 study participants were recruited during the study period of 1 year , of which 40% were females and 60% were males and majority of the subjects belong to the age group 41 to 50 years. In cases 28% had DM, 26% had HTN, 8% had family history psoriasis and 26% were on Psychiatry Medication. In Controls 24% had DM, 22% had HTN, none had family history and 8% were on Psychiatry Medication. There was a statistically significant difference in Family history and Psychiatry Medication which shows P value of 0.041 and 0.017 respectively. 18% had arthritis and 50% had nail changes and hence a statistically significant P value of 0.002 and <0.001 respectively. Mean duration of Psoriasis among cases was found to be 10.8 ± 12 months and Mean PASI score was 20.5 ± 5.4.

Table No : Past History comparison between two groups

		Group				P value
		Cases		Controls		
		Count	%	Count	%	
DM	No	36	72.0%	38	76.0%	0.648
	Yes	14	28.0%	12	24.0%	
HTN	No	37	74.0%	39	78.0%	0.640
	Yes	13	26.0%	11	22.0%	
Family H/O	No	46	92.0%	50	100.0%	0.041*
	Yes	4	8.0%	0	0.0%	
Psychiatry Medication	No	37	74.0%	46	92.0%	0.017*
	Yes	13	26.0%	4	8.0%	

Table No 2: Mean ACTH and Cortisol Levels comparison between two groups

	Group				P value
	Cases		Controls		
	Mean	SD	Mean	SD	
ACTH (pg/ml)	51.2	13.2	35.0	11.0	<0.001*
Cortisol (mg/dl)	8.9	4.1	14.8	3.1	<0.001*

In study subjects, mean ACTH was 51.2 ± 13.2 pg/ml and in controls it was 35 ± 11 pg/ml and hence mean ACTH was significantly higher (p<0.001) among study subjects than in controls. And also in study subjects mean Cortisol was 8.9 ± 4.1 mg/dl and in controls it was found to be 14.8 ± 3.1 mg/dl and hence Mean ACTH levels was significantly (p<0.001) lower in study subjects than in controls.

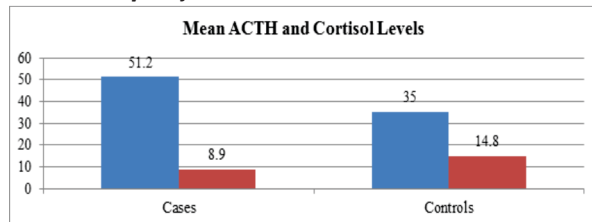


Figure No 1 : Bar diagram showing Mean ACTH and Cortisol Levels comparison between two groups

For this study population, a correlation between PASI, ACTH and cortisol was elicited using Pearson correlation and it was found that there was a significant positive correlation between PASI and ACTH levels among cases, i.e. with increase in PASI severity there was increase in ACTH levels and vice versa. And also a significant negative correlation between PASI and Cortisol levels in cases, i.e. with increase in PASI severity there was decrease in Cortisol levels and vice versa.

Table No 3: Correlation between PASI, ACTH and Cortisol among cases

		PASI	ACTH (pg/ml)	Cortisol (mg/dl)
PASI	Pearson Correlation	1	0.800**	-0.880**
	P value		.000	.000
	N	50	50	50
	N	50	50	50

Another correlation between the duration of psoriasis, ACTH and cortisol was also elicited and it was found that study there was positive correlation between PASI and ACTH levels among cases, i.e. with increase in PASI severity there was increase in ACTH levels and vice versa. But the correlation was not statistically significant. There was negative correlation between PASI and Cortisol levels in cases, i.e. with increase in PASI severity there was decrease in Cortisol levels and vice versa. But the correlation was not statistically significant.

IV. DISCUSSION

This study is done to determine how the severity of psoriasis correlates with the dysregulation of hypothalamo pituitary adrenal axis by measuring serum ACTH and cortisol to determine the influence of daily stressors on the above mentioned levels in patients with psoriasis. In this study the mean ACTH was significantly higher whereas mean cortisol levels was significantly lower in cases as compared to controls and P value was found to be statistically significant which was found in concordance with a literature that [12,13] showed that the daily stressors are negatively associated with cortisol levels and ACTH can be increased in case of chronic stress

respectively. Another study[14] concluded that the psoriasis patients whose disease appears to be stress responsive, exhibit an altered HPA response to acute social stress thus implicating that such patients may perhaps be primed to flares of their psoriasis. In this study a significant positive correlation between PASI and ACTH levels and a significant negative correlation was seen between PASI and cortisol levels among psoriatic patients. A study showed that there is a negative association between cortisol levels and they showed an increase in the severity of psoriasis one month later[12]. In another study it is indicated that HPA dysfunction may be seen in psoriasis because the bedtime cortisol levels was correlated with psoriasis severity[15]. In this study there was a positive correlation seen between duration of the disease, PASI and ACTH and a negative correlation between duration of the disease, PASI and cortisol but the correlations were not statistically significant. A study stated that the patients who are persistently experiencing high levels of daily stressors are possibly more stress reactive and so they had relatively lower mean cortisol levels suggesting that the HPA axis is hypoactive in these individuals, which might directly influence the disease-related outcome[12]. In another literature a comprehensive review was done where the distribution and function of the central and peripheral HPA axis in various stress-related skin diseases and they also mentioned that some previous studies have shown altered expression of central and peripheral HPA axis hormones in chronic inflammatory skin diseases and skin tumours, and that the hyper-active lesional HPA axis hormones may negatively feedback to the central HPA axis and interact with some cytokines and neuropeptides thereby leading to deterioration of symptoms thus providing an evidence-based understanding of the expression of the central and peripheral HPA axis in common skin diseases and its association with disease activity[16]. But since this is a pilot study hence further study needs to be done.

V. CONCLUSION

Chronic plaque psoriasis is one of the most common non contagious dermatological condition seen, that is mostly associated with high levels of psychological distress and considerable life impact. This study also shows the influence of daily stressors on the disease outcome by affecting cortisol and ACTH levels at moments of high stress. Furthermore, patients with persistently high levels of stressors were characterized by a psychophysiological profile of lowered cortisol levels and increased ACTH levels and so they may be particularly vulnerable to the influence of stressors on their psoriasis severity. This have important implications for evaluation and surveillance of patients with psoriasis. Screening of HPA axis should become standard practice in patients with psoriasis for decreasing the severity of psoriasis by appropriate management. It is also recommended that for the treatment of psoriatic patients it is necessary to collaborate with the psychiatrists for counselling and treatment of psychiatric disorders if present, as it decreases the psoriasis severity and also is associated with a decreased need for systemic management of psoriasis.

Conflict of interest : nil

REFERENCES

- Okhandiar RP, Banerjee BN. Psoriasis in the tropics: An epidemiological survey. J Indian Med Assoc 1963;41:550-6.
- Dominguez PL, Han J, Li T, Ascherio A, Qureshi AA. Depression and the risk of psoriasis in US women. J Eur Acad Dermatol Venereol 2013;27:1163-1167. doi: 10.1111/j.1468-3083.2012.04703.x.
- Rampton DS. The influence of stress on the development and severity of immune-mediated diseases. J Rheumatol Suppl 2011; 88: 43-47. doi: 10.3899/jrheum.110904.
- Coplan JD, Mathew SJ, Smith EL, et al. (July 2001). "Effects of LY354740, a novel glutamatergic metabotropic agonist, on nonhuman primate hypothalamic-pituitary-adrenal axis and noradrenergic function". CNS Spectrums. 6 (7):607-12,617.
- Kim JE, Cho BK, Cho DH, Park HJ (July 2013). "Expression of hypothalamic-pituitary-adrenal axis in common skin diseases: evidence of its association with stress-related disease activity". Acta Dermatovenereologica. 93 (4):387-93. doi:10.2340/00015555-1557

6. Verhoeven EWM, Kraaimaat FW, van de Kerkhof PCM et al. Stress and psoriasis: a prospective study. *J Invest Dermatol* 2009; 129:2075-7.
7. Evers AWM, Lu Y, Duller P et al. Common burden of chronic skin diseases? Contributors to psychological distress in adults with psoriasis and atopic dermatitis. *Br J Dermatol* 2005; 152:1275-81.
8. Tagen M, Stiles L, Kalogeromitros D et al. Skin corticotropin-releasing hormone receptor expression in psoriasis. *J Invest Dermatol* 2007; 127:1789-91.
9. Arck PC, Slominski A, Theoharides TC. Neuroimmunology of stress: skin takes center stage. *J Invest Dermatol* 2006; 126:1697-704.
10. Paus R, Theoharides TC, Arck PC. Neuroimmunoendocrine circuitry of the 'brain-skin connection'. *Trends Immunol* 2006; 27:32-9.
11. Lindegard B et al. Diseases Associated with Psoriasis in a General Population of 159,200 Middle-Aged, Urban, Native Swedes. *Dermatologica* 1986; 172:298-304
12. F.Z.Zangeneh and A.Fazeli. The significance of stress hormones in psoriasis. *Acta Medica Iranica* 2008; 46(6):485-488.
13. Van de Kar, L.D., & Blair, M.L. (1999). Forebrain pathways mediating stress-induced hormone secretion. *Frontiers in Neuroendocrinology*, 20(1), 1-48
14. H.L.Richards et al . response of the hypothalamo - pituitary adrenal axis to psychological stress in patients with psoriasis. *British Journal of Dermatology* 2005 153, pp1114-1120.
15. A.R.Brunoni, I.S.Santos et al . Psoriasis severity and hypothalamic - pituitary - adrenal axis function : results from the CALIPSO study. *Brazilian journal of medical and biological research*. 2014. 47(12):1102-1106
16. Jung Eun Kim et al . Expression of Hypothalamic-Pituitary-Adrenal Axis in Common Skin Diseases: Evidence of its Association with Stress-related Disease Activity *Acta Derm Venereol* 2013; 93:387-393