

Peroxisome Proliferator Activated Receptor-Gamma Tissue Expression and Gene Polymorphism in Alopecia Areata in an Egyptian Sample

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Abstract

Background: The nuclear receptor PPAR- has several roles in controlling metabolic and cellular activities. Recent years have brought increased focus on the roles played by inflammation, lipid metabolism, and immune response regulation in the development of dermatological diseases. PPAR- has several functions in skin biology, and expanding our knowledge of these might help in the treatment of a variety of skin problems. This review aims to evaluate the role of PPAR- in skin diseases. We also discuss its significance in skin biology, from keratinocyte regulation to sebaceous gland function. The use of PPAR- agonists in the treatment of inflammatory skin disorders, viral infections, autoimmune diseases, and hair difficulties is something we want to raise awareness of. PPAR- is emerging as a complicated player in dermatology, and our findings demonstrate its profound impact on skin health and disease. This protein regulates inflammation, lipid metabolism, and the immune response, making it a promising therapeutic target. Psoriasis, atopic dermatitis, and scarring alopecia may all benefit from PPAR- agonists in the future as new therapy alternatives.

Keywords: PPAR- γ , Conditions affecting the skin, swelling; lipid metabolism, the immune response.

Introduction

Alopecia The hair follicle is preserved and hair loss is temporary in alopecia areata, an autoimmune condition. When hair loss is severe, it often follows a relapsing-remitting pattern that may be chronic (5).

Alopecia areata is a mysterious aetiology that has yet to be determined. Alopecia areata, it is generally believed, is a T-cell-mediated autoimmune illness that is more common in those with a certain genetic predisposition (8). It has been hypothesised that endogenous or external triggers initiate and numerous substances cooperate to sustain a T-cell driven autoimmune process. Based on what we know about its origins, hair loss is caused by a complicated cycle of inflammation that feeds on itself. The cytokines secreted by the keratinocytes trigger the endothelial cells to become activated, which then attract the T cells and macrophages, which in turn secrete even more cytokines. (2).

A breakdown of this immunological privilege zone due to an unidentified autoantigen has been postulated to underlie alopecia areata. Once IFN- and IL-2 are present, CD8+, CD4+, and other inflammatory cells may be induced to enter the immunological privilege zone. All of these changes may cause hair follicle irritation, which can lead to hair loss (5).

Upregulation of pro-inflammatory cytokines must play a crucial role in the pathogenesis of AA, just as it does in other autoimmune disorders. Overexpression of ICAM-1 and MHC molecules on hair follicle keratinocytes and dermal papilla cells, as well as abnormal

lesional expression of tumour necrosis factor-(, interferon-(, IL-2, and IL-1, are all features of the immune response in AA. Increased levels of IL-1, IL-6, IL-15, IL-17A, and IFN- were seen in the blood of individuals with AA. (3).

PPARs are a subfamily of ligand-activated nuclear receptors that control gene transcription in response to dietary fatty acids. Different genes code for and distribute the three PPAR isoforms: PPAR-, PPAR-, and PPAR-. PPAR- functions as an anti-inflammatory agent, aids in the differentiation and storage of fat in adipose tissue, and controls glucose metabolism via insulin sensitization (5).

In addition to its role in regulating inflammation, PPAR- has been connected to the function of sebaceous glands. The sebaceous glands' role in producing sebum is essential to the normal life cycle of hair follicles. Inflammatory responses often occur in pilo-sebaceous units, which are created alongside hair follicles (7). Many aspects of the inflammatory response are suppressed by PPAR- because it modulates cytokine expression. T cells, monocytes/macrophages, vascular smooth muscle cells, and endothelial cells all use different receptors and adhesion molecules (1). TNF-(, IL-1, IL-6, RANTES, and MCP-I are all inflammatory cytokines that are inhibited by PPAR- agonists in macrophages (4).

Hair matrix keratinocytes, hair shaft cortex, hair cuticle, inner root sheath, outer root sheath, dermal papilla cells, sebocytes, and the

connective tissue sheath all express PPAR- in human skin (5).

Aim of the Work

The aims of this work are to:

- Assess Alopecia areata patch skin PPAR-mRNA expression levels.
- Investigate the risk of alopecia areata development in a group of Egyptian patients by looking at the relationship between PPAR- gene polymorphism and alopecia areata.
- Check how PPAR- polymorphisms relate to PPAR- expression in alopecia areata hotspots.

Subjects and Methods

Type of study

Case Research with a "control" group.

Subjects

- This Ten participants will be selected from the outpatient clinic at Benha University's Department of Dermatology, Venereology, and Andrology. There will be two distinct sets of subjects:
- Five people who seem to be in good health will make up the "control group" in this study.
- Five alopecia areata patients will make up this study's patient group.
- Thoughts about ethics
- The Benha Faculty of Medicine's local ethics committee will provide their stamp of approval to the project. Each person who takes part in the research will first provide their informed permission.
- Criteria for exclusion:
- No participant will be included in the research if they have any of the following:
- Telogen effluvium, androgenetic alopecia, and cicatricial alopecia are only few of the other hair loss conditions.
- Significant medical illnesses occurring at the same time, such as cancer, diabetes, liver, kidney, or heart disease.
- Systemic or skin illness characterised by inflammation, infection, or autoimmunity.

Methods

The following applies to all patients:

Comprehensive research of the past

Results

Table (1) Socio-demographic characteristics of the sample.

Variable	No.	%
	N=10	
Age (mean ± SD)	37.50± 14.67	(22-70)
Sex:	Female	2
	male	8
BMI	24.60± 3.06	(21-30)

When it started, how long it lasted, how it was treated, what other skin conditions the patient had, and what medications they used all had a role.

Physical Checkup:

Full physical to rule any other systemic conditions.

A full skin inspection and a clinical evaluation of the alopecia areata lesion will be performed to find out:

Where the wounds are located and how big they are.

Amount of fixes.

The alopecia areata type (patchy alopecia, ophiasis, alopecia totalis, alopecia universalis).

The sickness has returned.

Disease severity as measured by the SALT scale

The following molecular biology tests will be performed on all participants:

Peroxisome proliferator-activated receptor (PPAR-) gene expression in skin samples was analysed by quantitative reverse transcription polymerase chain reaction (qRT-PCR). Tissue samples will be frozen at -80 degrees until further analysis is performed. The following procedures will be used to estimate gene expression levels in accordance with the manufacturer's guidelines:

RNA isolation from biological materials.

The process of making cDNA from mRNA.

PCR amplification in real time.

Gene analysis: 2- ct estimate based on (Lissac et al., 2005).

Procedure for estimating PPAR- gene polymorphism using RFLP-PCR, as per manufacturer's instructions:

DNA isolation from body fluids and tissue samples.

To amplify through polymerase chain reaction (PCR).

Polymorphism in the Pro12Ala gene: genotyping (rs1801282).

Modeling Statistics

The data will be entered into a statistics software programme for the social sciences, where appropriate statistical tests will be run on the compiled data (SPSS)

(mean \pm SD)

The average age of the participants was shown to be 37.5014.67 in Table 1, with almost 60% being males and a mean body mass index of 24.603.06.

Table (2) Case clinical summary tabulated (2).

Variable		No. N=5	%
Type of alopecia	patchy	4	80.0
	Totalis	1	20.0
Number of patches (mean \pm SD)		7.5 \pm 6.8 (1-15)	
Course	Progressive	4	80.0
	Stationary	1	20.0
	Scalp	2	40.0
Site of patches	Scalp, Beard	1	20.0
	Scalp, Eye brows	1	20.0
	Scalp, beard, eye brows, eye lashes	1	20.0
Nail affection	Yes	3	60.0
	No	2	40.0
Previous treatment response	Good	2	40.0
	Poor	3	60.0
Recurrence	Yes	3	60.0
	No	2	40.0
Family history	Yes	0	0.0
	No	5	100.0
Associated disease	Yes	1	20.0
	No	4	80.0

Eighty percent of patients reported experiencing patchy alopecia, with 40% of those areas located on the scalp (see Table 2). Sixty percent of patients had nail affection, only twenty percent of cases had an accompanying condition, and in every instance there was no alopecia in the family history.

Table (3) Gene polymorphism analysis: a comparison of cases and controls.

Gene polymorphism	cases N=5		controls N=5		Test sig.	of p-value
	No.	%	No.	%		
CC	3	60	2	40	0.53	0.76
CG	1	20	2	40		
GG	1	20	1	20		

There were no significant variations in gene polymorphism between patients and controls, as shown in Table 3 (P= 0.76).

Table (4) Tissue expression in both case and control patients is compared in Table 4.

Tissue expression	cases N=5		controls N=5		Test sig. t-test	of p-value
	Mean \pm SD		Mean \pm SD			
PPAR-g1	0.45 \pm 0.18		1 \pm 0.01		6.96	<0.001
PPAR-g2	0.56 \pm 0.15		1.02 \pm 0.03		6.74	0.002

According to Table (4), PPAR-g1 (P0.001) and PPAR-g2 (P=0.002) Tissue expression differed significantly between patients and controls.

Discussion

Alopecia areata is the most common kind of alopecia that does not leave scars, behind only male and female pattern baldness. Between 0.1 to 0.2% of the population has this condition (9). and less than 1% of Egypt's total population (10). Depending on the severity and pattern of hair loss, alopecia areata is divided into numerous subtypes, the most frequent of which is called "patchy alopecia" (10). Cell-mediated autoimmunity is the predominant theory for the aetiology of alopecia areata, in which autoreactive cytotoxic T lymphocytes target melanocytes in response to recognition of melanocyte-associated proteins such tyrosinase. T-helper 17 cells, natural killer (NK) cells, mast cells, plasmacytoid dendritic cells (pDCs), and regulatory T (Treg) cells have all been involved in addition to the "core actors," CD8+ T cells. T-reg cells are a kind of regulatory lymphocyte that plays an important role in maintaining self-tolerance and immunological balance (11).

Conclusions

The multifunctional Significant effects of Proliferator-Activated Receptor gamma (PPAR-) on skin health and disease have been shown. This protein regulates inflammation, lipid metabolism, and the immune response, making it a promising therapeutic target. Psoriasis, atopic dermatitis, and scarring alopecia may all benefit from PPAR- agonists in the future as new therapy alternatives.

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