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Estimation of Interferon Kappa Level in Psoriasis

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Abstract:

Introduction: Cases who suffer from psoriasis exhibit an elevated type I interferon signature. human interferon kappa (IFN-κ), often known as Interferon-κ, is a group of interferons belonging to the type I interferon family. Keratinocytes are predominantly responsible for its expression. For this investigation, we are examining whether IFN-κ has a role in the etiology of psoriasis.

Aim of the study: To determine whether IFN-κ, a type I interferon that is constitutively generated by keratinocytes, was implicated in the etiology of psoriasis.

Subjects and Methods: Twenty cases had psoriatic arthritis & twenty healthy participants who served as the control group. A comprehensive clinical examination was carried out, and measurements were taken of the levels of IFN-k in both the tissue and the serum.

Results: In our study, we observed that there was a significant elevation in human IFN-κ levels in serum and tissue for psoriasis patients compared to the control group, we also found that there were no significant correlations detected between human IFN-κ levels in serum and tissue for psoriasis patients & the degree of severity of the illness

Conclusion: Taking into consideration the results of our investigation, it can be speculated that INF-k can contribute to the etiology of psoriasis.

Keywords: Psoriasis; Interferon-kappa; Psoriasis Area; Severity Index.

1. Introduction

Although psoriasis is a problem that affects both children and adults all over the world, the prevalence of the condition differs from population to population. The prevalence of psoriasis was found to range from 0.5 to 11.4% in adults and from 0 to 1.4% in children, according to a comprehensive review that was conducted all over the world. Psoriasis is more likely to be found in those who live further away

from the equator by a significant margin. [1]. Furthermore, psoriasis can manifest itself at any age; nevertheless, it is of a lower prevalence in children compared to adults. The start of psoriasis is most common among the ages of 30 and 39, among the ages of 50 and 69 years [2].

One of the most frequent skin conditions is psoriasis which is characterized by chronic inflammation and can express itself in several different clinical ways. One of the most prevalent subtypes of psoriasis, chronic plaque psoriasis, is distinguished by erythematous plaques that are clearly defined and have a coarse scale that covers them at the surface. Additional major subtypes of psoriasis include pustular psoriasis, which can manifest as a subacute, acute, otherwise chronic pustular eruption; guttate psoriasis, which is distinguished by the acute onset of numerous small, inflammatory plaques; and erythrodermic psoriasis, which is characterized by cutaneous erythema and scale that affects the majority otherwise all of the body's surface area. In terms of psoriasis, there is no discernible gender preference [3].

It has been suggested that there are several risk factors for psoriasis. Genetic predisposition is thought to be a significant influence, while behavioral and environmental factors may also play a role in the progress of the condition. Psoriasis patients are more likely to engage in dangerous behaviors such as smoking than the general population, being overweight, and drinking alcohol. In addition, some medications and infections have been recognized as potential variables that might either initiate or exacerbate psoriasis [4].

There is one of the members of the type I Interferon family is interferon-kappa, often known as IFN-κ. It is composed of 207 amino acids, which includes a signal peptide that is 27 amino acids long and a series of cysteine that is retained in type I interferon, and it shares around 30% of its homology with other members of the family [5]. A restricted number of cell sources, involving keratinocytes, are capable of expressing interferon-gamma (IFN-κ) [6]. Through its utilization of receptors of the IFNRA1/IFNRA2 family, In the same way that other members of the family do, it activates the same set of genes. Recently, it has been discovered that interferon-gamma (IFN-κ) is linked to autoimmune diseases like cutaneous lupus erythematous. An increase in its expression has been observed in keratinocytes derived from lupus erythematous skin disease, and its function

has been hypothesized to be the promotion of inflammatory reactions [7].

A member of the type I interferon family, IFN-κ is expressed constitutively by keratinocytes to a significant degree. In this research, we investigated whether or not IFN-κ has a significant role in the progress of psoriasis.

2. Subjects & Methods

2.1.Study design

Conducting this case-control investigation at the Dermatology outpatient clinic, El-Kasr Al-Ainy, Faculty of Medicine, Cairo University, with the Dermatology Research Ethical Committee's (Derma REC) approval. Written consent was obtained from all individuals who participated.

2.2.Subjects

20 cases with psoriasis participated in the research. and 20 age, sex and during the period spanning from October 2019 to March 2020, their skin type was identical to that of healthy controls.

Inclusion Criteria

Patients meeting the inclusion criteria were Egyptian patients with psoriasis from both genders and were 18 years old and above and with no systemic therapy for a minimum of one month previous to the introduction of this research.

Exclusion Criteria

However, we excluded pregnant patients, lactating females and people who have other autoimmune illnesses that affect the skin or the body as a whole, such as SLE.

2.3.Methods

Data Collection

Personal history (including name, sex, age, occupation, skin type, marital status, residence, and smoking), present history (including course, onset, period of illness, any medications, and precipitating factors), family history of psoriasis, and history (including associated systemic otherwise dermatological illnesses) were all taken into consideration during the process of taking a detailed history from all of the cases and the control group. Each case was evaluated to ascertain the degree of psoriasis

(in percentage terms) and the severity of the condition.

Skin biopsy and serum samples were taken from every participant. Rule nine was utilized to assess the extent of the illness [8].

To evaluate the severity of the disease, the Severity Index and Psoriasis Area were utilized. This index is the instrument that is utilized the most frequently in clinical trials to evaluate the severity of the illness in cases who have psoriasis. Erythema, scaling, and thickness of lesions are all measured by the PASI, which is then weighted based on the region of involvement. Four places are evaluated: the head, the trunk, and the upper and lower extremities. The PASI scale is a scale that ranges from 0 to 72, which is calculated by multiplying the score for erythema by the sum of the scores for scaling and thickness. The extent of involvement is classified as follows: 0 (0%), 1 (1–9%), 2 (10–29%), 3 (30–49%), 4 (50–69%), 5 (70–89%), or 6 (90–100%). The scores that are used for thickness, scaling, and erythema are every rated on a scale ranging from 0 to 4, with 0 being the least severe and most severe [9].

Quantitation of serum and tissue level of Human Interferon Kappa

The serum level of Human Interferon Kappa (IFN-κ), was measured using an ELISA kit provided by Bioassay Technology Laboratory (Shanghai, China). As regards the skin biopsy, each biopsy was weighed and homogenized in 400ul of PBS (pH 7.4). Then centrifugation was done at 5000xg and following the separation of the supernatant, the same kit was utilized to determine the human IFN-κ. This kit employs an ELISA that is based on the Biotin double antibody sandwich technique.

2.4.Statistical Analysis

The statistical software for social science (SPSS 17.0) (Windows 8.1) was utilized to carry out the analysis of the data. In the case of qualitative data, descriptive analysis was carried out using numerical indicators and percentages. The arithmetic means were computed as a measurement of the central tendency, and the standard deviation was computed as a measure of the dispersion for the quantitative parametric data. To compare the measures of two independent groups, an independent student t-test was utilized. When comparing more than two independent groups, a one-way analysis of variance (ANOVA) test was

utilized, and Bonferroni post-hoc was utilized to test for significance at a p-value of less than 0.05. For comparisons between more than two independent groups, the Kruskal-Wallis test was utilized. To ascertain whether or not there was a significant difference amongst more than two independent groups, the Mann-Whitney test was utilized. Using a two-tailed Pearson correlation test to determine the significance of the relationship among the various groups, a bivariate Pearson correlation test was performed. To ascertain the degree of significance of the situation, a p-value of less than 0.05 was used.

3. Results

This instance control research was conducted on 20 psoriatic cases and twenty healthy volunteers who acted as controls. There was observed no significant variance amongst both groups concerning age (p =0.948), and sex (p =0.617). Regarding laboratory biomarkers, there was a statistically significant elevation in human IFN-κ values in serum for psoriasis cases compared to the control group. We observed a statistically significant elevation in IFN-κ values in tissue for Psoriasis patients compared to the control group (**Table 1**).

Table 1: Age, gender and laboratory biomarkers distribution among patient groups.

Parameters		**Psoriasis (N=20)**	**Control (N=20)**	**p-value**
Age (years)		40.85 ±2.73	40.71 ±2.57	0.948
Sex	**Female**	5 (25%)	6 (30%)	0.617
	Male	15 (75%)	14 (70%)	
Human IFN-κ	Serum (ng/L)	72.81 ±11.45	41.77 ±2.48	0.010*
	Tissue (ng/gm)	14439.46 ±4504.19	4056.23 ±573.45	0.024*

*significant.

Regarding Human IFN-κ levels in serum for psoriasis cases with clinical data, there was no statistically significant relation of human IFN-κ levels in serum for psoriasis cases with family history. There was a statistically significant relation of human IFN-κ levels in serum for Psoriasis cases with hypertension, with mild and moderate cases according to the PASI index. There was no statistically significant relation of

human IFN-κ levels in serum for Psoriasis patients with diabetes mellitus, and with extent of disease (**Table 2**).

Regarding the relation of human IFN-κ levels in tissue for psoriasis patients with clinical data, there was no statistically significant relation of human IFN-κ levels in tissue for psoriasis patients with family history, with the extent of disease and with hypertension. There was a statistically significant relation of human IFN-κ levels in tissue for psoriasis patients with Diabetes mellitus and with moderate cases according to the PASI index (**Table 2 & Figure 1**).

Table 2: Relation of Human IFN-κ levels in serum for Psoriasis patients with clinical data.

Variables		Serum	*P*-value	Tissue	*P*-value
Family History	No (16 (80%))	78.51 ±12.85	0.347	16206.23 ±5565.97	0.404
	Yes (4 (20%))	50 ±25.22		7372.368 ±1426.27	
Hypertension	No (17 (85%))	81.27 ±12.38	0.001*	15559.29 ±5268.20	0.429
	Yes (3 (15%))	24.87 ±3.01		8093.77 ±1740.00	
Diabetes mellitus	No (18 (90%))	72.53 ±12.10	0.824	15389.59 ±4965.87	0.05*
	Yes (2 (10%))	75.36 ±50.04		5888.27 ±680.13	
Extent	<20%	92.42 ±64.84	0.167	5692.88 ±1674.26	0.067
	>20%	66.27 ±46.68		17354.99 ±22659.16	
PASI	Mild	145.02 ±19.61	0.011[a], 0.024[b], 0.020[c], 0.924[d], 0.671[e], 0.05[f]	4389.19 ±818.93	0.071[a], 0.359[b], 0.05[c], 0.444[d], 0.99[e], 0.198[f]
	Moderate	65.36 ±12.87		16900.98 ±6333.80	
	Severe	69.13 ±33.83		8936.90 ±2017.18	
	Very Severe	43.71 ±0.01		16586.41 ±1.11	

*significant.

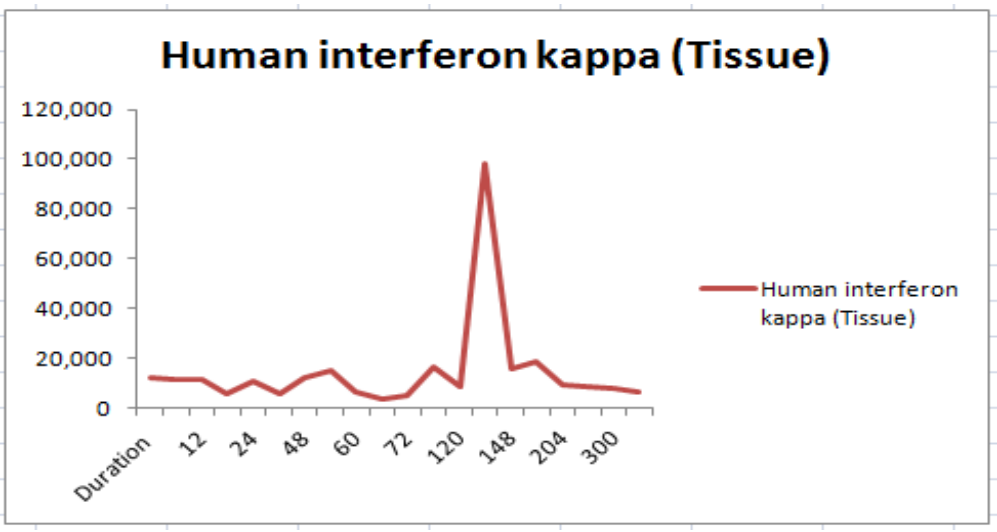

Figure 1: Relation of Mean levels of Human IFN-κ in tissue and patients' disease duration.

Regarding the correlation between Human IFN-κ in serum and patients' data, there were no statistically significant correlations detected between human IFN-κ in serum and patients' age, patients' gender, severity of the disease, extent of the illness and duration of the illness. Regarding the correlation between Human IFN-κ in tissue and patients' data, there were no statistically significant correlations detected between human IFN-κ in tissue and patients' age, patients' sex, severity of the disease, degree of the illness and the duration of the illness (**Table 4**).

Table 4: Correlation between Human IFN-κ in serum and tissue and patients' data.

Variables		r	Sig.	90% CI
Age	Tissue	-0.2309	0.3273	-0.6110 to 0.2357
	Serum	-0.05922	0.8041	-0.4889 to 0.3936
Sex	Tissue	0.2801	0.2317	-0.1855 to 0.6429
	Serum	-0.01395	0.9534	-0.4537 to 0.4312
PASI	Tissue	-0.02604	0.9132	-0.4632 to 0.4213
	Serum	-0.2168	0.3585	-0.6016 to 0.2496
Extent of the disease	Tissue	-0.01899	0.9367	-0.4577 to 0.4271
	Serum	-0.1458	0.5396	-0.5527 to 0.3172
Duration of the disease	Tissue	0.04145	0.8622	-0.4086 to 0.4753
	Serum	-0.1294	0.5867	-0.5409 to 0.3322

4. Discussion

About 2% of the population is affected with psoriasis, which is a skin disorder that is often found, persistent, immune-mediated, inflammatory, and polygenic. Although psoriasis is one of the dermatological disorders that has received the greatest focus of attention shown by researchers, the pathophysiology of the illness is not yet fully understood. [10]. Understanding of the pathophysiology of psoriasis has radically altered within the past ten years. While it was initially seen as an epidermal disorder, the interaction amongst KCs, microvascular endothelium, DCs, neutrophils, and various T cell subsets, which results in the generation of a cycle of inflammation that is self-sustaining centered on the TNF/IL-23/IL-17 axis, is currently

recognized to be a complicated disease that presents with autoimmune and autoinflammatory components [11].

Cytokines of the type I interferon are generally created in response to infections caused by viruses and play an essential part in the defense mechanisms of the host [12]. They accomplish this by inducing the production of anti-viral genes, which prevent replication of the virus within host cells and eliminate cells that have been infected. In addition to this, they induce the development of dendritic cells and have a part to play in the process of activating the adaptive immune system. Within the type I interferon family, there are currently thirteen subtypes of Interferon -α, namely Interferon -β, -κ, -ε, -σ, -ω, and -δ. These subtypes differ in their origins, receptor affinities, and biological activity, as stated in reference [13]. Psoriasis patients have been found to have skin lesions that exhibit elevated levels of type I interferon-inducible signals, according to the findings of certain researchers [14]. In addition, treatment with interferons can either cause psoriasis to develop in those who do not already have it or make psoriasis worse [15].

While there is significant evidence of type I Interferon signaling in psoriasis, it is unclear where type I Interferon cytokines originate from in the skin of psoriatic lesions. Previous research that looked for the origins of type I IFNs in psoriasis skin only found weak Interferon -α mRNA by the use of in situ hybridization; no Interferon -α protein or Interferon -β mRNA/protein was found [16].

In our study we observed that there is a significant elevation in Human interferon kappa levels in serum and tissue for Psoriasis cases compared to the control group, suggesting that Human interferon kappa is involved in psoriasis etiology. Li et al. (2019) found that the epidermis of psoriasis lesions exhibited a large rise in IFN-κ protein, which is similarly raised in the peripheral blood serum of a subset of psoriasis cases. These findings are consistent with our findings [17]. According to Yao et al. (2008) findings on the presence of protein expression of type I IFNs-prompted ISG15 and STAT1, they discovered that Interferon -κ in psoriatic lesions was situated in the epidermis, in the suprabasal layers of the KC [18]. IFN-κ mRNA was shown to be elevated in psoriasis in the tissue of the skin lesions, which agrees with our findings [18].

IFN-κ of epidermal keratinocytes may be the cause of elevated type I

Interferon -prompted signatures in psoriasis [17]. Nevertheless, Zheng et al. (2016) demonstrated Interferon -β positive staining in recently frozen slices of biopsies taken from the skin from lesions associated with psoriasis, though they did not state the number of participants they examined [19]. In our study, we found that there is no significant correlations were detected between Human interferon kappa levels in serum and tissue for Psoriasis patients and the severity of the disease, although there is a statistically significant relation between Human interferon kappa levels in serum and tissue for Psoriasis patients with moderate cases according to PASI index, this findings was concordant with Li and colleagues which revealed that There was insufficient strength for the correlation study amongst IFN-κ and the severity of psoriasis because the size of the sample taken from human individuals was too small [17].

We also observe in our study that there is no correlation between IFN-k levels in serum and tissue for Psoriasis patients and the duration and extent of the disease, these findings may be explained by a small number of patients. As of now, psoriasis cases are not being treated with antagonistic IFN-k methods. Our research provides a fresh perspective on whether IFN-k is a promising target for the therapy of psoriasis.

5. Conclusion

Based on the findings of our research, it can be speculated that INF-k can contribute to the etiology of psoriasis. Studies on a Large scale are needed to study the relation of the psoriasis with severity and duration of the disease.

Ethical approval and consent to participate:

Before beginning the research, the IRB of the Fayoum University Faculty of Medicine granted research approval. Before participation, every patient provided written, informed consent. The study's purpose and objectives were made clear to the study's subjects by the researcher.

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Conflicts of Interest: All authors declare they have no conflicts of interest.

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