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Brief Report

Single nucleotide polymorphism of IGF-1R (rs2229765) in acne and/or its severity

Parul Kamboj[1], Amanjot Kaur Arora[1], Ramandeep Kaur[2], Sohini Banerjee[3], Garima Dhawan[3], Navya Gupta[2], Dipankar De[1]

Departments of [1]Dermatology, Venereology and Leprology, [2]Biochemistry, [3]Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

ABSTRACT

Acne vulgaris is a common inflammatory disease of pilosebaceous glands diagnosed by dermatologists in teenagers. During puberty, a peak in the levels of hormones (growth factors and its terminal mediator insulin-like growth factor-1 (IGF-1)) is observed that plays a vital role in acne pathogenesis. IGF-1 and its polymorphism are known to positively correlate with acne and/or its severity. However, the role of polymorphism of IGF-1 receptor (IGF-1R) in acne and/or its severity has not yet been elucidated. Therefore, the study aimed to assess the association of IGF-1R polymorphism with the occurrence of acne and its severity. IGF-1R polymorphism was analyzed in acne patients (n = 100) and controls (n = 100) by the restriction fragment length polymorphism. IGF-1R polymorphism was found to be evenly distributed among the controls and patients. Although IGF-1 polymorphism positively correlates with acne and/or its severity, the polymorphism of its receptor IGF-1R was not significantly associated with acne. Furthermore, no significant association was observed between IGF-1R polymorphism and IGF-1R expression at messenger ribonucleic acid (mRNA) and protein level. A similar study with a larger study populations may be planned to validate or refute the observed findings.

Keywords: Acne, genotype, IGF-1 receptor (IGF-1R), Insulin like growth factor -1 (IGF-1), single nucleotide polymorphism

INTRODUCTION

Acne vulgaris is a common inflammatory skin disease among adolescents.[1] It is associated with elevated insulin-like growth factor-1 (IGF-1) level that exerts a wide range of biological effects[1] via activation of its tyrosine kinase receptor (IGF-1R).[2] IGF-1 level and its polymorphism positively correlate with acne and/or its severity.[3] Studies in various carcinomas and autoimmune diseases have shown an important role of single nucleotide polymorphism (SNP) of IGF-1R (rs2229765).[4] The role of IGF-1 in acne pathogenesis has been suggested by various studies, but the role of IGF-1R polymorphism in acne and/or its severity is still not established. In this study, we tried to assess whether an association exists between IGF-1R polymorphism and occurrence of acne or its severity.[4]

MATERIAL AND METHODS

The case–control study was conducted after approval from the Ethics Committee (Ref no. NK/2606/Study/116 dated 10.03.2016). Written informed consent was obtained from all the recruited patients and controls. Clinically confirmed patients with acne vulgaris (n = 100) were recruited after proper examination by an experienced dermatologist in daylight. An equal number of age and gender matched controls (n = 100), patients attending our outpatient department for another disease and not having acne, were recruited.

To study the polymorphism of IGF-1R, 2 ml venous blood sample was collected under aseptic precautions from all study participants in ethylenediaminetetraacetic acid (EDTA) vial for deoxyribonucleic acid (DNA) isolation using NucleoSpin® Blood DNA kits (Macherey-Nagel, Germany, REF 740951.250). The isolated DNA was amplified and digested overnight at 37°C by 1U Mn1I restriction enzyme (Thermo Scientific; Cat no-ER1071). Polyacrylamide gel electrophoresis (15%) was used to visualize the digested products on the Gel DOC System (Alpha Imager, USA) [Supplementary Figure 1].

***Corresponding author:** Dr. Dipankar De, Department of Dermatology, Venereology and Leprology, Postgraduate Institute of Medical Education and Research, Sector 12, Chandigarh-160012, India. dr_dipankar_de@yahoo.in

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For expression studies, two biopsies (2 mm) from any two facial acne lesions of acne patients (n = 100) were taken under local anesthesia. One of the biopsy samples was used to study the expression of IGF-1R at gene level and the other one was used to study the expression of IGF-1R at protein level. From healthy controls (n = 20), one facial skin biopsy was taken under local anesthesia to study the gene expression of IGF-1R. For gene expression studies, ribonucleic acid (RNA) was isolated by TRIzol (Thermo Invitrogen, Cat no. 15596026) and converted to complementary DNA (cDNA) (Verso cDNA synthesis kit by Thermo Scientific; Cat no. #AB-1453/A) followed by Real Time-Plymerase chain reaction (RT-PCR) (Thermo Scientific; Cat no–F-416X) using SYBR green. Protein expression was analyzed by immunohistochemistry using a primary antibody against IGF-1R in formalin-fixed sample (Biorad, Cat no. MCA2344) [Supplementary Figure 2].

Statistical tests were carried out using SPSS version 16.

RESULTS

The mean age of controls and cases were 24.24 ± 4.8 and 23.09 ± 5.8 years, respectively. The genotypic distribution of IGF-1R polymorphism in controls and cases was nearly the same, that is, 16.7% of controls and 16.3 % of cases exhibited homozygous AA genotype; 52.2% of controls and 57% of cases had homozygous GG genotype; and 26.7% and 31.1% controls and cases had heterozygous GA genotype respectively [Supplementary Figure 3]. The association between the genotypes and acne or its severity was analyzed using the Chi-square test. It was observed that none of the genotypes were associated with acne (likelihood ratio 0.476, p = 0.788) and/or its severity (p = 0.965). The mRNA expression of IGF-1R was found to be significantly decreased (p = 0.0418) in cases (0.46 ± 0.82, 95% CI 0.25–0.67) as compared to controls (1.52 ± 2.11, 95% CI 0.53 – 2.57) [Figure 1]. At the protein level, 66.6% of the acne cases showed IGF-1R positivity of grade 2+ and 3+. However, the effect of polymorphism on the expression of IGF-1R at the mRNA level (spearman correlation, r = 0.135, p = 0.25) or protein level (spearman correlation, r = 0.17, p = 0.11) in acne patients was not found to be significantly correlated.

DISCUSSION

IGF-1 interaction with IGF-1R initiates a downstream cascade that leads to the regulation of genes/factors required in acne pathogenesis.[1,2] All three genotypes (homozygous AA and GG and heterozygous AG) were equally distributed between controls and cases, suggesting that IGF-1R polymorphism is not associated with acne or its severity. However, discrepancy observed at mRNA and protein levels suggests that transcript levels alone might not be sufficient to determine the protein expression.[5] Furthermore, IGF-1R expression at mRNA and protein level was not associated with its polymorphism. Overall, it was inferred that IGF-1R polymorphism was not associated with acne and/or its severity, and IGF-1R genotype did not have an effect on the expression of IGF-1R at mRNA or tissue level. A formal sample size calculation was not done because of absence of data to do so. Sample size was limited by funds available. Results of this pilot study do not project a signal toward an association between IGF-1R polymorphism and acne or its severity. A similar study may be planned in a larger study population to validate or refute the observed findings.

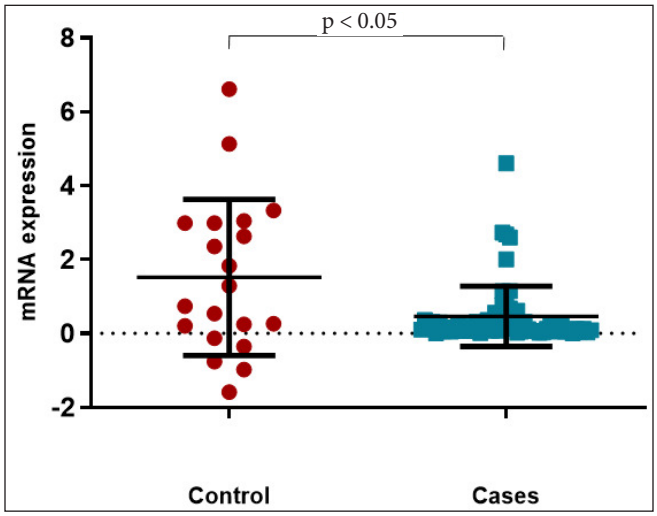

Figure 1: IGF-1R expression: Dot plot representing mRNA expression of IGF-1R in controls and cases. (Each red dot and blue box respectively represents individual healthy controls and acne patients recruited in the study.)

CONCLUSION

IGF-1 and its polymorphism is known to play an important role in pathogenesis of acne and/or determines its severity. Binding of IGF-1 to its receptor (IGF-1R) initiates cascade of events that regulate genes/factors affecting acne pathogenesis. In our study, we observed that single nucleotide polymorphism (SNP) of IGF-1R was evenly distributed in controls and cases and was not associated with acne or its severity. Furthermore, no effect of IGF-1R polymorphism was observed at genetic and protein level. These findings suggest that IGF-1R polymorphism does not play any significant role in acne and/or its severity.

Authors' contributions

PK: Data collection, analysis and interpretation, manuscript drafting; AKA: Recruitment of patients and healthy controls;

NG: Sample collection; RK, SB and GD: Data collection; DD: Conceptualization, funding acquisition, patient recruitment, supervision, manuscript editing.

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Ethical approval

The research/study approved by the Review Board at Postgraduate Institute of Medical Education and Research, number NK/2606/Study/116, dated 10th March 2016.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Deplewski D, Rosenfield RL. Growth hormone and insulin-like growth factors have different effects on sebaceous cell growth and differentiation. Endocrinology 1999;140:4089-94.
2. De Meyts P, Whittaker J. Structural biology of insulin and IGF1 receptors: Implications for drug design. Nat Rev Drug Discov 2002;1:769-83.
3. Rahaman SMA, De D, Handa S, Pal A, Sachdeva N, Ghosh T, *et al*. Association of insulin-like growth factor (IGF)-1 gene polymorphisms with plasma levels of IGF-1 and acne severity. J Am Acad Dermatol 2016;75:768-773.
4. Liu TC, Hsieh MJ, Liu MC, Chiang WL, Tsao TC, Yang SF. The clinical significance of the insulin-like growth factor-1 receptor polymorphism in non-small-cell lung cancer with epidermal growth factor receptor mutation. Int J Mol Sci 2016;17:763.
5. Liu Y, Beyer A, Aebersold R. On the dependency of cellular protein levels on mRNA abundance. Cell 2016;165:535-50.

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