Short Communication

Lack of Association between the SNP rs2010963 G>C of VEGF and Psoriasis: A Meta-Analysis Study

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Abstract

Background: Many studies have investigated the possible associations between the VEGF rs2010963 single nucleotide polymorphisms (SNPs) and psoriasis risk in various populations. However, results from different studies have been inconsistent.

Objectives: We perform a systematic review on data from published case-control studies to derive a more precise estimate of the association between the VEGF rs2010963 polymorphisms and psoriasis risk.

Methods: The PubMed, Medline, China National Knowledge Infrastructure (CNKI) database were searched to identify relevant published studies.

Results: Five studies with 1578 cases and 1738 controls were included for meta-analysis. The overall psoriasis risk was not associated with the CC variant genotype in Asian (for CC vs GC+GG OR 1.17, 95% CI: 0.96-1.42; \(P_{\text{heterogeneity}} 0.10\)) or in Caucasian subgroup (for CC vs GC+GG OR 1.15, 95% CI: 0.93-1.42; \(P_{\text{heterogeneity}} 0.08\)) (\(P>0.05\)). Meanwhile, the C allele did not significantly increase the risk of psoriasis compared with G allele.

Conclusion: Our findings suggest that VEGF rs2010963 G>C polymorphisms may not influence psoriasis susceptibility.

ABBREVIATIONS

VEGF: Vascular Endothelial Growth Factor; SNPs: Single Nucleotide Polymorphisms; OR: Odds Ratio; CI: Confidence Interval; HWE: Hardy-Weinberg Equilibrium; KC: Keratinocyte; PBMCs: Peripheral Blood Mononuclear Cells

INTRODUCTION

Over the last few years, several studies have shown that VEGF expression was increased in psoriatic skin lesions, and that serum levels of VEGF were significantly increased in patients with psoriasis [1,2]. One study found the Single Nucleotide Polymorphisms (SNPs) at positions rs2010963 had an impact on VEGF expression and psoriasis risk [3], whereas another study failed to find any such association [4]. This inconsistency may be due to inadequate statistical power, racial and ethnic differences, publication bias, small sample size or other limitations. We performed a meta-analysis of the published case-control precise estimate of the association between VEGF rs2010963 polymorphisms and psoriasis risk.

MATERIALS AND METHODS

The PubMed, Medline, China National Knowledge Infrastructure (CNKI) database were searched to identify case-control studies published from 1998 to May 31, 2013. Search terms used were “VEGF”, “polymorphism”, “SNPs”, “rs2010963(or +405)” and “psoriasis”. No language restrictions were imposed. References of retrieved articles and related articles also were screened. Inclusion criteria were: (1) evaluation of the VEGF rs2010963 G>C polymorphism and psoriasis risk, (2) case-control studies, (3) enough published data for estimating an odds ratio (OR). Exclusion criteria were: (1) no control population, (2) duplicate publication, (3) the number of genotypes could not be ascertained, (4) the control population deviated from Hardy-Weinberg Equilibrium (HWE).

Two investigators independently extracted the data from all eligible publications. The investigators reached a consensus on all the items entered into the database.

A \(\chi^2\)-test was used to determine if the observed frequencies of genotypes in both cases and controls conformed to HWE.
strength of the association between the VEGF rs 2010963 G>C polymorphisms and psoriasis risk was measured by OR with 95% CIs. Heterogeneity assumption between-study was checked by the χ²-based Q test. If the P value was greater than 0.05 for the Q-test, indicating a lack of heterogeneity among studies, the summary OR estimate of each study was calculated by the fixed-effects model [5]. Otherwise, the random-effects model was used [6]. All the statistical tests were performed with Review Manager (RevMan 5.0.17).

RESULTS AND DISCUSSION

The literature search identified 9 potentially relevant publications. According to inclusion criteria and exclusion criteria, 4 studies were excluded. They were studies on VEGF receptor and other polymorphisms (2 publications), studies on responsiveness to efalizumab and retinoid (2 publications). Finally, a total of 5 studies (2 Caucasian, 3 Asian) were retrieved based on the search criteria for psoriasis susceptibility related to the VEGF rs 2010963 G>C polymorphisms [3,4,7-13]. There were a total of 1578 cases and 1738 controls included. All studies indicated that the distribution of genotypes in the controls was consistent with HWE.

Table 1 lists the main results of this meta-analysis. Overall, individuals carrying the CC genotype had no significant increase in psoriasis risk compared to individuals with the GC+ GG genotype in the Asian subgroup (OR 1.17, 95% CI 0.93-1.42, \( P_{heterogeneity} 0.10, P>0.05 \)) and this association was observed in the Caucasian subgroup too (OR 1.15, 95% CI 0.93-1.40, \( P_{heterogeneity} 0.08, P>0.05 \)). However, whether in Asians or in Caucasian, we found a nonsignificant effect for GC genotype on psoriasis risk (in Asians, OR 0.90, 95% CI 0.79-1.04, \( P_{heterogeneity} 0.61, P>0.05 \); in Caucasian, OR 0.89, 95% CI 0.77-1.04, \( P_{heterogeneity} 0.34, P>0.05 \)). Meanwhile, our meta-analyse indicated that the C allele did not significantly increase the risk of psoriasis (in Asian, OR 0.96, 95% CI 0.70-1.20, \( P_{heterogeneity} 0.02, P>0.05 \); in Caucasian, OR 0.87, 95% CI 0.64-1.19, \( P_{heterogeneity} 0.02, P>0.05 \)).

Many studies have investigated the possible associations between VEGF rs 2010963 G>C polymorphisms and psoriasis risk in various populations [4]. However, results from different studies have been inconsistent. To better understand whether the VEGF rs 2010963 G>C SNPs contribute to psoriasis susceptibility; we performed a meta-analysis. To the best of our knowledge, this is the first meta-analysis designed to investigate the association.

Our results indicated that the VEGF rs 2010963 CC genotype was not potential risk factors for psoriasis, especially, in Asian subgroup. This finding is converse with Young et al. This discrepancy could have occurred owing to the stratified difference in choiced psoriasis. As some of the studies did not provide the information on disease severity, we cannot further stratify the cases in our study.

We also found the CG genotype and C allele were not significantly associated with psoriasis susceptibility as a whole and Asians subgroup. In summary, our study demonstrated that the VEGF rs 2010963 G>C SNPs is not significantly associated with psoriasis susceptibility. The rs 2010963 G>C SNPs has been reported to be MZF1-binding site and the occurrence of a C allele should decrease VEGF gene transcription and protein production [15]. It is possible that our findings are attributable to chance because of the relatively small numbers in the group. It is now widely accepted that differences in ethnic distributions between case and control groups in population studies may be a source of potential bias, which might confound the results of a pooling analysis. Considering the limited studies and total population numbers of Caucasian patients included in the meta-analysis, our results should be interpreted with caution.

It is difficult to tell whether the polymorphisms themselves or linked genes are responsible for our results. The present analysis was limited to one SNP’s with in the VEGF gene, did not consider the haplotype association. Therefore, functional studies and larger-scale studies are needed to further confirm these findings. More sophisticated gene–gene and gene–environment interactions should also be considered in future analysis, which should lead to further understanding of the association between the VEGF promoter polymorphisms and psoriasis risk.

CONCLUSION

Our findings suggest that VEGF rs 2010963 G>C polymorphisms may do not influence psoriasis susceptibility.

REFERENCES


