

Association between acne and smoking: systematic review and meta-analysis of observational studies

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To the Editor: Acne is a chronic inflammatory disease commonly found in areas with abundant sebaceous glands. It is more likely to produce permanent atrophic or hypertrophic scars that can cause serious psychosocial consequences and reduce the quality of life of the patients.^[1] Acne fades in most people after puberty and can continue into middle age in a small percentage of people. The occurrence of acne is caused by endogenous and exogenous factors, and many environmental factors can induce acne, such as occupational exposures, birth control pills, diet, certain cosmetics, and the menstrual cycle of the women.

The clinical report on the relationship between smoking and acne is currently controversial. Some previous studies have shown that smoking can aggravate acne, and other studies have not confirmed this association and have even shown protective effects. To our knowledge, three related systematic reviews have been published. Mannocci *et al*^[2] conducted a systematic review and meta-analysis on the relationship between acne and smoking in 2010. A total of six cross-sectional studies were included. A significant correlation between smoking and the occurrence of acne was not observed. One similar study was conducted in 2015 and found that smokers, especially males, have a higher risk to develop acne.^[3] However, only three case-control studies were included in this study, and the conclusions are not reliable. Bhutani *et al*^[4] also conducted a meta-analysis and found unconvincing evidence that smoking can increase or decrease the risk of acne. To provide further evidence, this study explores the correlation between smoking and acne based on the different methodological characteristics of the studies.

The meta-analysis was completed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Eligible studies were identified by two authors independently through a

comprehensive search of the following databases: the Cochrane Library (up to June 2019), PubMed, Ovid, and EMBASE. The search terms and text terms used were: (acne OR acne vulgaris OR common acne) AND (smoking OR cigarette OR tobacco OR nicotine). Language limitation was not imposed. We included studies that met the following criteria: (1) observational studies that reported the relationship between acne and smoking; and (2) independent estimates of the association from the original studies or sufficient data to calculate them. Non-original articles (eg, case reports, letters to editors), reviews, and duplicated publications were excluded. (3) Special types of acne such as acne inversa, acne medicamentosa, and acne cosmetica were excluded. The exposure of interest must be a history of cigarette smoking. The study classified smoking status as smoking and non-smoking. Smoking refers to current smokers and non-smokers included people who had never smoked and people who had quit smoking. This meta-analysis has been registered, and the protocol can be accessed at PROSPERO (CRD42019138518). Two authors independently extracted the data from all included studies and performed a methodological quality assessment. Disagreements were resolved through consultation. If they failed to reach a consistent conclusion, differences were resolved by the third author. We used the Newcastle-Ottawa Scale (NOS) to evaluate the methodological quality of the included case-control studies. In addition, the quality assessment of the included cross-sectional studies was assessed by the Agency for Healthcare Research and Quality (AHRQ). The analyses were performed using Review Manager v.5.33 (Nordic Cochrane Centre, Cochrane Collaboration).

Twenty studies met the inclusion criteria; after excluding three articles with similar data, 17 studies were eventually included. The flow diagram for the study selection is shown

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in Supplementary Figure 1, <http://links.lww.com/CM9/A409>. This study included seven case-control and ten cross-sectional studies. The study population was mainly distributed in Europe and Asia. The subjects were included in small and large sample studies ($n=98$ cases to $n=10,521$). The subjects were not limited by gender or age, and patients with both adolescent acne (aged 12–25 years) and adult acne (aged >25 years) were included. For the quality of the included ten cross-sectional studies, the AHRQ scores ranged from 5 to 6 and were considered to be of moderate quality. Of the seven case-control studies, five studies had NOS scores ≥ 5 , which were considered to be of high quality, only one study had a score of 4, which was in low quality, and another case-control study did not have the full text available and was not graded. The main characteristics and quality assessment of the included studies are presented in Supplementary Table 1, <http://links.lww.com/CM9/A410>.

The pooled odds ratio (OR) for smoking in patients with acne in comparison with those without acne was 1.21 (95% confidence interval [CI] 0.93–1.57). The pooled ORs, based on seven case-control studies and ten cross-sectional studies, were 1.21 (95% CI 0.81–1.81) and 1.21 (95% CI 0.84–1.74), respectively. Significant heterogeneity can be seen in the overall results and the sub-group analysis [Supplementary Figure 2, <http://links.lww.com/CM9/A409>]. The pooled ORs for smoking in patients with acne compared with those without acne in adults and adolescents were 1.43 (95% CI 1.10–1.87) and 1.04 (95% CI 0.79–1.38), respectively. Significant heterogeneity was observed in the adolescent sub-group and the adult sub-group [Supplementary Figure 3, <http://links.lww.com/CM9/A409>]. The sub-group analysis based on the different geographic areas showed that the pooled ORs for smoking in patients with acne compared with those without acne were 2.60 (95% CI 1.90–3.56) in Asia and 1.04 (95% CI 0.79–1.38) in Europe. Heterogeneity was not observed in the Asian population, but there was significant heterogeneity in the European population; Supplementary Figure 4, <http://links.lww.com/CM9/A409> shows the overall forest plots by the geographic region. The funnel plot was essentially symmetrical, indicating no clear evidence of publication bias. Evaluation of the contribution of each study to the pooled ORs was performed to assess the sensitivity analysis. We excluded one study at a time and then recalculated the pooled P or ORs estimates for the remaining studies. The study had an undue influence on the summary ORs in the Asian population. After excluding this study, smoking became a risk factor for acne.

This study systematically analyzed smoking in observational studies of the population with and without acne and found that smoking has no protective effect on reducing the risk of acne. Furthermore, smoking was a risk factor for acne in the adult group. Smoking increased the risk of acne in the Asian population. A significant association between smoking and acne in the European population was not observed. The heterogeneity is significant in the

European population, which may be related to regional differences, genetic differences, and smoking habits, which needs to be further explored.

The specific mechanism linking smoking and acne is still unclear. Nicotine and other components in cigarette smoke cause vasoconstriction and hypoxemia and have anti-inflammatory effects on neutrophil and lymphocyte chemotaxis. However, keratinocytes also have nicotine acetylcholine receptors, which can induce hyperkeratosis at high concentrations. In addition, cigarette smoke contains large amounts of arachidonic acid and polycyclic aromatic hydrocarbons, which can stimulate the phospholipase A2-dependent inflammatory pathway and aggravate acne.

The results of this meta-analysis are based on observational studies, along with information collected from physician diagnoses and patient self-reported acne, which may have contributed to some inherent bias. Some studies include small sample size and may have selection bias. Large population studies need to be further developed.^[5] Considering the possible adverse health effects of smoking on the human body, it is unethical to conduct prospective clinical studies on the relationship between acne and smoking. This study is essential to provide correct information about the effects of tobacco on acne, which may help in anti-smoking information programs.

We conclude that this meta-analysis provides evidence that smoking is a risk factor for acne in the Asian population and adult acne. However, due to the existing limitations of this study, we should make further efforts to confirm these findings and clarify the underlying mechanisms.

Conflicts of interest

None.

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