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Protocol: HLA and Nasal Polyposis susceptibility: A meta-analysis of worldwide studies

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We use this protocol and it's working

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Abstract

Nasal polyposis (NP) is a common and recurrent condition of the upper respiratory tract that can lead to significant morbidity. NP are noncancerous growths that develop on the lining of the nasal passages and sinuses whose pathophysiology involves a complex interplay of genetic, environmental, and immunological factors. Several studies have explored the association between human leukocyte antigen (HLA) class II alleles and NP, but the results have been conflicting. The aim of this meta-analysis is to investigate the association between HLA class II alleles and NP risk.

Troubleshooting

Administrative Information

1 **Support**

Sources: No financial sources utilized
Sponsor: Albany Medical Center
Role of sponsor: Research oversight

2 **Title**

Protocol: HLA and Nasal Polyposis susceptibility: A meta-analysis of worldwide studies

3 **Registration**

Registration is via protocols.io

4 **Authors**

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5 **Amendments**

None

Introduction

6 **Rationale**

Nasal polyposis is a common and recurrent condition of the upper respiratory tract that can lead to significant morbidity. NP are noncancerous growths that develop on the lining of the nasal passages and sinuses whose pathophysiology involves a complex

interplay of genetic, environmental, and immunological factors. Several studies have explored the association between human leukocyte antigen (HLA) class II alleles and NP, but the results have been conflicting. This meta-analysis of HLA and nasal polyposis will provide a comprehensive examination of these alleles and their potential prognostic value. By identifying the predisposition to the disease at an earlier stage, it may be possible to alter the disease course through timely treatment interventions.

7 **Objective**

To conduct a meta-analysis to determine the significance of HLA-DRB1, HLA-DQA1, and HLA-DQB1 alleles are linked with odds of developing nasal polyposis.

Methods

8 **Eligibility criteria**

For analysis eligibility, only studies published after 2000 will be considered. Studies that are inaccessible, not in English, insufficiently report data on the experimental or control population, or present data that is difficult to interpret will be excluded.

9 **Information Sources**

The databases utilized for data acquisition will include PubMed, Google Scholar, ScienceDirect, and Cochrane Library. Institutional access will be employed for acquiring the data. However, if access is not available, no attempts to contact authors will be made. The data gathering process will take approximately 1 month.

10 **Search Strategy**

Searching will be conducted using the following terms “HLA and nasal polyp”, “HLA-DRB1 and nasal polyp”, “HLA-DQA1 and nasal polyp”, “HLA-DQB1 and nasal polyp”. When an available database feature is available, both HLA and Nasal Polyp will be required to appear in the title in order to limit the search. One researcher, Ryan Witcher will be assigned the role of searching, data collection, and statistical analysis. Ryan Witcher and Sugosh Anur will be responsible for manuscript assembly and review. Final review will be by Dr. Jordan Grube.

11 **Study Records**

Data Management

The data collected during the search process will be stored in Google Sheets for analysis with RevMan statistical software.

Selection Process

To be included in the study, relevant data should be easily accessible in the publication, and the minimum requirement is to report the presence or absence of nasal polyp among both experimental and control groups. Any HLA allele that satisfies the above criteria will be recorded, but only those alleles that occur a minimum of three times will be included in the statistical analysis. The case group will be considered acceptable if it includes nasal polyps with or without comorbidities, but if there is a subgroup that exclusively

reports nasal polyps, that data will be utilized. Acceptable control groups will consist of unrelated individuals without nasal polyps.

Data that does not provide data that is a direct comparison between HLA alleles and the presence or absence of nasal polyps, or that was published before the earliest acceptable date of 2000, will not be included. Additionally, studies that report data on multiple alleles that fall under a general genotype will not be matched with separate studies that provide data solely on the general genotype. However, a study that provides data on a single allele within a general genotype can be matched with a separate study that reports data on the general genotype. For instance, if a study presents genotypic frequency on both HLA-DRB1*0301 and HLA-DRB1*0305, the data cannot be combined under the single serotype HLA-DRB1*03, and thus will be excluded. Conversely, if a study only provides data on one allele, such as DRB1*0301, it can be categorized under the investigative group of HLA-DRB1*03.

Data collection Process
Data will be collected by one researcher onto one Google Sheets. If the legitimacy of data or the study being assessed is questionable, Ryan Witcher and Sugosh Anur will discuss the topic. If there is disagreement as to the best option the principle investigator Dr. Jordan Grube will have the final decision on any topic.

12 **Data items:**
Data collected included the number of cases of nasal polyp with the presence or absence of specific HLA alleles, as well as the healthy controls with the presence or absence of the specific HLA alleles. Odds ratios and confidence intervals that were found were also recorded.

13 **Outcomes and Prioritization**
Data on the frequency of HLA alleles with respect to nasal polyps will be collected. For inclusion in the analysis, data must have been reported in at least three separate publications and exhibit a significant odds ratio interval with an I2 heterogeneity value of less than 25%. Significance will be determined by evaluating the confidence intervals of the odds ratio and effect size.

14 **Risk of bias in Individual Studies**
Assessment of bias will be performed using the NIH Quality Assessment Tool for Case Control Studies (cited below). If the allele meets all selection criteria, a DOI plot will be generated using MetaXL.

National Heart, Lung, and Blood Institute. Study Quality Assessment Tools. Available from: **https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools**. Updated 2021 July.

15 **Data Synthesis**

A: Statistical analysis will be performed using the Revman 5.4 software (referenced below). The forest plot analysis will require inputs such as the number of cases with a distinct HLA, the total number of cases, the number of controls with a distinct HLA, and the total number of controls.

B: The odds ratios and their respective confidence intervals of each study will be evaluated to generate a combined odds ratio and confidence interval for each HLA allele. The level of heterogeneity in the data will be measured using I^2. A heterogeneity value greater than 25% will be considered moderate to high and will be disqualified from an assessment of significance.

C: Sensitivity analysis may be performed via Revman or other software such as MetaXL.

D: See above.

Review Manager (RevMan) [Computer Program]. Version 5.4, The Cochrane Collaboration, 2020.

16 **Meta-bias and Confidence in Cumulative Evidence**

GRADE criteria will be used (cited below).

Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Harbour RT, Haugh MC, Henry D, Hill S, Jaeschke R, Leng G, Liberati A, Magrini N, Mason J, Middleton P, Mrukowicz J, O'Connell D, Oxman AD, Phillips B, Schünemann HJ, Edejer T, Varonen H, Vist GE, Williams JW Jr, Zaza S; GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ. 2004 Jun 19;328(7454):1490. doi: 10.1136/bmj.328.7454.1490. PMID: 15205295; PMCID: PMC428525.