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A Short Note on Hodgkin lymphoma

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Abstract

Hodgkin lymphoma (HL) is the most common lymphatic system cancer in teenagers and young adults (TYAs) worldwide. Several conditions that disrupt immune regulation have been linked to an increased risk of HL in TYAs. These include infectious mononucleosis (IM) following an EBV infection, HIV infection, immunosuppressive therapy, and a number of autoimmune diseases like multiple sclerosis, systemic lupus erythematosus, and rheumatoid arthritis. Genetic studies have also found that certain HLA genes that regulate the immune system in human subjects are associated with an increased risk of

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Introduction

As a possible explanation for the underlying cause of immune system dysfunction during HL development, the antigenic stimulation hypothesis has been proposed. There is a growing body of evidence supporting this hypothesis and demonstrating that a number of immune-related cancers, including leukemia, occur as a consequence of immune system malfunction in early life. Allergic diseases, including asthma, eczema, and allergic rhinitis, are among the most common perpetrators of chronic immune stimulation. This hypothesis proposes that conditions with chronic immune stimulation predispose subjects to hematologic malignancies, such as multiple myel the relationship between allergic diseases and HL has only been the subject of a small number of studies, and the results have been inconsistent and inconclusive. Previous studies may not have been able to detect associations because they relied on a small number of exposed subjects. Electronic health records from primary care, where allergic disease is mostly diagnosed and treated, or from the population of the United Kingdom (UK), which has one of the highest rates of both HL in TYAs and allergic disease worldwide have not been the subject of any studies. They mostly work by suppressing the immune system, so their use is usually reserved for more severe cases that have not responded to conventional first-line treatments. Therefore, the effects of steroids may be intertwined with any association between allergic disease and HL: Because steroids are used to treat a variety of immune-related diseases that may also be risk factors for HL, their use could either alter or confuse any effect—they are a marker of the severity of allergic disease. This interplaying role must therefore be taken into consideration in any study of allergic diseases. Steroids have been linked to an increased risk of lymphoma in some studies; however, there has been no link found in others; More importantly, it isn't clear if taking steroids is a risk factor on its own, a measure of how bad an allergy is, or a proxy for other immune-related diseases. In addition, many of the studies focused solely on topical steroids or did not differentiate between lymphoma types, adding to the uncertainty regarding the relationship between steroid treatment and HL risk.

Using linked primary care electronic health records, we investigated whether individuals with a history of allergic disease (asthma, eczema, or allergic rhinitis) are more likely to develop HL in later life and whether steroid exposure affected HL risk. Using inpatient Hospital Episode Statistics (HES) and index of multiple deprivation (IMD) data from the UK Clinical Practice Research Datalink (CPRD), we carried out a matched case-control study [1-5].

Discussion

The prospectively collected, anonymized data from UK primary care consultations can be found in the CPRD database, which is an electronic health record. It is the largest source of longitudinal primary care data, with information on 22 million patients-roughly 9% of the UK population in 2013-43. These data are available since the founding of CPRD in 1987. Clinical symptoms, diagnoses (coded using Read codes), investigation outcomes, medications, and specialist recommendations are all included. Before practices are declared "up to standard" (UTS) for research purposes, they are regularly audited to ensure high data quality and that 95 percent of prescribing and morbidity events are captured.43 The CPRD data used in this study were enhanced by prelinkage to HES. Every visit to a National Health Service hospital in England (approximately 125 million episodes annually) is recorded in the HES database. The International Classification of Diseases, Tenth Revision (ICD-10) is used to code the clinical information in each episode, which includes information about procedures, diagnoses, and previous medical history. Patients whose practices have consented to data linkage (54 percent of all contributing CPRD practices in the UK) can access the data starting in April 1997.44 CPRD data were also prelinked to information on quintiles of IMD scores in practices that had consented to data linkage. Based on the income, employment, disability, educational attainment, and other characteristics of a postcode's Local Super Output Area, these can be thought of as a composite ecological (small area-based) measure of a patient's socioeconomic status (SES). The latter typically have populations of 1,000 to 3,000 people. Each patient's general practice's Local Super Output Area was represented by an aggregate IMD score. The July 2016 CPRD builds and the linked data from Set 13 were used to collect the data for this study.

In the beginning, we talked about the cases and control subjects' basic characteristics. Odds ratios (ORs) were calculated for the

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relationship between each exposure variable and HL using univariable conditional logistic regression, which was matched on age at index date, sex, and duration of follow-up. Multivariable conditional logistic regression was then used to adjust for all other variables in the model. After that, interaction terms were added to look into how age, sex, and SES might change the relationship between HL incidence and allergic disease.

In order to account for the large number of allergic diagnoses, a subsequent analysis of the final regression model classified allergic disease as a linear rather than binary variable. By comparing models in which allergic disease was added as a nonlinear versus a linear term, we investigated departure from linearity and assessed for linear trend by number of allergic diagnoses. First, we estimated the linear effect using likelihood ratio tests. To reduce the likelihood of a type 1 error, we utilized 95% confidence intervals and an implied 5% level of statistical significance.

We carried out the analyses once more using various definitions of exposure, this time taking into account each individual allergic disease. To begin, we created a cross-tabulation to compare the prevalence of allergic disease combinations in cases and control subjects. After adjusting for each other and other variables in the model, we then repeated the conditional logistic regression analysis that was mentioned earlier, but this time we included asthma, eczema, and allergic rhinitis as separate variables to see how they affected HL incidence on their own. To see if the estimated risk for each allergic disease by age, sex, and SES strata-as well as for any other allergic disease-could be affected in any way, interaction terms were added. We used likelihood ratio tests in supplementary analyses for each of the three allergic diseases separately to see if a model with them classified as infant/childhood/adult onset differed from one with them classified as yes-no variables independent of age of onset. Estimation of stratum-specific adjusted odds ratios (aORs) was done whenever there was evidence of heterogeneity [6-10].

Conclusion

Secondary analyses by comparing effect estimates before and after adjusting for steroid use, secondary analyses were conducted to assess for potential effect modification when stratifying by steroid use and to investigate the extent to which the effect of variables might be confounded by steroid treatment. Before and after adjusting for other variables, the effect of steroids was also evaluated, both collectively (any use of steroids) and stratified by method of administration (inhaled, topical, oral, or intravenous/intramuscular). By estimating the linear effect of the number of steroid prescriptions before the index date on HL risk and by route of administration (ordered according to strength/level of systemic absorption), we used likelihood ratio tests to check for a potential dose-response relationship. The Independent Scientific Advisory Committee for MHRA Database Research and the London School of Hygiene and Tropical Medicine Ethics Committee approved the project's protocol. A National Research Ethics Service Committee has granted universal ethical approval for observational studies utilizing anonymized CPRD data and receiving approval from an Independent Scientific Advisory Committee. The Declaration of Helsinki was followed when conducting the study.

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