Asthma and vaccination history in a young adult cohort

Abstract

Background: It has been suggested that childhood vaccinations may be associated with the onset of asthma. We investigated the association between asthma, atopy and vaccination history in a cohort of young adults living in Melbourne, Australia.

Methods: Subjects were aged between 22 and 44 years and were surveyed by an interviewer-administered questionnaire. Questions were asked about vaccinations to measles, mumps and rubella (MMR), triple antigen (DTP), hepatitis B and Sabin polio vaccine (OPV). Atopy was assessed by skin prick testing to common aeroallergens.

Results: There was no significant association observed for subjects diagnosed with asthma who had received measles or MMR vaccinations compared with those who did not receive measles or MMR vaccinations (RR 1.33, 95% CI 0.98-1.80). Non-significant associations were also observed for OPV and hepatitis B vaccinations (RR 3.27, 95% CI 0.50-21.3 and RR 1.08, 95% CI 0.83-1.41, respectively). However, subjects reporting full immunisation were found to be at higher risk to asthma (RR 1.52, 95% CI 1.09-2.11) but not atopy.

Conclusions: Our results show relatively weak support for the hypothesis that childhood vaccinations may lead to increased risk of asthma, but caution is advised due to possible recall bias.

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There have been conflicting reports in recent years regarding the increased risk of atopic diseases such as asthma being related to increased vaccination rates.[1-5] Some of these studies have suggested that infection in early life could have a protective role by acting as a catalyst for the maturation of the T helper 1 (T_{H1}) immunity phenotype over the T_{H2} immunity phenotype that leads to IgE antibody responses. Thus the increase in vaccinations undertaken during infancy in many Western countries has led to a situation where the T_{H2} phenotype may predominate and hence increase the rate of atopic diseases.

The idea that increasing childhood vaccination rates may indirectly increase the rates of atopic diseases such as asthma in a population has serious public health implications. In the latter half of the 20th century, childhood immunisations have contributed to significant reductions in infant and adult morbidity and mortality. However, effectiveness relies on high rates of immunisation (herd immunity) and a link between vaccinations and increased risk of atopic diseases such as asthma may undermine public confidence in full immunisation.

The purpose of this study was to determine whether childhood vaccinations were associated with atopy and asthma in a cohort of young adults in Melbourne, Australia.

Subjects and Methods

We conducted a cohort study in Melbourne, Australia, as part of the European Community Respiratory Health Survey (ECRHS) between 1992 and 1998. This study originally included 27 study centres in 14 countries with more than 10,000 subjects. The full details of the sampling protocol have been described elsewhere.[6,7] Briefly, in 1992, 4,500 adults were randomly selected from electoral rolls in Melbourne and sent postal questionnaires. More than 3,200 subjects (72%) returned the postal questionnaires and random (n=1642) and symptomatic (n=433) samples were invited to the laboratory for the second phase of the study.[8] Subjects were surveyed by a validated interviewer-administered questionnaire covering: history of asthma; details of home and occupation environment; smoking history; medications; dietary information; and respiratory symptoms. The respiratory symptoms included wheezing or whistling in the chest, shortness of breath, chest tightness, and cough and phlegm during the previous 12 months.

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Atopy was assessed by skin prick testing to common aeroallergens. Of the 637 subjects in the laboratory stage of the study aged between 20-44 years, 205 (32.1%) reported that they had asthma, of whom 187 (29.3%) had asthma confirmed by a doctor. For the analysis, asthma was ascribed to those subjects reporting that they had their asthma confirmed by a doctor prior to the commencement of the study. The mean (SD) age of the first asthma attack was 16.2 (12.2) years. The range of the first asthma attacks was 0-45 years and the quartiles were <5 years, 5-15 years, 16-27 years and >27 years, respectively.

The aeroallergens used were Dermatophagoides pteronyssinus, cat, rye grass pollen, Cladosporium herbarium, Aspergillus fumigatus, Alternaria tenuis, cypress, olive, plantain and ragweed (Bayer, Sydney), together with positive (histamine) and negative controls. Atopy was defined as having a wheal of three millimetres or greater in diameter for any allergen. Atopy status was established in 456 subjects who presented to the laboratory.

Since the Melbourne centre was one of the first of the ECRHS centres to undertake the follow-up in 1998, a preliminary version of the questionnaire was used. This questionnaire included vaccination history questions, which were not included in the questionnaire used by the other study centres. Vaccination history included measles or measles, mumps and rubella vaccinations (MMR); hepatitis B; Bacille Calmette-Guérin (BCG); oral polio vaccine (OPV); and diphtheria, tetanus and whooping cough (DTP). The standard schedule (NHMRC, 1993) for MMR, DTP and OPV is for ages from two months to five years or prior to school entry. Subjects simply answered 'yes', 'no' or 'don't know' to questions for each of the vaccinations. History of other vaccinations such as influenza, typhoid, cholera, smallpox and yellow fever were also recorded, if reported by the subject. Relative risks (RR) were calculated for asthma, each vaccination type, atopy and for subjects reporting full immunisation. The dates of asthma onset were recorded but dates of vaccinations were not recorded. For the early childhood vaccinations we expected all to precede the onset of asthma. However, vaccinations related to overseas travel and influenza may have been received after the onset of asthma.

Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS) computer package.[9] Relative risks are given with the 95% confidence intervals (95% CI) used to assess statistical significance.[10]

Results

Atopy for one or more of the common aeroallergens tested was found in 271 (59.4%) of the 456 young adults who presented to the laboratory. The relative risks and 95% CI for the outcomes of asthma and atopy have been tabulated in Table 1, for each type of vaccination. Measles and OPV vaccinations were not significantly associated with increased risk for asthma or atopy. However, full immunisation (MMR, OPV and DTP) or influenza vaccination was associated with a significantly increased risk for asthma. Only 34 participants did not report receiving at least one of the three childhood vaccinations and 273 (42.7%) reported full immunisation (measles or MMR, DTP and OPV). This figure may appear low in light of the reported full immunisation rate in Australia of 53% in 1990,[11] but given that measles vaccine was first licensed for mass use in Australia in 1968 and rubella in 1970, many of the older subjects missed these vaccinations. The total numbers of subjects reporting the various vaccines are given in Table 1.

The 'don't know' answers reported by the subjects for the different vaccinations ranged from 2.5% for OPV to 22.2% for measles or MMR. A further analysis was performed correcting for age of the 'don't know' respondents, to investigate whether the 'don't know' responses were related to the age of the subjects. No correlation or significant associations were found relating age to the 'don't know' answers (these results have not been presented here).

Discussion

We found an increased risk of asthma but not atopy for full immunisation in a cohort of young adults. Although associations were observed for asthma and measles or MMR, OPV, hepatitis B, none were statistically significant. The associations for atopy and vaccinations appeared consistently weak for all vaccinations investigated. This is a very important finding since the hypothesis that atopic asthma is associated with vaccination history would also necessarily demand a strong association with atopy. Our findings therefore only provide relatively weak support to the hypothesis that vaccinations undertaken during infancy may favour the T_{H2} phenotype and hence increase the rate of atopic disease. Significant associations were found between influenza vaccination and both asthma and atopy, but we believe this is not a causal relationship, since nearly all of the subjects reported onset of asthma prior to the commencement of influenza immunisation in early infancy in Victoria, Australia. Additionally, influenza triggers asthma attacks, hence influenza vaccine is commonly recommended for people with asthma.

Table 1: Association of doctor-diagnosed asthma and atopy with vaccination history for 637 young adults.

Vaccination type (no. vaccinated)	RR[a] for asthma	95% CI for asthma	RR[a] for atopy	95% CI for atopy
Measles or MMR (n=309)	1.33	0.98-1.80	1.07	0.88-1.30
DTP (n=548)	0.80	0.36-1.75	1.03	0.54-1.97
OPV (n=562)	3.27	0.50-21.3	1.14	0.57-2.30
Full immunisation[b] (n=273)	1.52	1.09-2.11	1.10	0.89-1.36
Hepatitis B (n=183)	1.08	0.83-1.41	1.05	0.89-1.24
BCG (n=469)	0.95	0.70-1.29	0.87	0.72-1.05
All vaccinations (n=73)	1.25	0.89-1.74	0.82	0.62-1.09
Influenza (n=139)	1.69	1.33-2.16	1.23	1.05-1.45

Notes:
(a) Relative risk.
(b) Full immunisation is defined as measles or MMR, DTP and OPV.

The major strengths of this study are that it has the advantages of the cohort design and that relatively large numbers of subjects were recruited (n=637). A further strength of this study was that large differences did not exist in subject numbers between most of the groups investigated e.g. balanced numbers in the vaccinated and non-vaccinated groups. Since the overwhelmingly majority of children born later than 1988 in Australia were vaccinated with the MMR vaccine and most other significant infectious childhood disease vaccines, attempts by future studies to recruit sufficient numbers of non-vaccinated subjects will become increasingly more difficult.

The results of previous studies investigating childhood vaccinations and asthma or atopy have been mixed. Recent reports by Hurwitz and Morgenstern[12] and Yoneyama et al.[13] found that DTP vaccinations were associated with an increase in atopic disorders. Yoneyama et al.[13] also found that vaccination to BCG inhibits the development of atopic disorders. This is in contrast to reports by Anderson et al.[5] and Wickens et al.[4] who found no significant associations of atopy or asthma and the various childhood vaccinations investigated in this study. However, most of the previous studies were limited by either weak design (ecological studies, e.g. Anderson et al.[5]), small overall subject numbers (Yoneyama et al.[13]), or had small numbers in the non-vaccinated groups. Small numbers in the non-vaccinated groups in studies may introduce confounding by atopic families deciding it could be dangerous to undertake vaccinations because of the risk of anaphylaxis, or asthmatic families wanting additional protection. The present study avoids these confounding issues and may be difficult to repeat in future years.

Typically, studies of young adults where information of vaccination history is self-reported may be subject to significant recall bias. Caution is therefore advised in the interpretation of our results. Future studies might obtain more accurate data from maternal and child health records or general practitioners' notes. Since the mean age of asthma onset in our study is only 16.2 years, occupational asthma is unlikely to significantly affect our results. The numbers of subjects who reported 'don't know' to specific questions regarding vaccination history in this study was small for OPV (2.5%). However, although we performed a subanalysis correcting for age, the 22% of subjects who answered 'don't know' for measles and MMR vaccination may have adversely affected the results of our analysis. It is unlikely that subjects reporting 'don't know' were confounded by socio-economic status since all subjects came from suburbs with relatively homogenous socio-economic status, in the south-eastern part of Melbourne.

An alternative hypothesis that we are unable to investigate in this study is that parents of children with asthma are more likely to have their children vaccinated. This may be investigated with the future development of the Australian Childhood Immunisation Register, which commenced operating on 1 January 1996. None the less, we can conclude that it is unlikely early childhood vaccination significantly increases the risk of atopy or asthma in adulthood.

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