Antibiotic use in children: another increased risk of asthma?

The aim of this work was to explore, in a large population-based cohort, the association between exposure to antibiotics in the first year of life and the subsequent development of asthma.

Methods

This was a longitudinal study cohort that enrolled all live births in British Columbia (Canada) from January 1997 to December 2003. Children enrolled in the study should have at least two years of follow-up from the time of birth. Linked administrative health data (physician service, hospital admissions, outpatient dispensing episodes of prescription drugs) were used to assess potential antibiotic exposure, potential confounders and outcome. Asthma medications included: short acting b-agonists, inhaled corticosteroids, ipratropium, ketotifen, leukotriene receptor antagonists. Exposure to antibiotics in the first year of life was measured in 3 ways: a) ever dispensed versus never dispensed; b) number of antibiotic courses (0, 1-2, 3-4, >4); c) type of antibiotic (penicillins, cephalosporins, macrolides, sulfonamide or others). Cox proportional hazards regression analysis was used to estimate hazard ratios (HRs) and their 95% confidence intervals (CIs) for the association between exposure to antibiotics and subsequent risk of asthma, adjusted for potential confounders (gender, family socioeconomic status at birth, living area, birth weight, gestational age, delivery method, frequency of physician visits, specialist visits, hospital visit involving surgery, congenital anomalies, upper and lower airways disease).

Results

251,817 live births were included in the study; 50% were male, 85% were born in urban areas and there was an even distribution across socioeconomic quintiles. 43% of children were prescribed at least 1 antibiotic in their first year of life; in specific 56.7% never received antibiotics in their first year of life, 33.2% received 1-2 antibiotic courses, 7.3% received 3-4 courses and 2.8% >4 courses. 7% of children developed asthma over the follow-up period (mean time 5.5 years) and the overall incidence of asthma was 2.3% per person-years (PY) of follow-up; however the rate ranged from 2.7% PY for diagnosis at 2-3 years to 1.7% PY for diagnosis at 5-9 years. The association between asthma and exposure to antibiotics in the first year of life was stronger for diagnoses earlier in the follow-up period. There was a higher risk of asthma associated with: male sex; living in an urban area; having lower socioeconomic status, first cesarean, forces or vacuum extraction, no congenital anomalies, specialist visit, increased bronchitis, upper or lower respiratory airways infection, otitis media diagnoses. Regarding the type of antibiotics, macrolides showed the strongest association with subsequent asthma.

Conclusion

A small but significant association between antibiotic use and the subsequent development of asthma was demonstrated. Authors found an increasing risk of asthma with the increasing number of antibiotic courses during the first year of life, too.

Original article
Editorial comment

Nowadays this is the largest cohort study that investigates the possible association between antibiotic exposure and the subsequent development of asthma. Since last decade several studies [1–7] tried to evaluate this relationship, with conflicting results, although some studies [2, 5] found an association similar to the present study. The base of this speculation is the “hygiene hypothesis”, originally formulated by Strachan [8], who found an inverse relationship between family size and development of atopic diseases. Afterward, it becomes more and more important the idea that a lower microbial exposure (sanitation, antibiotics use, vaccines) could “switch” the immune system toward “self” instead of “non-self” antigens, with a consequent increasing of autoimmune and atopic diseases. In the last years this hypothesis has been discussed, and some Authors underlined that the hygiene hypothesis alone could not be an adequate explanation for the increase in atopic diseases [9]. It’s interesting the observation made by Mattes et al. [10], who undertakes that, regarding the relationship between antibiotic use, infections and atopy, “it’s difficult to disentangle from the potential confounders such as whether the key exposure relates to the infection or the antibiotic”. Other factors have been analysed to explain the increase of atopic diseases, among which socio-economic status, nutrition and diet, and, more recently, overweight and obesity. According to us, another possible explanation could be that atopic patients could be more prone to respiratory infections, so requiring more antibiotic courses. Moreover, in this study, even if well conducted, there is not a control group, but, as the authors highlight, this would be unethical. Probably more studies, analyzing all above mentioned potential confounding factors, are needed to firmly assess the relationship between antibiotic use and the increasing risk of asthma.

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References

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