

Increased risk of childhood asthma from antibiotic use in early life

Chest

June 2007;131(6):1753-9

Kozyrskyj AL, Ernst P, Becker AB.

FROM ABSTRACT:

BACKGROUND:

To address the major methodological issues of reverse causation and selection bias in epidemiologic studies of antibiotic use in early life and the development of asthma, we undertook a cohort study of this association in a complete population of children.

METHODS:

Using the health-care and prescription databases of Manitoba, Canada, this longitudinal study assessed the association between antibiotic prescription use during the first year of life and asthma at age 7 years in a 1995 birth cohort of 13,116 children.

RESULTS:

Independent of well-known asthma risk factors, asthma was significantly more likely to develop in children who had received antibiotics in the first year of life at age 7 years.

The association with asthma was observed for antibiotic use in non-respiratory tract infections ([86% increased risk]).

The risk of asthma was highest in children receiving more than four courses of antibiotics.

Broad-spectrum (BS) cephalosporin use was more common in these subpopulations of children.

CONCLUSIONS:

Antibiotic use in early life was associated with the development of childhood asthma, a risk that may be reduced by avoiding the use of BS cephalosporins.

THESE AUTHORS ALSO NOTE:

"Asthma is one of the most common chronic diseases worldwide, significantly impacts quality of life, and represents a significant cost to the health-care system."

The prevalence of asthma has increased drastically in industrialized countries over the last 25 years.

"The Hygiene Hypothesis postulates that growing up in a more hygienic environment with less microbial exposure may promote the fetal immune response, which is skewed in the atopic T-helper (Th) type 2 direction, whereas microbial pressure would drive the immune system toward a balanced Th-1 and Th-2 immunity."

Studies indicate that exposure early in life to endotoxins from the membranes of dead bacteria "may be the key element of less hygienic environments, which results in a lower prevalence of allergy and asthma."

The Microflora Hypothesis of allergic disease points out that the early in life commensal microbial intestinal flora is responsible for proper T cell immunologic maturation and function, and that early in life exposure to antibiotics alters gastrointestinal microflora and diminishes Th-1 immune responses and increases allergic airway disease. **[Important]**

"Since oral antibiotics are frequently prescribed for upper and lower respiratory tract infections in children, an understanding of the relation between antibiotic use and asthma is critical to clinicians and health-care policymakers worldwide."

RESULTS

In this study cohort of 13,116 children, 65% had received at least one antibiotic prescription during the first year of life, and in all but 3% the antibiotic was a broad spectrum antibiotic. **[Amazing]**

40% received the antibiotic because of otitis media.

28% received the antibiotic for other upper respiratory tract infections.

19% received antibiotics for lower respiratory tract infections.

7% received antibiotics for non-respiratory tract infections.

After adjusting for other potential asthma causing variables, "antibiotic use in the first year of life (vs. no use) was significantly associated with greater odds of the development of asthma at age 7."

"This likelihood [of asthma] increased with the number of antibiotic courses."

"Children who had received more than four courses of antibiotics were almost twice as likely to have asthma develop."

"In a model that adjusted for all risk factors for asthma, asthma was significantly more likely to develop in children receiving antibiotics in a dose-dependent manner."

"The highest risk of asthma occurred among children receiving more than four courses of antibiotics."

"Asthma at age 7 years was almost twice as likely in children receiving one or more antibiotic prescriptions for non-respiratory tract infections in comparison to children who had not received antibiotics."

DISCUSSION

"Children receiving more than four courses of antibiotics were at 1.5 times the risk of having asthma develop than were children not receiving antibiotics."

Asthma prevalence is lowest in rural children "which may be attributed to the protective effect of endotoxin exposure in farming communities."

Antibiotics may alter the protective effect of gut flora in children.

All antibiotics decrease anaerobic gut microflora in infants, but broad-spectrum antibiotics significantly alter gut microflora.

Antibiotic disruption of intestinal microflora impairs the gastrointestinal barrier function leading to allergen penetration and subsequent inflammation.

It is prudent to avoid the unnecessary use of broad-spectrum antibiotics in the first year of life.

KEY POINTS FROM DAN MURPHY

- 1) "Asthma is one of the most common chronic diseases worldwide, significantly impacts quality of life, and represents a significant cost to the health-care system."
- 2) The prevalence of asthma has increased drastically in industrialized countries over the last 25 years.
- 3) "The Hygiene Hypothesis postulates that growing up in a more hygienic environment with less microbial exposure may promote the fetal immune response, which is skewed in the atopic T-helper (Th) type 2 direction, whereas microbial pressure would drive the immune system toward a balanced Th-1 and Th-2 immunity."
- 4) Studies indicate that exposure early in life to endotoxins from the membranes of dead bacteria "may be the key element of less hygienic environments, which results in a lower prevalence of allergy and asthma."
- 5) The Microflora Hypothesis of allergic disease points out that the early in life commensal microbial intestinal flora is responsible for proper T cell immunologic maturation and function, and that early in life exposure to antibiotics alters gastrointestinal microflora and diminishes Th-1 immune responses and increases allergic airway disease. **[Important]**

- 6) In this study cohort of 13,116 children, 65% had received at least one antibiotic prescription during the first year of life, and in all but 3% the antibiotic was a broad spectrum antibiotic. **[Amazing]**
- 7) After adjusting for other potential asthma causing variables, “antibiotic use in the first year of life (vs. no use) was significantly associated with greater odds of the development of asthma at age 7.”
- 8) “This likelihood [of asthma] increased with the number of antibiotic courses.”
- 9) “Children who had received more than four courses of antibiotics were almost twice as likely to have asthma develop.”
- 10) “In a model that adjusted for all risk factors for asthma, asthma was significantly more likely to develop in children receiving antibiotics in a dose-dependent manner.”
- 11) Antibiotic disruption of intestinal microflora impairs the gastrointestinal barrier function leading to allergen penetration, subsequent inflammation and asthma.
- 12) It is prudent to avoid the unnecessary use of broad-spectrum antibiotics in the first year of life.