Allergy

RISK FACTORS, PREVENTION, AND THE HYGIENE HYPOTHESIS

Acetaminophen Versus Ibuprofen in Young Children With Mild Persistent Asthma

Sheehan WJ, Mauger DT, Paul IM, et al. *N Engl J Med*. 2016;375(7):619–630

PURPOSE OF THE STUDY. With previous observational data, researchers have suggested an association between the frequent use of acetaminophen and possible asthma-related complications in children. The authors of this study specifically address this, evaluating the number of asthma exacerbations in children who received acetaminophen versus ibuprofen for fever or pain alleviation.

STUDY POPULATION. This study included 300 children (aged 12–59 months) with mild persistent asthma. Children were determined eligible if they met the criteria of current use of Step 2 asthma controller therapy. Children were excluded if they had any history of adverse reaction to the trial medications or if there was evidence suggestive of possible poor adherence to the trial medication regimens or study procedures.

METHODS. This was a prospective, randomized, double-blind, parallel-group trial in which enrolled children were assigned to receive either acetaminophen or ibuprofen as needed for management of fever, pain, or discomfort. Patients were managed over 48 weeks and received standardized asthma-controller therapies. The primary outcome was the number of asthma exacerbations that required systemic glucocorticoid treatment. A standardized list of criteria for treatment with systemic glucocorticoids was used when assessing asthma exacerbations. Prespecified secondary outcomes included: percentage of asthma-control days, average use of albuterol as a rescue, and frequency of unscheduled health care visits for asthma.

RESULTS. One hundred and fifty children were initially assigned to each treatment group. One hundred and sixteen patients in the acetaminophen group completed the trial compared with 110 patients in the ibuprofen group. There was no significant difference in the median number of doses of acetaminophen versus ibuprofen received ($P = .47$). No significant difference in number of asthma exacerbations was observed between the 2 groups (relative rate of asthma exacerbations in the acetaminophen versus ibuprofen group: 0.94; confidence interval: 0.69–1.28; $P = .67$). The acetaminophen group had 49% of participants with at least 1 asthma exacerbation compared with 47% in the ibuprofen group. Furthermore, no significant difference was noted between the 2 groups in regard to percentage of asthma control days, use of albuterol rescue inhaler, unscheduled asthma-related health care visits, and overall adverse events.

CONCLUSIONS. In young children with mild persistent asthma, the use of acetaminophen for as-needed pain or fever management was not shown to be associated with a higher incidence of asthma exacerbations or overall worse asthma control compared with the use of as-needed ibuprofen.

REVIEWER COMMENTS. This topic has been debated for some time on the basis of several observational studies revealing an association between impaired asthma control and use of acetaminophen in children and adults. However, in other studies, researchers have suggested that the association is confounded simply by the fact that children with asthma who have more frequent symptomatic respiratory tract infections will often take acetaminophen for management of fever and malaise. The authors of this study explored this concept and observed that greater use of antipyretic or analgesic medications was associated with concurrent respiratory illnesses, and respiratory illnesses were associated with asthma exacerbations that required systemic glucocorticoids. Overall, there was no difference in rate of asthma-related complications in patients given acetaminophen versus ibuprofen.

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Areas With High Rates of Police-Reported Violent Crime Have Higher Rates of Childhood Asthma Morbidity

Beck AF, Huang B, Ryan PH, Sandel MT, Chen C, Kahn RS. *J Pediatr*. 2016;173:175–82

PURPOSE OF THE STUDY. To assess the association between population-level violent (and all) crime rates and population-level childhood asthma utilization and patient-level risk of asthma reutilization after hospitalization.

STUDY POPULATION. Four thousand six hundred and thirty-eight children aged 2 to 17 years who visited the emergency department (ED) or were hospitalized for asthma at Cincinnati Children's Hospital Medical Center between January 1, 2011, and December 31, 2013.

METHODS. In this retrospective cohort study, we identified subjects by using diagnosis code 493.XX and classified them demographically by using electronic medical record information. Street addresses were geocoded and linked to 2010 census tracts. The population- and patient-level asthma utilization rates were calculated by dividing the number of asthma ED and hospitalizations per tract by number of children aged 2 to 17 years within that tract. This

measurement was annualized over the data collection period. Patient-level reutilization was calculated for 981 hospitalized children who were followed for ≥12 months to identify time to first asthma-related ED revisit and/or rehospitalization. Cincinnati Police Department data were used to calculate violent crime rates (VCRs) and all crime rates (ACRs) by dividing the crime per tract by total people residing in the tract. Crime rates were then stratified as low, low medium, high medium, and high. Poverty rate, unemployment, asthma-related housing code violation density, and traffic-related air pollution were identified as covariates of the study.

RESULTS. Both VCRs and ACRs were associated with asthma utilization with the average asthma utilization rate of 28.0 per 1000 patients and the average VCR and ACR of 10.5 per 1000 patients and 118.7 per 1000 patients per year, respectively. There was a trend toward hospitalized children being more likely to reutilize if they lived in an area with a higher VCR and ACR in unadjusted models.

CONCLUSIONS. Crime data may help facilitate early identification of risk factors or stressors relevant to asthma utilization patterns.

REVIEWER COMMENTS. Asthma, as any other chronic illness, is affected by social and environmental factors. Crime rates can be used to assess the stress imposed by the environment on a child's health, particularly in instigating an acute exacerbation, compliance with controller medication, and follow-up with the primary care provider. In this study, a basis is provided for identifying potentially modifiable population-level and patient-level environmental factors which play an important role in the management of asthma, the most common pediatric chronic illness.

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Breastfeeding and Asthma Outcomes at the Age of 6 Years: The Generation R Study

den Dekker HT, Sonnenschein-van der Voort AM, Jaddoe VW, Reiss IK, de Jongste JC, Duijts L. *Pediatr Allergy Immunol*. 2016;27(5):486–492

PURPOSE OF THE STUDY. To investigate the association of duration and exclusiveness of breastfeeding with asthma outcomes in children aged 6 years and determine association with atopy or infection.

STUDY POPULATION. Prospective cohort study of 5675 children from the prenatal period until young adulthood in the Netherlands.

METHODS. Information about breastfeeding was collected through questionnaires. At age 6, airway resistance and exhaled nitric oxide (FeNO), a marker of eosinophilic airway inflammation, were measured. Follow-up questionnaires inquired about wheezing patterns and current asthma.

RESULTS. Children who were not breastfed had increased risk of late and persistent wheezing (odds ratio [95% confidence interval]: 1.69 [1.06 to 2.69] and 1.44 [1.00 to 2.07], respectively) and lower FeNO levels (estimated percentage difference [95% confidence interval]: −16.0 [−24.5 to −7.5]). Shorter duration of breastfeeding was associated with early wheezing (as was less exclusive breastfeeding) and current asthma at age 6 years. Breastfeeding duration and exclusiveness were not associated with FeNO or airway resistance. The associations were explained partly by lower respiratory tract infections in early life and to a lesser extent by lower respiratory tract infections in later life.

CONCLUSIONS. Breastfeeding patterns may influence wheezing and asthma in childhood, which seems to be partly explained by infectious mechanisms.

REVIEWER COMMENTS. In this study, the researchers add longitudinal data about breastfeeding and asthma outcomes among a cohort in the Netherlands through age 6 years. Interestingly, those who were never breastfed had increased risk of late and persistent wheezing but lower FeNO levels. In addition, the risk of wheezing associated with lack of breastfeeding seemed to be at least partially mediated by respiratory infections. Limitations include the potential for selection bias because the characteristics of the participants who were lost to follow-up were different than those included in the study. Finally, 70% of participants were of European ethnicity, which may affect generalizability of these findings.

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Breastfeeding, Maternal Asthma and Wheezing in the First Year of Life: A Longitudinal Birth Cohort Study

Azad MB, Vehling L, Lu Z, et al. *Eur Respir J*. 2017;49(5):1–9

PURPOSE OF THE STUDY. To examine the association of breastfeeding and wheezing in the first year of life in a pregnancy cohort, with attention to maternal asthma and infant sex.

STUDY POPULATION. The study included 2773 infants born to women enrolled in the Canadian Healthy Infant Longitudinal Development (CHILD) Study, a population-based birth cohort, from 2009 to 2012.

METHODS. Caregivers reported on infant wheezing and infant feeding via questionnaire at 3, 6, and 12 months of life.

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