Asthma Publications: Year in Review

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Factors Contributing to the Development of Asthma

- Evaluated the relationship between early viral illnesses, allergic sensitization and persistence of wheezing/asthma in children at risk for atopy

- Prospective study of 217 children from birth to 13 years old

- Gathered information about viral illnesses during ages 0-3 years, allergic sensitization at different time points and asthma diagnosis
Interaction of Atopy and Infections

Study Summary

“In a high-risk birth cohort, the persistence of asthma at age 13 years was most strongly associated with early wheezing illness with *Rhinovirus* and aeroallergen sensitization early in life”
How could infections promote development of asthma?\(^1\)

- Viral infections enhance airway epithelial production of IL-33 which promotes airway inflammation.

- Viral wheezing illnesses may damage the airway making it more susceptible to remodeling/obstruction.

- Respiratory infections and treatment may lead to airway dysbiosis.

- Allergic airway inflammation can promote impaired viral immunity.


Chung KF. Airway microbial dysbiosis in asthmatic patients: A target for prevention and treatment? JACI. April 2017:1071-80

- Bacteria in the digestive track and airway can affect both the development and progression of asthma

- Bacteria are present in the normal lung, but can be dysregulated in those with asthma

- Newer lab techniques (16s rRNA sequencing) has allowed for improved understanding of what bacteria are present in the lung
Airway Dysbiosis and Asthma

- Microbiome in the lung influenced by mode of delivery, diet, microaspiration, antibiotics, environment, and microbial exposures

- Bacteria in the normal lung is similar to oral microbiome

- Colonization of the upper airway in children with certain respiratory bacteria is associated with the development of asthma (*Haemophilus, Streptococcus, Moraxella*)
Study Summary

Improved understanding of the changes in the lung microbiome with asthma may lead to novel therapeutic targets

Environmental Determinants of Asthma

Early Exposures

- High levels of exposure to endotoxin in mattresses have been associated with reduced risk of asthma development\(^1\)

- Farm exposure, reduced risk of asthma in Amish vs. Hutterite\(^2,3\)

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Study Summary

Asthma risk may be reduced by environmental exposures to microbial dust which may be mediated, in part, through modulation of the innate immune inflammatory response. 


Asthma Interventions

- Reviewed various clinical trials and observational studies assessing the impact of Omalizumab on uncontrolled severe persistent asthma in the pediatric population.

- The data reviewed efficacy and safety of Omalizumab.

- Uncontrolled severe persistent asthma was defined as continued symptoms of asthma despite high dose inhaled corticosteroid plus a second controller agent.

Omalizumab

- Pediatric indication for omalizumab: Add-on therapy for uncontrolled severe asthmatic patients who are 6 years and older, first approved by EMA (2009), then the FDA (2016).

- Omalizumab is believed to work by binding to free IgE, thereby blocking IgE receptor binding on the surfaces of various allergic type cells. When this connection is broken, less inflammatory activation occurs. Overtime, this interplay is believed to cause further down-regulation of the inflammatory cascade by reducing levels of free IgE.
Omalizumab Efficacy Outcomes

*Overall reduction of daily corticosteroid requirement
*Decrease in incidence and frequency of exacerbations, both seasonally and out of season.
*Possible anti-inflammatory effect as evidenced by reduction of FENO levels while on omalizumab therapy.
*Possible preventative effect in regards to seasonal exacerbations when started 4-6 weeks prior to fall season

- Milogram (2001), Lanier (2009), PROSE study

Omalizumab Safety Outcomes

*Prescribing information focuses on two warnings: risk of malignancy and risk of anaphylaxis
*Risk of primary malignancy was similar in control and Omalizumab groups (EXCELS study)
*No statistically significant difference in overall risk of anaphylaxis between control and omalizumab groups (ICATA study and 2 studies involving 1381 patients)
*When anaphylaxis did occur, it was most frequently observed within first 3 doses and usually within 1 hour of dosing.

- EXCEL study, ICATA study
Study Summary

- Overall, Omalizumab is efficacious and safe for uncontrolled severe persistent asthma as an add-on therapy in the pediatric population.


- Background: Asthma in pregnancy has been associated with higher risk of hypertension during pregnancy. Historically there is limited data to show link between hypertensive disorders of pregnancy (HDP) and use of long acting bronchodilators.

- Hypertensive disorders of pregnancy include: gestational hypertension, preeclampsia, and eclampsia.

- Approximately 13% of pregnancies involve diagnosis of asthma.

- The importance of controlling asthma during pregnancy is underscored by health of mom and health of baby.
Asthma Control During Pregnancy

- Previous studies have found no significant increased risk of HDP with first-line inhaler corticosteroids or short acting beta-agonists.
- Long-acting beta-agonists are the second most utilized controller therapy for asthma but data is lacking.
- A few recent studies found increased HDP risk from LABA use however there were obvious limitations with both studies that encouraged further study, thus the advent of Blais’ study.

Methods

- Blais et al. study: Retrospective cohort study with data spanning over 20 years. Women had at least one asthma diagnosis prior to pregnancy.
- Fetal age 20-45 weeks gestation
- Maternal age 15-45 years
- Maternal asthma during pregnancy
- Excluded: Patients with documented chronic HTN or with HDP that were diagnosed prior to 20 weeks gestation, patients with filled LABA without ICS, patients with kidney disease/PCOS/Lupus/or on DMARDS.
Results

- 7853 women
- Mean age of mother was 26 years old
- Primarily urban population
- Most of the women had mild asthma
- Around 10% were impacted by HDP. outcomes were similar between women exposed to LABA and those not exposed to LABA

Study Summary

- Findings from this article suggest that women that require LABA during pregnancy that reach 20 weeks of gestation, are at no increased risk of developing HDP.
- There is strong evidence that poorly controlled asthma during pregnancy is detrimental to both mother and unborn child.
- Potential limitations: Use of medications was based on fill history not actual use.

- The review is beneficial as it finds limitations with original study that need to be considered.
- Original study found correlation between cockroach extermination and improved asthma in children in urban homes. Particularly, the children sensitized to cockroach were associated with most of the change.

Allergen exposure and Asthma

- Background: Idea of allergen exposure being linked with asthma morbidity dates back to 1964. Though there has been much association, there has been difficulty from an experimental standpoint. This may be why environmental measures are not focused on as much as medications in regards to asthma treatment.
- Dust mite: minimal effects
- Mouse: possibly some improvement
Take Home Messages

- Cockroach numbers tend to fall quickly with extermination but in Rabito's study, asthma symptoms improved slowly over a 6 month period.
- Cockroach allergen is in saliva, body part debris, and excretions from the cockroach. These things can remain despite exterminating the bug.
- Overtime, the level of allergen is reduced as continued cleaning occurs.
- Weaknesses with study: unblinded, possible investigator bias, modeled comparison between groups but no actual data for asthma-related outcomes.


- Pharmacists frequently receive refill requests for albuterol (SABA) and are often the first member of the health care team who is contacted when a patient’s asthma is not well controlled.
- When a refill request was made, a pharmacist investigated reason for refill and followed a protocol based on patient history and reason for refill to provide the refill, education or recommend a clinic visit with provider.
Results

- 84 patients included in the study (retrospective review)

- 50% of SABA requests were able to be refilled by the pharmacist

- 26% of those requesting refills were well controlled, 38% not well controlled and 36% very poorly controlled

- Pharmacists facilitated a clinic visit in 49% of requests and 61% of these attended the appointment

- Asthma education was delivered to 82% of caregivers
**Study Summary**

Evaluating asthma control when patients request a SABA refill can help identify those who need evaluation/are not well controlled

A large % of patients (50%) requesting SABA refill needed an appointment/evaluation

Pharmacists can provide meaningful point of care asthma education

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- Study evaluated the safety and efficacy of adding on tiotropium to either high dose ICS or medium dose ICS with 2 or more controller therapies in children aged 6-11 years old
- 12 week, double blind, placebo controlled trial
- The primary end point was peak FEV1 3 hours after dosing (comparing before vs. after intervention)
- Participants continued their standard controller therapies
- Also evaluated for side effects
### Study Summary

- The addition of Tiotropium 5ug daily to standard therapy improved peak FEV1 after dosing compared to placebo.

- Safety and tolerability comparable with placebo.

### Asthma Education

- Youth are often not active participants in asthma visits
- Only 13% of adolescents asked questions about their asthma management despite high rate of asthma-related problems or concerns
- Most asthma visits are dominated by parents and providers

- Enrolled 359 children aged 11-17 with persistent asthma (and parents) from 4 pediatric clinics (rural and suburban)
- Randomized to either standard care OR standard care + intervention which including watching an asthma video on an iPAD and reading an asthma question prompt list
- Video was 11 minutes (triggers, staying active, symptoms, how to keep parents off your back about asthma, how to talk to your provider and having self-management confidence)
- Question prompt list introduced common questions people have about asthma and management
- Office visits were then taped and analyzed
Results

- Intervention dramatically increased children’s question asking about medications, triggers and environmental control

- Caregiver (parental) question asking unchanged

- Providers were much more likely to spend time educating youth who asked questions

Study Summary

Use of videos or discussion prompt lists help youth become more actively involved in their asthma visits and management

It’s important to remember that providers were less likely to offer education if the youth did not ask questions.

- Historically poor inhaler technique has been linked to poor asthma outcomes. This study investigated different types of inhaler technique mistakes and how they related to asthma outcomes.

- 5000 adults (16 years and older) from 2011 to 2014. Utilized iHARP database (an asthma review service). Inhaler errors were verified by HCP trained in inhaler technique.

- Analysis of device cohorts: Metered-dose inhalers vs. Dry-powder. 3 cohorts total: Turbo-haler Symbicort (DPI), Diskus-Seretide (DPI), and Seretide (MDI).

- Error frequency, asthma symptom control, and exacerbation rate were all analyzed to pinpoint errors in inhaler use.

- Inclusion: Diagnosis of asthma. Exclusion: Diagnosis of COPD or other chronic respiratory disease.

- Primary outcome was asthma control. Secondary outcome was exacerbation rate in 12 month period.

Results

- 4276 patients were available to study but final sample was 3660.

- Of the study sample: 46% controlled asthma, 34% partly controlled asthma, 19% uncontrolled asthma

- Common errors: insufficient inhalation (lack of fast/forceful inhale in DPI, lack of slow/deep inhale in MDI, not having head tilted and chin up in all devices, not breathing out to empty lungs first) AND twist errors (not hold device upright in turbohalers, not twisting base twice in turbohalers)

- The authors define the most Critical Errors to be: Insufficient inspiratory effort with DPIs and poor coordination between the start of inhalation and actuation of dose with MDIs.

- Inhaler errors were associated with risk of uncontrolled asthma status. In Turbohaler and MDI cohorts, 8 of 14 errors had significant association. In DPI cohort, 4 of 14 had significant association.

- Inhaler errors were associated with increased rate of exacerbation
Association between Errors and Asthma Symptoms

Study Summary

The importance of teaching inhaler technique is underscored as poor inhaler technique is associated with poor asthma outcomes.

Changing Practice: Value of reviewing technique with each visit and checking technique when able.

- Inhaler technique is an important part of medication delivery and hence asthma control.
- Inhaler errors have been observed in up to 86% of asthma/COPD patients.
- Certain critical errors are associated with poor asthma control and asthma exacerbations.
- In person educational models for teaching inhaler techniques have been effective but memory of proper inhaler use can wane over time.
- This study looked at outcomes related to virtual education for inhaler techniques once patients were discharged from the hospital.
- Surveys of educations model and in person focus groups were used to assess access, functionality, and quality of the virtual educational program.
- 18 years and older, English speaking, asthma/COPD diagnosis (2 different cohorts)

Results

- 48 participants, predominately Female and African American
- Internet access and use was generally high across all participants but Asthma cohort tended towards smart phones and COPD cohort preferred computers and has less access to wifi
- Willingness to use virtual education post hospital-discharge was high across groups, access to virtual education was available for all in some form or another.
- Themes: 1) Internet access and technological literacy were imperative for access to educational materials. 2) Usefulness and teaching strategy were important for functionality of educational materials. 3) Clarity, ease of use, and length of video were identified as quality measures.
Study Summary

Overall the virtual teach-to-goal educational module for inhalers is a feasible option for continuing asthma education once outside of the hospital setting.

Changing Practice: Value of this particular educational module for patients is likely helpful for patients post-clinic as well (not just hospital). Understanding that modules should be tailored to different groups in order to address cultural and socioeconomic differences.

References

3. Chung KF. Airway microbial dysbiosis in asthmatic patients: A target for prevention and treatment? JACI. April 2017;1071-80