ASTHMA IN ADULTS AND ADOLESCENTS UPDATE INCORPORATING THE 2020 FOCUSED UPDATES TO THE ASTHMA MANAGEMENT GUIDELINES (NAEPP) AND THE 2019GLOBAL INITIATIVE FOR ASTHMA (GINA)

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(No conflicts to report)

CASE 1

- 44 yo M with mild intermittent asthma presents with 5 days of wheezing, chest tightness, cough, SOB
- BP 130/80, pulse 92, sat 92%
- Has been using his albuterol inhaler Q4 hours
- How would you treat?

ASTHMA PEARLS

- Asthma will affects 40 million people in their lifetimes
- 78% of asthma care is done by PCPs
- New Guidelines released in 2019 and 2020 (GINA (Global initiative for Asthma & NAEPPCC National Asthma Education and Prevention Program coordinated by the NHLBI)
- New evidence favors using combined ICS along with BD for flares – even in mild intermittent

LET'S START WITH THE DEFINITION

- GINA (Global Initiative for Asthma) Asthma is a heterogenous disease usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, SOB, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation.
- NAEPP (National Asthma Education and Prevention Program). Asthma is common chronic disorder of the airways that is complex and characterized by variable and recurring symptoms, airflow obstruction, bronchial hyperresponsiveness and an underlying inflammation.

DEFINITION HAS SIGNIFICANT OVERLAP WITH COPD

- COPD generally has less reversibility
- Smoking history and age are factors to be considered
- Asthma – COPD overlap is not uncommon
- Common disease in childhood with a variable course over time
- Some evidence for adult onset
- Sub-types: occupational, aspirin sensitive, eosinophilic asthma

COMMON TRIGGERS:

Allergens (dust mites, molds, cockroaches, pollen, cats, dogs and other animals

Viral infection

Exercise

Cold air

Mold

Smoke

Aspirin (cough, wheeze chest tightness) about 7% of adults with asthma – rare in kids

CONTRIBUTING FACTORS

- Poor inhaler technique
- Smoking
- Treatment nonadherence
- Environmental exposure
- GERD
- Social dominants of care
- OSA
- Chronic sinusitis
- Other cardiopulmonary conditions

EVALUATION PART 1 SPIROMETRY

- FEV1/FVC ratio will be <0.7 - obstructive pattern
- Severity of obstruction graded by degree of reduction in FEV1
- FEV1 > 70% predicted mild
- FEV1 50-69% of predicted moderate
- FEV1 <50% predicted severe

EVALUATION PART 2 BRONCHODILATOR RESPONSE

- Acute reversibility of airflow obstruction is tested by giving 2-4 puff of short acting bronchodilator and repeating spirometry in 1-15 minutes
- 12% and 200ml improvement (or 20% increase in PEF) is still is used in GINA recs
- 2020 NAEPPCC guidelines: post BD value –Pre BD value X 100/predicted value where value is either FEV1 or FVC. An increase >10% is significant
- False normal in cough variant asthma, scarring, use of controller meds, minimal sxs/obstruction at the time of testing

BRONCHOPROVOCATION TESTING

- Inhaled methacholine, mannitol, exercise, or hyperventilation of dry air
- Can follow with bronchodilator
- False + in about 5%
- False negatives rare

PEAK FLOW

- Simple, inexpensive
- Good for monitoring patients with known asthma rather than diagnosis
- Repeat X3; use the highest

NORMAL BASED ON HEIGHT, AGE, SEX

- Not used for diagnosis
- Spirometry with BD challenge is preferred for diagnosis

DIAGNOSIS: CLINICAL VS TESTING

- Pt with repeated episodes of typical symptoms triggered by typical stimuli with wheezing and response to medication.
- NAEPP and GINA recommend validation with objective data but many would forgo spirometry in typical cases and use spirometry for patients with less typical, more persistent, or refractory symptoms

GOALS OF TREATMENT

- Control asthma related symptoms, maintain normal activities, and minimize risk for exacerbations.
- Good control means minimal cough, wheeze, SOB, 2 or less night time awakenings per month, 2 or less rescue meds per week

ASSESSMENT OF ASTHMA SEVERITY -INTERMITTENT

- Daytime sxs 2 or less per week
- 2 or less awakenings per mo due to asthma
- Use of SABA 2 or fewer times per week
- FEV1 >80 % between exacerbations
- FEV1/FVC normal between exacerbations
- 1 or no exacerbations requiring oral steroids per year

MILD PERSISTENT

- Sxs > 2 per week < than daily
- 3-4 nocturnal awakenings per mo due to asthma
- SABA >2 but less than 7 per week
- Minor interference with normal activities
- FEV1 > 80% of predicted

MODERATE PERSISTENT

- Daily sxs of asthma
- Nocturnal awakenings from asthma weekly
- Daily need for SABA
- Some limitation of normal activity
- FEV1>60 and <80 % and FEV1/FVC below normal

SEVERE PERSISTENT

- Asthma sxs throughout the day
- Frequent night time awakenings from asthma
- SABA multiple times per day
- Extreme limitation in activites

THERAPY FOR INTERMITTENT ASTHMA

- As needed SABA (albuterol or levalbuterol)
- A new approach advocated by the Global Initiative for Asthma (GINA) is budesonide-formoterol 80-4.5 1-2 puffs BID PRN (Symbicort)
- Formoterol has both a rapid onset and long duration of action
- This approach is off label
- Alternative is to use a low dose ICS whenever a LABA is used
- Prior to exercise can use 2 puffs SABA or can use budesone-formoterol combo

EVIDENCE TO SUPPORT ICS+SABA

- Reliever triggered inhaled glucocorticoid in Black and Latinx adults with asthma. NEJM 22 Feb 26
- Albuterol-Budesonide Fixed Dose Combination Rescue Inhaler for Asthma NEJM 22 June 2

RESEARCH SUMMARY

Reliever-Triggered Inhaled Glucocorticoid in Black and Latinx Adults with Asthma

Israel E et al. DOI: 10.1056/NEJMoa2118813

CLINICAL PROBLEM

Black and Latinx adults are disproportionately affected by asthma, and attempts to address this disparity have been largely unsuccessful. Use of a single inhaler containing a glucocorticoid and a β_2-agonist for both maintenance and as-needed reliever therapy can reduce asthma exacerbations in patients with moderate-to-severe asthma but has not been well studied in Black and Latinx patients, who may face barriers to its use.

CLINICAL TRIAL

Design: A pragmatic, open-label, randomized trial enrolled 1201 Black and Latinx adults with moderate-to-severe asthma.

Intervention: Participants were assigned either to use a patient-activated, reliever-triggered inhaled glucocorticoid strategy plus usual care or to continue usual care. Participants in the intervention group received one-time instruction on using the glucocorticoid inhaler, which delivered a metered dose of 80 μg of beclomethasone dipropionate, each time they used their quick-reliever inhaler or nebulizer. The primary end point was the annualized rate of severe asthma exacerbations.

RESULTS

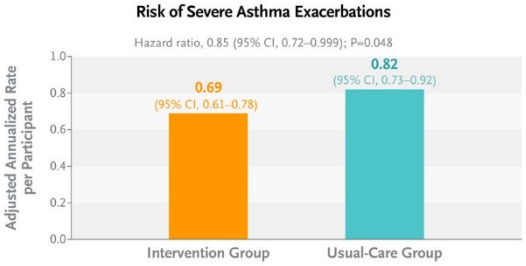
Efficacy: At a median follow-up of 15 months, the annualized rate of severe asthma exacerbations was significantly lower in the intervention group than in the control group.

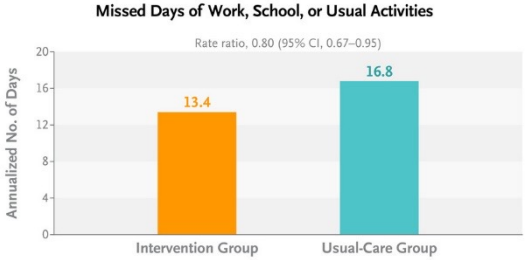
Safety: The incidence of serious adverse events was similar in the two groups.

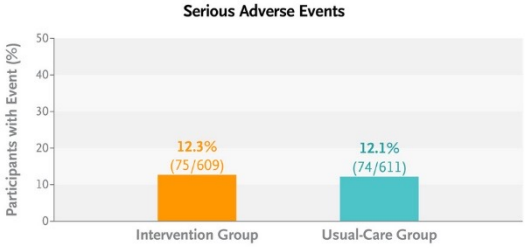
LIMITATIONS

- The trial was open-label, and inhaled glucocorticoids were provided at no cost, which could have affected the findings.
- Most of the trial participants were women, so the findings may not be as generalizable to men.
- Participants identified as Black or Latinx, but the trial included many different ethnic groups that may differ in asthma morbidity and in responsiveness to this treatment strategy.

Links: Full Article | NEJM Quick Take | Editorial







CONCLUSIONS

Adding inhaled glucocorticoids to as-needed reliever therapy led to a lower rate of severe asthma exacerbations among Black and Latinx adults with moderate-to-severe asthma.

MILD PERSISTENT

- Los dose ICS daily or low dose ICS LABA
- Alternative (GINA) budesonide-formoterol PRN (off label)
- Leukotriene modifier (i.e. montelukast)

MODERATE PERSISTENT

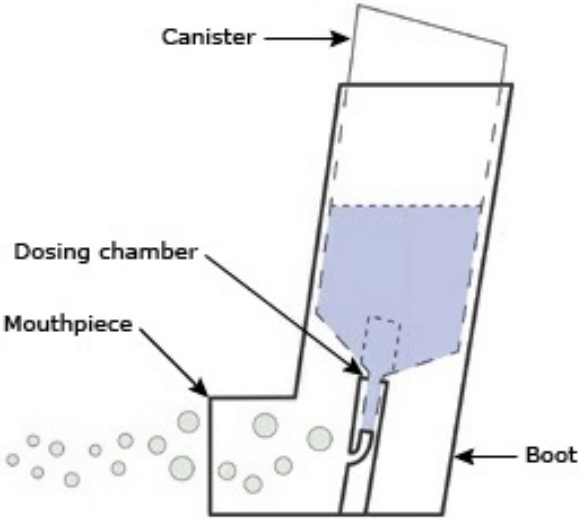
- Low dose ICS + LABA
- If using budesonide formoterol; can do both daily + quick relief of symptoms SMART (single inhaler maintenance and reliever therapy). Likely can do the same with mometasone-formoterol (Dulera)
- LABAs no longer carry any black box warnings
- Alternate to SMART is ICS + LABA and SABA PRN
- LAMA (tiotropium) can be used in place of LABA if pt intolerant of LABA

SEVERE PERSISTENT

- Medium or high dose ICS + LABA
- Leukotriene modifier Montelukast, zafirlukast, zileuton), tiotropium or biologic
- Addition of LAMA to ICS is helpful but not if already on ICS/LABA
- Triple tx (ICS, LABA, LAMA) approved for tx of severe persistent (Trelegy)

	Low Dose	Medium Dose	High Dose
Beclomethasone HFA (QVAR Redihaler) 40mcg, 80mcg	80-160 mcg 2 divided doses	>160-320 mcg 2 divided doses	>320-640 mcg 2 divided doses
Budesonide DPI (Pulmicort Flexhaler) 90mcg, 180mcg	180-360 mcg 2 divided doses	>360-720 mcg 2 divided doses	>720-1440 mcg 2 divided doses
Ciclesonide HFA (Alvesco) 80mcg, 160mcg	160 mcg 2 divided doses	320 mcg 2 divided doses	640 mcg 2 divided doses
Fluticasone propionate HFA (Flovent HFA) 44mcg, 110mcg, 220mcg	176-220 mcg 2 divided doses	>220-440 mcg 2 divided doses	>440-1760 mcg 2 divided doses
Fluticasone propionate DPI (Flovent Diskus) 50mcg, 100mcg, 250mcg	100-250 mcg 2 divided doses	>250-500 mcg 2 divided doses	>500-2000 mcg 2 divided doses
Fluticasone propionate DPI (Armonair Digihaler) 55mcg, 113mcg, 232mcg	110 mcg	226 mcg 2 divided doses	464 mcg 2 divided doses
Fluticasone furoate DPI (Arnuity Ellipta) 50, 100, 200mcg	50 mcg	100 mcg	200 mcg
Mometasone DPI (Asmanex Twisthaler) 110mcg, 220mcg	220 mcg	>220-440 mcg	>440 – 880 mcg 2 divided doses
Mometasone HFA (Asmanex HFA) 100mcg, 200mcg	200 mcg 2 divided doses	>200-400 mcg 2 divided doses	>400-800 mcg 2 divided doses

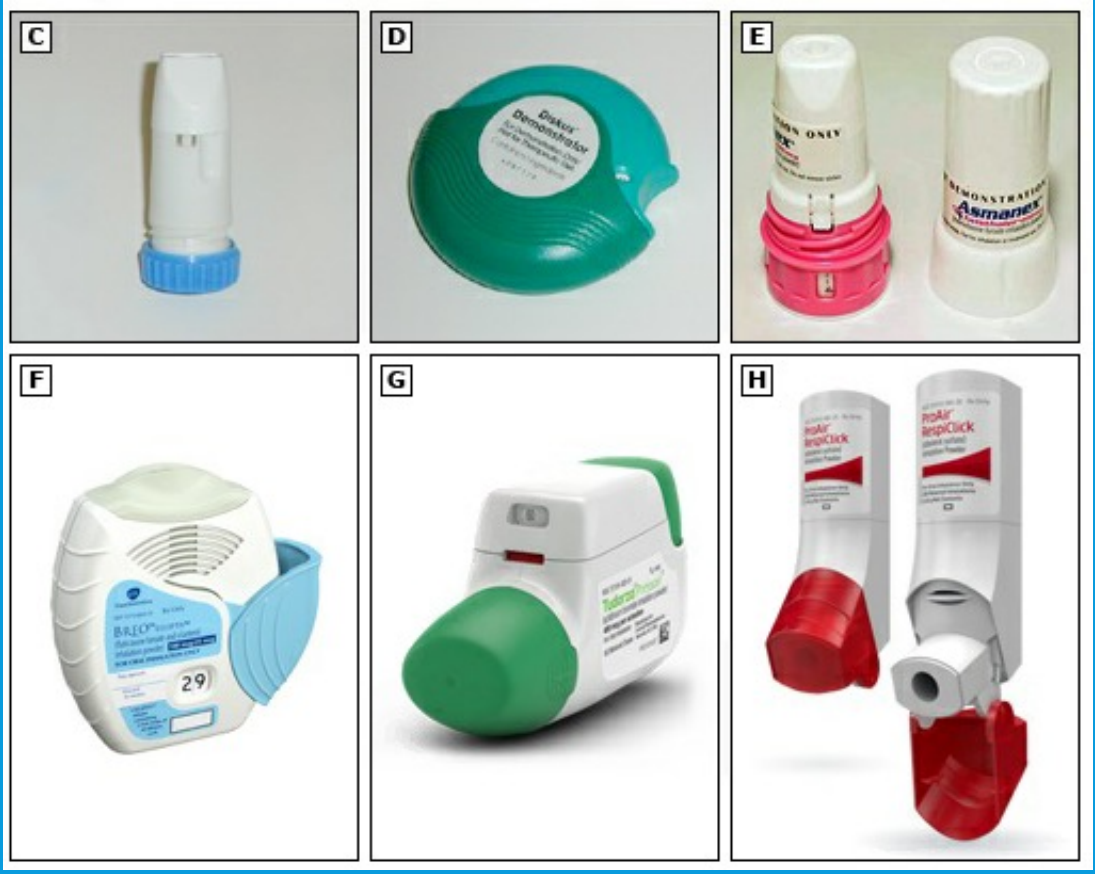
METERED DOSE INHALERS



Medication is stored under pressure in the canister and released from the dosing chamber when the canister is pressed downward.

Graphic 62613 Version 4.0. 2022. UpToDate. Uptodate.com.

DRY POWDER INHALERS



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RESEARCH SUMMARY

Albuterol–Budesonide Fixed-Dose Combination Rescue Inhaler for Asthma

Papi A et al. DOI: 10.1056/NEJMoa2203163

CLINICAL PROBLEM

Patients typically treat acute asthma symptoms with short-acting β_2-agonist (SABA) rescue therapy. However, SABAs do not treat inflammation, leaving patients at risk for severe exacerbations. Whether rescue therapy with a fixed-dose combination of a SABA (albuterol) plus a glucocorticoid (budesonide) can improve outcomes is unknown.

CLINICAL TRIAL

Design: A multinational, phase 3, double-blind, randomized trial evaluated the safety and efficacy of as-needed use of a fixed-dose combination of albuterol and budesonide, as compared with albuterol alone, in patients with uncontrolled moderate-to-severe asthma receiving inhaled glucocorticoid-containing maintenance therapy.

Intervention: Adults and adolescents were randomly assigned to receive, on an as-needed basis, 180 μg of albuterol plus 160 μg of budesonide, 180 μg of albuterol plus 80 μg of budesonide, or 180 μg of albuterol; the treatments were delivered through a single metered-dose inhaler. Children 4 through 11 years of age were assigned only to the lower-dose combination group or the albuterol-alone group. Participants continued their baseline glucocorticoid-containing maintenance therapies. The primary efficacy end point was the first severe asthma exacerbation in a time-to-event analysis.

RESULTS

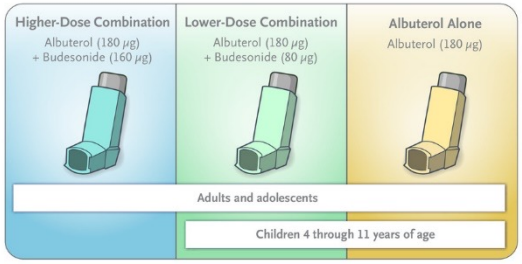
Efficacy: 3123 patients were assessed with respect to the efficacy end points. During a minimum follow-up of 24 weeks, the higher-dose combination of albuterol–budesonide significantly reduced the risk of severe asthma exacerbations, as compared with albuterol alone. The difference between the lower-dose combination and albuterol alone was not significant.

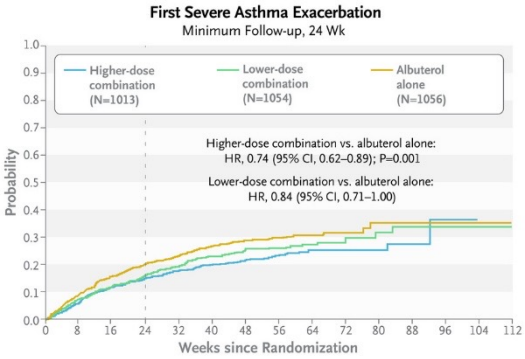
Safety: The incidence of adverse events was similar across the three trial groups.

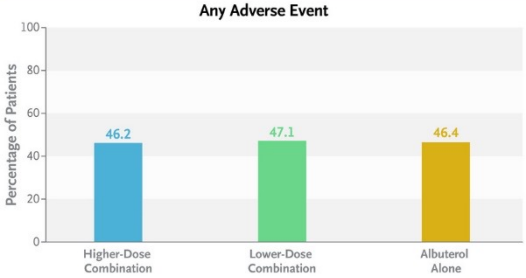
LIMITATIONS AND REMAINING QUESTIONS

- The fraction of exhaled nitric oxide level was not measured, a limitation that precludes direct assessment of antiinflammatory effects.
- A small number of children 4 to 11 years of age were included; thus, no conclusions in this age group could be drawn.

Links: Full Article | NEJM Quick Take | Editorial







CONCLUSIONS

Among patients with uncontrolled moderate-to-severe asthma receiving inhaled glucocorticoid-containing maintenance therapy, as-needed use of 180 μg of albuterol plus 160 μg of budesonide reduced the risk of severe asthma exacerbations, as compared with albuterol alone, without increasing the incidence of adverse events.

IN SEVERE ASTHMA MAY CONSIDER DETERMINING PHENOTYPE

- Type 2 asthma includes allergic and eosinophilic asthma
- Non Type 2 asthma is associated with obesity and smoking and is driven by neutrophils
- About 50% of severe asthma patients are Type 2 and respond to new biologics
- It is identified by eosinophils in blood > 150 per UL or sputum > 2% or elevated ferrous nitrous oxide > 20 parts per billion
- Current biologics: omalizumab (Xolair), mepolizumab (Nucala), reslizumab (Cinqair), dupilumab (Dupixent), benralizumab (Fasenra)

MONITORING RESPONSE

- Asthma Control Test (ACT)
- Spirometry
- PEF monitor
- Fractional exhaled nitric oxide (FENO)
- Sputum eosinophils

ADJUSTING MEDICATION

- Asthma is inherently variable so adjusting medication to achieve control and minimize adverse effects makes sense
- In addition to increasing the potency of the ICS, addition of LAMA, or leukotriene modifier, or referral to specialist may be appropriate.
- Dupilumab is approved for severe eosinophilic asthma
- Reducing medication is important to reduce long term exposure to high doses of inhaled corticosteroids

UNCONTROLLED, DIFFICULT TO TREAT AND SEVERE ASTHMA

- Uncontrolled is characterized by poor symptom control or frequent exacerbations
- Difficult to treat is uncontrolled despite adherence to ICS + second controller and need for frequent OCS
- Severe asthma is a subset of difficult to treat asthma in which the disease is uncontrolled despite adherence to optimal management or worsen when high intensity therapy is decreased.

UPDATED ASTHMA DIAGNOSIS AND MANAGEMENT RECOMMENDATIONS FROM GINA (GLOBAL INITIATIVE FOR ASTHMA)

- As needed SABA not recommended
- As needed low dose ICS/formoterol combo preferred in adolescents and adults with asthma
- When PRN ICS/formoterol not controlling symptoms, change to daily dosing

ASTHMA MANAGEMENT GUIDELINES FOCUSED UPDATE 2020 NIH/NHLBI

- First US Update in 10 years; focuses on 6 key areas
- For mild to moderate persistent asthma, single maintenance and reliever therapy (SMART) is preferred
- For moderate to severe asthma, SMART with ICS/formoterol daily + PRN is preferred. This is not FDA approved. Advair is not an alternative. Unknown if fluticasone/vilanterol (Breo) or Mometasone/formoterol(Dulera) are appropriate for SMART
- Indoor allergy mitigation is conditionally recommended
- Immunotherapy is conditionally recommended as an adjunct for patients with mild to moderate allergic asthma

ASTHMA MANAGEMENT GUIDELINES FOCUSED UPDATE 2020 NIH/NHLBI CONTINUED

- Fractional Excretion of Nitric Oxide (FeNO) has limited utility for guiding care in primary care setting. Should not be used to predict asthma in patients from birth to four years of age.
- In pts with asthma not controlled with ICS alone, add LABA first. Only use LAMA when LABA is not tolerated.

CASE 1

- 44 yo M with mild intermittent asthma presents with 5 days of wheezing, chest tightness, cough, SOB
- BP 130/80, pulse 92, sat 92%
- Has been using his albuterol inhaler Q4 hours
- How would you treat?

DETERMINE SEVERITY OF EXACERBATION

What is the peak flow? Can use best or calculated to determine %

Daytime sxs

Nighttime sxs

Wheezing

O2 sat

Work of breathing

OPTIONS ABOUND

- Nebulized albuterol in clinic 2.5 mg (can repeat q20min for 1 hr)
- 4 puff MDI (can repeat Q20 min for 1 hr)
- For milder exacerbations can start formoterol/budesonide as shown to be effective in the studies above. Can take 1-2 inhalation q 20 for 1 hour (6 puffs) with a max of 12 puff per day
- Prednisone 40-60mg daily for 5 days (for moderate to severe exacerbations (PEF 5-80% of predicted or best)
- If pt was on ICS could quadruple the dose for 14 days instead of oral prednisone

THANK YOU!