The role of inhaled steroids and bronchodilators in asthma

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Objectives

Describe the role of therapy based on GINA and EPR-3 recommendations

Compare and contrast the mechanism of action and effectiveness of inhaled steroids and bronchodilators for the management of persistent asthma

Highlight device characteristics to aid in device selection/matching with patient characteristics
ROLE OF THERAPY BASED ON GINA AND EPR-3

Asthma guidelines

GINA
Updated yearly
Stepwise management - pharmacotherapy

**Asthma guidelines**

EPR-3 2007

GINA 2016, Box 3-5 (2B) (upper part)
MECHANISM OF ACTION AND DEVICES

Common treatments for the medical management of Asthma

Quick-relief “rescue”
- Short-acting bronchodilators pm (beta 2 agonists - SABAs - preferred)
- “Burst” of systemic corticosteroids

Long-term control
- Inhaled corticosteroids (ICS)
- Long-acting muscarinic antagonist (LAMA)
- Combination therapy (inhaled corticosteroids and long-acting beta 2 agonists (ICS/LABA)
- Leukotriene modifiers
- Biologic agents
Mechanism of Action:
short-acting beta 2 agonists (SABAs)
**Dry powder** albuterol
Proair Respiclick Open-Click-Inhale

Quick-relief "rescue"

SABAs preferred: Ventolin, Proventil. Proair MDI and Respiclick - ALL ALBUTEROL, Xopenex (LEVALBUTEROL), Atrovent (IPRATROPIUM), Duoneb, Combivent (BOTH ALBUTEROL & IPRATROPIUM), Spiriva (Tiotropium)

OCS: Prednisone, Medrol, Prelone

Relative Risk of Hospitalization in the US

Donahue et al. JAMA. 1997;277:887-891.
Common treatments for the medical management of Asthma

**Quick-relief “rescue”**
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Mechanism of action: ICS
Effects of Inhaled Corticosteroids on Inflammation

Pre- and post-3-month treatment with budesonide (BUD) 600 mcg b.i.d.

Low-dose ICS and the Prevention of Death From Asthma in Canada

Rate Ratio for Death from Asthma

Number of Canisters of ICS per Year
Relative Risk of Hospitalization in the US

Donahue et al. JAMA. 1997;277:887-891.

Common treatments for the medical management of Asthma

Introduction of generic fluticasone propionate: ArmonAir

Long-term control
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Common treatments for the medical management of Asthma

Introduction of QVAR RediHaler
breath-actuated MDI device

Long-term control
- Inhaled corticosteroids (ICS)
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Introduction of Arnuity Ellipta - different fluticasone esters (furoate vs. propionate)

FF confers higher affinity for lung tissue compared with FP
Translates to enhanced lung residency and once-daily efficacy in asthma
Some evidence that the characteristics of FF may result in superior symptom reduction compared with FP
Common treatments for the medical management of Asthma

- **Long-term control**
  - Inhaled corticosteroids (ICS)
  - Long-acting muscarinic antagonist (LAMA)
  - Combination therapy (inhaled corticosteroids and long-acting beta 2 agonists (ICS/LABA))
  - Leukotriene modifiers
  - Biologic agents

- **Spireva Respimat (tiotropium)**
  - FDA approved for 6+ Feb 2017
  - 2 inhalation once daily

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Ellipta Steps

1. PREPARE
2. INHALE
3. CLOSE
Mechanism of Action:
long-acting muscarinic antagonist (LAMA)
Stepwise management - pharmacotherapy

Respirmat SMI
Respimat SMI

PRIME FOR FIRST-TIME USE

The following steps are needed to fill the dosing system the first time you use it and will not affect the number of doses available. After preparation and initial priming, your SIRVA RESPIMAT inhaler will be able to deliver the labelled number of doses.

Proper priming of the inhaler is important to make sure the correct amount of medicine is delivered.

1. Hold the inhaler upright, with the base cap closed, to avoid accidental release of dose.
2. Tilt the clear base in the direction of the black arrows on the label until it clicks (half a turn).
3. Flip the base cap until it snaps fully open.
4. Point your SIRVA RESPIMAT inhaler toward the ground away from your face. Press the dose-release button. Close the base cap.
5. Repeat steps 5, 6, and 7 until a spray is visible.
6. Once the spray is visible, you must repeat steps 5, 6, and 7 three more times to make sure the inhaler is prepared for use.

Your inhaler is now ready to use. These steps will not affect the number of doses available. After preparation and initial priming, your SIRVA RESPIMAT inhaler will be able to deliver the labelled number of doses.

Respimat Daily Use  T-O-P (Turn, Open, Press)
Common treatments for the medical management of Asthma

Black box warning removed against all LABAs Dec 2017
Mechanism of Action:
long-acting beta 2 agonists (LABAs)

Common treatments for the medical management of Asthma

New combinations
Breo Ellipta: fluticasone furoate (vs. propionate) and vilanterol (vs. salmeterol) allows for once a day dosing (UICS/ULABA)

AirDuo Resp: salmeterol)
Asthma Topics

1. Role of Adjustable Medication Dosing in Recurrent Wheezing and Asthma
2. Role of Long Acting Anti-Muscarinic Agents (LAMAs) in Asthma Management as Add-on to ICSs
3. Role of Bronchial Thermoplasty in Adult Severe Asthma
4. Role of Fractional exhaled Nitric Oxide (FeNO) in Diagnosis, Medication Selection, and Monitoring Treatment Response in Asthma
5. Role of Remediation of Indoor Allergens (e.g., House Dust Mites/Animals/Pests) in Asthma Management
6. Role of Immunotherapy in Treatment of Asthma

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Adjustable Medication Dosing

“Intermittent Therapy,” adjusting the dosing regimen for ICSs

• cost savings
• sparing potential side effects of ICSs, especially in children
• possibly reducing the need for oral corticosteroids

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Triple therapy: ICS/ABA/LAMA

DEVICE CHARACTERISTICS
Respiratory and non-respiratory diseases use inhalational therapy

Requires treatment by inhalation to deliver to the lungs (max benefits) with least side effects.

Technically possible by modulating particle size through inhaler design, and by adjusting excipients and propellants.

Respiratory Tract Deposition

![Particle Size/Airway Deposition](chart)

<table>
<thead>
<tr>
<th>Particle Size</th>
<th>Result</th>
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<tbody>
<tr>
<td>&gt;5 μm</td>
<td>No clinical efficacy</td>
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<tr>
<td></td>
<td>Systemic absorption if swallowed</td>
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<tr>
<td>2-5 μm</td>
<td>Clinical effect</td>
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<tr>
<td>&lt;2 μm</td>
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</table>

Courtesy R. Pleasants
MDIs

Solutions
QVAR and Alvesco
No need to shake
< 2 microns in size - reach smaller airway
Pro-drug

Suspensions
All other MDIs are suspensions
Have to be shaken between puffs
> 3 microns in size – reach bronchial/conducting tubes

In-check Dial

Device used to check inhaler technique
Billable teaching
Should be used at every visit to confirm proper inhaler technique

Optimum Inspiratory Flow

<table>
<thead>
<tr>
<th>Inhaler</th>
<th>20</th>
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<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>80</th>
<th>90</th>
<th>100</th>
<th>110</th>
<th>120</th>
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<td>Accuhaler/Disku</td>
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<td>Turboshaker/Turbolizer</td>
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<td>Easi-breath/Surehaler</td>
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<td>Low resistance pMDI</td>
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June 2000
Original In-Check Dial

New In-Check Dial

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Respiratory and non-respiratory diseases use inhalational therapy

Requires treatment by inhalation to deliver to the lungs (max benefits) with least side effects

Technically possible by modulating particle size through inhaler design, and by adjusting excipients and propellants

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Excipient

Peanut can cross-react with soy but not enough to cause reaction

Lecithin is no longer used as an emulsifier in Atrovent
## Dry Powder Inhalers

<table>
<thead>
<tr>
<th>Metering</th>
<th>Dispersion</th>
<th>Oropharyngeal Deposition</th>
<th>Pulmonary Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passive</td>
<td>Passive/Active</td>
<td>Passive/Active</td>
<td>Active</td>
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</tbody>
</table>

Telko and Hickey (2005). Respir Care 50, 1209-1227.

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### Spacers and VHCs

Increase medication delivery to the lower airways by reducing oral deposition of particles and by enhancing hand-mouth coordination with activation.

Spacer is a generic term for any open tube placed on the MDI mouthpiece to extend its distance from the mouth.

VHCs are manufactured with a one-way valve that prevents exhalation into the device.

Activate only once into VHC/spacer.

Rinsing with diluted household detergents should prevent static electricity and enhance delivery to lungs (or use anti-static device).
Spacers and Inhaled Drug Delivery

Respiratory and non-respiratory diseases use inhalational therapy

Asthma & COPD

Requires treatment by inhalation to deliver to the lungs (max benefits) with least side effects

Technically possible by modulating particle size through inhaler design, and by adjusting excipients and propellants
HFA propellant allows for smaller particle size

Amounts of CFCs exempted, used, on hand at the end of each year (tons), 1996-2014
Metered dose inhalers and the Montreal Protocol

CFCs were replaced with HFAs (HFCs) in 2008 (US)
95% use HFC-134a
5% use HFC-227ea
HFAs are CFC-free but is still a GHG

Proportions of doses delivered by MDIs and DPIs in different regions, 2012
In 2014 630 million MDIs were manufactured using 9400 tons of CFC-free HFAs

Do HFAs have a carbon footprint - global warming potential (GWP)?

Digitized respiratory disease
Digitized respiratory disease

Transferable or embedded systems

– Reminder systems
– Smart sensors
  • Use
    – Records dose taken (time and date stamp)
    – Inhaler shaken
    – Flow detected by pressure changes/acoustic sensors
  • Location
  • Technique instructions

Connected devices

– Smart sensor data
– Gather patient-reported data
– Link to education/support
– Push alerts
– At the individual level may help patient, payer and provider to identify patterns
– BIG data
  • Population health
  • Personalized medicine

Your inhaler’s watching you: drugmakers race for smart devices

Ben Hirschler

LONDON (Reuters) - Makers of inhalers to treat asthma and chronic lung disease are racing to develop a new generation of smart devices with sensors to monitor if patients are using their puffers properly.