New Trends in Management of Asthma

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Why new trends in for Asthma management?

• Rise in Asthma Prevalence
• Increase acute exacerbations
• Increase morbidity
• Increase ED visits
• Increase hospitalizations
• Consumed more health care resources
Why do we need a new approach!

• Substantial advances in scientific knowledge about
  - Nature of asthma
  - Wide range of new medications
  - Understanding of important emotional, behavioural, social aspects of asthma care

• In spite of these efforts
  - Evidence of suboptimal asthma control
  - Poor adherence to existing guidelines
Why do we need a new approach!
Outline

New trends ......

• New GINA guideline
• Asthma Management
• Asthma Control
• Future treatment for asthma
New GINA guideline - 2015

The changes include

• Revised asthma definition
• Tools for assessing symptom control and risk factors for adverse outcomes
• Expanded indications for inhaled corticosteroid therapy
• Targeted treatment based on phenotype, modifiable risk factors & patient preference
• Optimisation of medication effectiveness by addressing inhaler technique and adherence
New GINA guideline - Updated

• A new definition of asthma –
  “Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.

• importance of individualising patient management not only by using genomics or proteomics, but also with “humanomics”
Clinical approach to a patient suspected of Asthma

- Arriving at a clinical diagnosis
- Excluding other possible differential diagnosis
- Assessing aggravating and relieving factors
- Assessing severity
- Assessing for accompanying asthma related co-morbidities
Goals for successful management of Asthma

• Achieve and maintain control of asthma symptoms
• Maintain normal activity levels, including exercise
• Maintain pulmonary function as close to normal as possible
• Prevent asthma exacerbations
• Avoid adverse effects from asthma medications
• Prevent asthma mortality
Key Priorities in Management of Asthma

The GINA cycle of asthma care

- Diagnosis
  - Symptom control and risk factors (including lung function)
  - Inhaler technique and adherence
  - Patient preference

- Assess
  - Asthma medications
  - Non-pharmacological strategies
  - Treat modifiable risk factors

- Adjust treatment
  - Symptoms
  - Exacerbations
  - Side-effects
  - Patient satisfaction
  - Lung function

- Review response

Good communication is essential – establish a partnership with the patient
- Consider health literacy, personal goals and fears, and cultural issues

Treatment choices
- Population-level decisions: efficacy, effectiveness, safety, cost, regulations
- Patient-level decisions for tailoring treatment: also discuss patient characteristics (phenotype) that predict response or risk; patient preference; practical issues inhaler technique, adherence, and cost; treat modifiable risk factors; use non-pharmacological strategies where appropriate

Stepwise medication adjustment
- Consider stepping up if uncontrolled symptoms, exacerbations or risks, but check diagnosis, inhaler technique, adherence, and cost; treat modifiable risk factors; use non-pharmacological strategies where appropriate
Management of Asthma

Basic principles
• Stepwise management of Asthma
• Divided into 3 groups based on age (0-4 y, 5-11 y, 12 y and older)
• Patients should be assessed every 1-6 months for asthma control
• At every visit, adherence, environmental control, and comorbid conditions should be checked
Management of Asthma - Severity

• Severity depends on the frequency of asthma symptoms.

• *Intermittent Asthma* –
  - Day time symptoms are < 2 per week
  - Night time symptoms are < 2 per month
  - No limitation of daily activity
  - No severe asthma attacks needing hospitalization or ICU care
  - Rescue medication use < 2 per week

If “yes” to all of the above classified as Intermittent Asthma
# Management of Asthma - Severity

## Persistent Asthma

<table>
<thead>
<tr>
<th>Type</th>
<th>Day time symptoms</th>
<th>Night time symptoms</th>
<th>*Use of rescue medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild Persistent</td>
<td>&gt; 2 times/wk, may affect daily activity</td>
<td>&gt; 2 times/month but &lt; 1 time/week</td>
<td>&gt; 2 times per week but not daily</td>
</tr>
<tr>
<td>Moderate Persistent</td>
<td>Daily symptoms, activity affected</td>
<td>&gt; 1 time per week</td>
<td>Daily use of rescue medication</td>
</tr>
<tr>
<td>Severe Persistent</td>
<td>Continuous symptoms</td>
<td>Frequent</td>
<td>Frequent</td>
</tr>
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</table>

*Rescue Medication = SABA (Short acting bronchodilators), LABA Long acting bronchodilators with rapid action also- fomoterol, theophylline preparations
Stepwise Management of Asthma

**Step 1**
- Preferred controller choice
  - Consider low dose ICS

**Step 2**
- Low dose ICS
  - Leukotriene receptor antagonists (LTRA)
  - Low dose theophylline

**Step 3**
- Low dose ICS/LABA*
  - Med/high dose ICS/LABA

**Step 4**
- Add tiotropium
  - High dose ICS + LTRA
  - Add tiotropium
  - Add low dose OCS

**Step 5**
- Refer for add-on treatment e.g. anti-IgE

**Reliever**
- As-needed short-acting beta₂-agonist (SABA)
  - As-needed SABA or low dose ICS/formoterol**
LTRA and ICS

Two parallel, multicenter

<table>
<thead>
<tr>
<th>First-Line Controller Therapy Trial</th>
<th>Add-on Therapy Trial</th>
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</thead>
<tbody>
<tr>
<td><strong>LTRA</strong></td>
<td><strong>LTRA</strong></td>
</tr>
<tr>
<td>(N = 148)</td>
<td>(N = 170)</td>
</tr>
<tr>
<td><strong>Inhaled Glucocorticoid</strong></td>
<td><strong>LABA</strong></td>
</tr>
<tr>
<td>(N = 158)</td>
<td>(N = 182)</td>
</tr>
<tr>
<td>Mean age — yr</td>
<td>51.0±16.0</td>
</tr>
<tr>
<td></td>
<td>49.7±16.1</td>
</tr>
<tr>
<td>47.6±16.5</td>
<td>44.1±16.4</td>
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</tbody>
</table>
LTRA and ICS

**Results** - LTRA is equivalent to both comparison drugs with regard to asthma-related quality of life at 2 months, but equivalence was not proven at 2 years.

ICS are superior to anti-leukotrienes when used as monotherapy in adults and children with persistent asthma - Cochrane review.
Higher level care and/or add-on treatment

Referral for specialist investigation and consideration of add-on treatment

• If symptoms uncontrolled or exacerbations persist despite Step 4

• Add-on omalizumab (anti-IgE) for uncontrolled on Step 4 treatment

• Options at Step 5
  – Tiotropium: for adults (≥18 years) with a history of exacerbations despite Step 4 treatment
  – Sputum-guided treatment
  – Add-on low dose oral corticosteroids (≤7.5mg/day prednisone equivalent): need close assessment and monitoring for osteoporosis
Anti-IgE Therapy

- Elevated serum IgE
- Biologic antibody therapy (Omalizumab; Xolair) binds IgE in the circulation and prevents it from activating mast cells and basophils
- In moderate to severe asthma, anti-IgE therapy reduced exacerbation rate and reduced steroid dose needed
- Anti IgE therapy is recommended as an add-on to optimized standard therapy in ≥ 12 years, who need continuous or frequent treatment with oral corticosteroids

Ann Intern Med. 2011 3;154(9):573-82
Cochrane Database Syst Rev. 2014 13;1
Bronchial Thermoplasty

Normal airway  
Asthmatic Airway

Principle:
Reduce airway smooth muscle mass through controlled thermal treatment to airways

Am J Respir Crit Care Med. 2012 Apr 1;185(7):709-14.
Am J Respir Crit Care Med. 2010 Jan 15;181(2):116-24
Asthma Control

Good asthma control is defined as:

• Minimal symptoms during day time and no symptoms at night time
• Minimal need for reliever or rescue medication (<2/wk)
• No exacerbations
• No limitation of physical activity
• Normal lung function (FEV1 and Peak Expiratory Flow > 80% of predicted or personal best)
INSPIRE study

• International Asthma Patient Insight Research (INSPIRE) study is the first multinational study to focus on patients with a physician-confirmed diagnosis of asthma who were receiving regular maintenance therapy with ICS, with or without a LABA. (2004-05)

• Aim - Assess patients' attitudes to asthma management
  - Levels of asthma control
  - Impact of the condition on patients' lives
  - Establish the frequency and severity of worsening & how patients respond to such events
INSPIRE study

- Oct 2004 and Aug 2005 in eleven countries
- 3415 adults aged ≥ 16 years with asthma were prescribed regular maintenance therapy with inhaled corticosteroids or inhaled corticosteroids plus long-acting β₂-agonists.
- Assess medication use, asthma control (ACQ), and patients' ability to recognise and self-manage worsening asthma
INSPIRE study

- 74% of patients using at least one rescue therapy every day during the 7 days before the interview took place.
- 51% having needed unplanned medical care (such as hospitalisation) as a result of an asthma attack on at least one occasion in the last year.
- 3.1% asthma-related unscheduled medical interventions in the year.
mean number of worsenings for the total population was 11.8/year
# Factors that Influence Asthma Control

<table>
<thead>
<tr>
<th>Reasons of poor control</th>
<th>Variables</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease-related</strong></td>
<td>Comorbidities</td>
<td>Rhinitis, rhinosinusitis, gastrooesophageal reflux, obstructive sleep apnoea, and obesity</td>
</tr>
<tr>
<td></td>
<td>Triggers</td>
<td>House dust mite, pollen, dust mite, passive smoking, new allergens, aspirin, and beta-blockers</td>
</tr>
<tr>
<td></td>
<td>Asthma type</td>
<td>Aspirin-sensitivity, nocturnal asthma, and allergic asthma</td>
</tr>
<tr>
<td><strong>Patient related</strong></td>
<td>Sociodemographic factors</td>
<td>Female sex, education below secondary level, adolescence, and elderly age</td>
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<tr>
<td></td>
<td>Adherence</td>
<td>Undertreatment, overtreatment, irregular visits to healthcare providers, insufficient monitoring of symptoms, and no modifications in lifestyle</td>
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<tr>
<td></td>
<td>Psychiatric comorbidity</td>
<td>Anxiety and depressive disorders</td>
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<tr>
<td></td>
<td>Psychological characteristics</td>
<td>Trait characterized by difficulty in identifying and verbally expressing sympotms, and in developing strategies</td>
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<tr>
<td></td>
<td>Perceptions</td>
<td>Tendency to tolerate symptoms, exacerbations and lifestyle limits as an inevitable consequence of asthma</td>
</tr>
<tr>
<td></td>
<td>Expectations</td>
<td>Low expectations and aspirations about the achievable degree of control</td>
</tr>
<tr>
<td></td>
<td>Behaviours</td>
<td>Smoking habits</td>
</tr>
<tr>
<td></td>
<td>Knowledge</td>
<td>Incorrect use of inhaler leading to ineffective/reduced drug delivery</td>
</tr>
<tr>
<td></td>
<td>Knowledge of current guidelines</td>
<td>Inadequate information about the disease's treatment</td>
</tr>
<tr>
<td></td>
<td>Misdiagnosis</td>
<td>Limited awareness of asthma prevalence inadequate assessment</td>
</tr>
<tr>
<td><strong>Doctor related</strong></td>
<td>Misdiagnosis</td>
<td>Lack of consciousness and familiarity about guidelines availability</td>
</tr>
<tr>
<td></td>
<td>Knowledge of current guidelines</td>
<td>Difficulty in accepting guidelines</td>
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<tr>
<td></td>
<td>Attitude towards guidelines</td>
<td>Lack of confidence in patient's adherence to guidelines</td>
</tr>
<tr>
<td></td>
<td>Guidelines implementation</td>
<td>Expectations of failure in following guidelines</td>
</tr>
<tr>
<td></td>
<td>Knowledge of current guidelines</td>
<td>Difficulty changing deep-seated routines</td>
</tr>
</tbody>
</table>
Future Treatment for Asthma

• Inhaled corticosteroid development - 40 years back
• First monoclonal antibodies used - 20 years back
• More effective drug-delivery devices
• Bronchial thermoplasty- developed 10 years ago

But the proportion of uncontrolled patients, unfortunately, remains stable

• Future ahead - to palpable personalised treatment for individual clinical (phenotype) or new biological (endotype)
Future Treatment for Asthma

Therapeutic options

• **New ICS** - Improving drug half-life to minimise side effects and Other routes of administration, eg Nasal

• **New long-acting β-agonists (LABA)**
  once-daily, very long-acting Indacaterol, vilanterol

• Long-acting muscarinic antagonists (LAMA) initially developed for COPD
  as an add-on therapy - tiotropium
Future Treatment for Asthma

Personalising medicine

Phenotyping severe asthma

Clinical approaches

A priori hypothesis
- Reversibility
  - Anti-IL-17
- Obesity
  - Bariatric surgery
- <3 exacerbations per year
  - Smooth muscle thermoplasty
- Viral exacerbation
  - IFN-β

Unsupervised clustering

Endotyping

Th2 low
- Neutrophilic
  - Azithromycin
  - Anti-CXCR2

Th2 high
- Paucigranulocytic
- Thermoplasty?

Atopic
- Total IgE
- Eos >300 per mm³
- Eos >400 per mm³
- ILC2?
- Periostin high

Omalizumab
- Anti-TSLP
- GATA3 DNAzyme
- Mepolizumab
- Dupilumab
- Benralizumab
- Reslizumab
- Anti-CRTH2
- Lebrikizumab
Lebrikizumab has been shown to selectively improve lung function in asthmatics with high levels of circulating periostin.
Causes for Concern

- **Allergic bronchopulmonary aspergillosis**
  - ? incompletely understood phenotype of asthma
  - Overlapping forms – mildest and the most severe disease

- **Eosinophilic granulomatosis with polyangiitis (EGPA)**
  - ANCA positivity for better diagnostic accuracy in many unclear clinical situations

- ??? TB
Summary

• Many advances in scientific knowledge about asthma
• In spite of these efforts suboptimal asthma control
• New GINA guideline – 2015 with a revised asthma definition
• Basic principles of management of asthma remains the stepwise approach
• ICS is in the fore front with others like LABA, LTRA
• Anti IgE is may need add-on to optimized standard therapy
• Good asthma control remain ever challenging
• Future treatment of asthma is personalizing according to pheno/endo typing
Thank You