Sherbet Fountains and Inhaler Devices – What do they have in common?

(Getting the most from inhaler devices)

Thursday 10th April 2008

Jon Bell
Who?

Pharmaceutical companies – sales & marketing, then clinical research

Medical device company – peak flow, spirometry, inspiratory (In-Check)

Present – independent research “inspiratory” – measurement & training

(Asthmatic; triggers - cat dander + lime cordial)

Aims / Goal?

1. Promote improved care through better understanding of basic aerosol science and device characteristics
2. Minimise waste with inhaled drug therapies
3. Increase respiratory MURs through application of knowledge of how devices work, and how to achieve optimum technique – no matter what device patient has.
Asthma and Pets

ALLERCA has produced the world’s first, scientifically-proven, hypoallergenic cats. These cats allow some of the millions of people with feline allergies to finally enjoy the love and companionship of a household pet without suffering from allergic symptoms.

CAT ALLERGIES
Currently most treatments for cat allergies focus on avoidance, allergy shots, and pharmaceuticals. This section provides more information on how to avoid the suffers of the ALLERCA cats, the choice that be made without live without a pet or make considerable alterations to one’s living environment.

HYPO-ALLERGENIC CATS
ALLERCA has produced the world’s first scientifically-proven hypoallergenic cats. This section provides some information on why an ALLERCA cat is the ideal companion for people with feline allergies. Please also take our quick survey and help us decide future breeds of hypoallergenic cats.

DEVELOPMENT
The ALLERCA research and development team has placed ALLERCA in a unique position to
### Medications for Asthma Management

**“Reliever” Meds**
- Taken as needed
- To relieve acute airflow obstruction and bronchoconstriction
- Primarily Beta$_2$-Agonists
  - “Blue” inhaler

**“Preventer” Meds**
- Taken daily, long-term
- To reduce inflammation
  - Primarily inhaled corticosteroids
    - “Brown” inhaler

**Combination products**
- “Purple” or “Red/White” inhaler
The importance of explaining asthma medications

Relievers
- Aspirin
- Tixylix
- Calpol Infant Suspension
- Rennie

Preventers
- Larlam
Consequence of poor compliance

Increased use of relievers ....

...and reduced protective effect
Could we do something similar to explain COPD medications?
An estimated 75% of hospital admissions for asthma are avoidable and as many as 90% of the deaths from asthma are preventable.

Asthma UK estimates that 2.1 million patients in the UK are suffering unnecessarily because they do not use their asthma treatment effectively.

http://www.asthma.org.uk/news_media/media_resources/for_1.html

Last accessed: 3rd October 2007
Guideline recommendations
(NICE COPD 2004)

Chronic obstructive pulmonary disease
Management of chronic obstructive pulmonary disease in adults in primary and secondary care

Delivery systems
Inhalers
- Most patients, whatever their age, can learn how to use an inhaler unless they have significant cognitive impairment.
- Hand-held devices are usually best, with a spacer if appropriate. D
- If a patient cannot use a particular device, try another. D
- Teach technique before prescribing an inhaler, and check regularly. D
- Titrate the dose against response for each patient. D

...but what if the half the dose is wasted each time the inhaler is used ....
“How do you inhale” challenge

Quick test of how you would inhale through commonly-used devices

- pMDI measurement first
- DPI measurement second

Need to:
1. Simulate resistance of device
2. Measure speed of inhalation

“How you would instruct the patient to inhale” using that type of inhaler

Single measurement

Results later …….
Mean resistance of various DPIs

Resistance in (cmH₂O)⁰²Ĺmin⁻¹

0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0

Aeroliser  Accuhaler  Turbohaler  Clickhaler  Twisthaler  Easyhaler

MDI / Spacer

Health Professionals speed of inhalation when asked to inhale as if using an MDI - “Slowly and Deeply”

- **60 L/min or less**: (n=179)
- **61 to 90 L/min**: (n=267)
- **91 L/min and above**: (n=2825)

Total = 3271 tests conducted: over 94% inhaled too fast

General Practitioners, Practice Nurses, Respiratory Nurses (Primary & Secondary Care), Pharmacists (Community, Retail and Hospital), Pharmacy Dispensers, Prescribing Advisors, Physiotherapists, Hospital Physicians (General Medicine and Thoracic), Pharmaceutical Company Employees (Representatives, Medical Advisors, Educational Staff)

Presented at ERS Annual Scientific Meeting, Stockholm 2007 (No. 91, Primary Care Day, 15/9/07): Jon Bell, Canday Medical Ltd. data collected between 1st June 2006 and 5th September 2007
Asthmatics - speed of inhalation through Metered Dose Inhaler

Speed of inhalation

90 L/min or less (n=36)

91 L/min and above (n=440)

Total = 476 individuals tested:
over 92% inhaled too fast

Fate of inhaled drugs – Good Technique

- **Mouth**: Inhaled drugs can be swallowed and reach the GI tract.
- **GI tract**: 80% of swallowed drugs are absorbed, 20% are deposited in the lungs.
- **Lungs**: Metabolism or absorption occurs from the lung.
- **Liver**: First-pass metabolism and oral bioavailability.
- **Systemic Circulation**: Absorption from the gut and mucociliary clearance from the mouth.

**Notes**:
- **80%**: Referred to as swallowed.
- **20%**: Referred to as deposited in the lung.
Fate of inhaled drugs – Poor Technique

- **95%** Swallowed
  - Mouth pharynx
  - GI tract
  - Absorption from gut
  - First-pass metabolism
  - Oral bioavailability

- **5%** Deposited in lung
  - Lungs
  - Metabolism or absorption from the lung
  - Systemic circulation

- **Fate of inhaled drugs**
  - Poor Technique
Why are there problems?

- Design of inhalers vary
  - Formulation of drug
  - Mechanical activation
    (passive MDI vs active DPI)
  - Internal resistance to airflow

- Patients vary
  - Pulmonary function
    (reversible Vs irreversible disease)
  - Ability to learn / be taught the correct technique
  - Physical size of lungs (child vs adult)
  - Effort varies from dose to dose
External shape hides internal differences

High resistance

Low resistance
Resistance of 3 Common Inhalers at different flow rates (placebo versions)

- **Dry powder device**
- **pMDI aerosol “puffer”**

Ref: J Bell 2004, data on file: jon@canday.co.uk
Changes in inspiratory flow affect the aerosol output from two types of portable inhaler.

<table>
<thead>
<tr>
<th>Inspiratory flow</th>
<th>Metered Dose Inhaler (MDI)</th>
<th>Dry Powder Inhaler (DPI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Lactose</td>
<td>Drug</td>
</tr>
<tr>
<td>Low</td>
<td>Drug</td>
<td>Lactose</td>
</tr>
</tbody>
</table>
Aerosol Deposition at varying Particle Size

<table>
<thead>
<tr>
<th>Micron size</th>
<th>Deposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Pharynx, larynx &amp; Upper respiratory tract</td>
</tr>
<tr>
<td>5</td>
<td>Optimal tracheobronchial deposition</td>
</tr>
<tr>
<td>2</td>
<td>Optimal alveolar deposition</td>
</tr>
<tr>
<td>0.5</td>
<td>Particles exhaled if &lt;0.5 micron</td>
</tr>
<tr>
<td>0</td>
<td>Particles exhaled if &lt;0.5 micron</td>
</tr>
</tbody>
</table>
n.b. note the angles of the airways
Particle Deposition In Respiratory Tract

Three mechanisms of aerosol kinetics govern the majority of particle deposition within the respiratory tract.

1. Inertial impaction  90%
2. Sedimentation  9%
3. Diffusion  1%

Mass

Speed

Gravity

Brownian motion*

* Whitley Bay Smoke Chamber
What have sherbet fountains got in common with inhalers .......

Twisthaler

pMDI

Handihaler

Turbohaler

Accuhaler
Implications

Metered Dose Inhalers
Lung deposition from pMDIs is influenced by inspiratory flow.

![Graph showing lung deposition from pMDIs at different inspiratory flows and lung volumes.](image)

- **Total lung deposition (% of inhaled dose)**
- **Inspiratory flows**:
  - 30L/min
  - 90L/min

**Metered Dose Inhaler (MDI)**

Implications

Spacer Devices
Spacer Devices – How they help

1. Capture aerosol avoiding coordination problems
2. Reduces large aerosol particles (associated with s/e)
Errors in Technique No. 129

Asthma patient audit: 1 patient, Male 55 yr
28 salbutamol MDI Rx in last 12 months
2000 mcg BDP
Poor inhaler technique
L. Vol. Spacer repeatedly prescribed
Implications

Dry Powder Devices
Lung deposition from Turbohaler is influenced by inspiratory flow

Total lung deposition (% of inhaled dose)

- 36L/min
- 58L/min

Lung deposition from a budesonide Turbohaler measured by gamma scintigraphy.

Total emitted dose at different flow rates

Application of PIF Measurement
Application of existing flow measurement technology

Measures speed of exhalation
PEF (l/min)

- Diagnosis for reversible airway disease
- Monitor response to treatment
- Identify provocative factors
- Objective input for self-management

Measures speed of inhalation
PIF (l/min)

- Measure inspiratory flow for inhaler used
- Identify poor inhalation technique
- Demonstrate optimal technique for inhaler
- Objective feedback on teaching success

(with facemask) monitors allergic rhinitis morbidity
(Peak NASAL inspiratory flow – PNIF)
1. Turn the DIAL to select the inhaler resistance

**Diskus / Accuhaler**
Multiple-dose powder inhaler

**Common pMDI**
Metered Dose Inhaler and MDI spacers with low resistance (e.g. AbleSpacer)

**Easibreathe**
Automatic pMDI

**Turbuhaler**
Turbulent flow inhaler

**Autohaler**
Automatic pMDI
2. Measure, then compare the inspiratory flow achieved with the optimum recommended for that device.

<table>
<thead>
<tr>
<th>Device</th>
<th>Optimum Inspiratory Flow Range (l/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple-dose powder inhaler Accuhaler</td>
<td>![Optimum or Effective]</td>
</tr>
<tr>
<td>Turbulent flow inhaler (old style) Turbuhaler®</td>
<td>![Optimum or Effective]</td>
</tr>
<tr>
<td>Turbulent flow inhaler (Synarex®) Turbuhaler®</td>
<td>![Optimum or Effective]</td>
</tr>
<tr>
<td>Auto inhaler Autohaler®</td>
<td>![Optimum or Effective]</td>
</tr>
<tr>
<td>Auto inhaler Easi-Breathe®</td>
<td>![Optimum or Effective]</td>
</tr>
<tr>
<td>Multiple-dose powder inhaler Clickhaler®</td>
<td>![Optimum or Effective]</td>
</tr>
<tr>
<td>Low-resistance aerosol pMDI</td>
<td>![Optimum or Effective]</td>
</tr>
</tbody>
</table>
Is there a difference between "effective" and "optimum"?

The optimum inspiratory flow range for each device has been ascertained after reference to pharmaceutical data - summary of product characteristics (SPC), promotional and educational literature (from the manufacturers) and clinical and laboratory studies.

1. Clinical effect observed
2. Oropharyngeal deposition is minimised
3. Clinical benefit is maximised
4. Side-effect risk is minimised
5. Inhaler provides greater dose consistency
What if asthma and COPD were treated with Chocolates and Champagne?

£5 to £20 a box

£15 to £35 a bottle

Would you allow people to waste 50% every time they had some?
Assessment & Training Devices
Monitoring inspiratory flow rate through the device

- Vitalograph’s Aerosol Inhalation Monitor (AIM)
- Clement Clarke’s In-Check and In-Check DIAL
- Fyne Dynamic’s MagFlo
- Canday Medical’s “2-Tone” Trainer
  (www.2ToneTrainer.com)
- Schering-Plough’s Twisthaler Trainer
- AstraZeneca’s Turbohaler Usage Trainer & Turbutesters
- Pharmaceutical Co.

Independent

60 L/min
35 L/min
Inhale Too Fast…. (e.g. pMDI)

High-speed aerosol cloud impacts in oropharynx
Inhale Too Slowly…. (e.g. DPI)

Reduced emitted dose and quality of aerosol at low speed
Inhale Optimally (e.g. pMDI)

Optimal PIF for inhaler efficiency and aerosol dynamics
Points to take away?

1. Internal resistance affects speed of inhalation
2. Speed of inhalation affects DPI device efficacy (less effect on MDI)
3. Speed of inhalation affects how much drug is deposited in the lungs – and how much in the mouth and throat
4. Teaching optimum technique (rather than just any technique that shows clinical effect) offers real and immediate benefits for both patient and professional.