Allergic Rhinitis - the need for better symptom control

Glenis Scadding
Conflict of interest

- Honoraria for articles, speaking engagements, and advisory boards with ALK, AstraZeneca, Britannia Pharmaceuticals, Capnia (UK) Ltd., Church & Dwight, Circassia, Grupo Uriach, GSK, Meda/Mylan, Merck, MSD, Ono Pharmaceuticals, Oxford Therapeutics, Sanofi-Aventis, and UCB
- Travel funding received from ALK, Bayer, GSK, and Meda
- Chair of BSACI rhinitis guidelines
WHY TREAT RHINITIS?

- SYMPTOMS
- CO-MORBIDITIES
- COMPLICATIONS
- QUALITY OF LIFE
- COSTS
Rhinitis symptoms

- Rhinitis means nasal inflammation, but is clinically defined as two or more of:
  - running nose
  - blocked nose
  - sneezing/itching
  - >1 hour per day rhinoconjunctivitis (in 50–70%)
  - allergic when IgE-mediated
High symptom burden

- Nasal congestion the most bothersome
- Followed by sneezing and runny nose

![Chart showing symptom burden]

Katelaris et al, Am J Rhinol Allergy 2012
8. Allergic rhinitis has a negative impact on sleep

• 73.5% of adults and 65.8% of children with AR report that their sleep disorders had prompted them to consult their physician.
• The most commonly observed sleep complaints
  – poor-quality sleep (50.3% of adults and 37.3% of children),
  – snoring (48.1 and 41.4%, respectively) and
  – nocturnal awakening (37.6 and 28.2%, respectively).

Leger et al, Allergy Asthma Clin Immunol 2017
AR: allergic rhinitis
1. Allergic rhinitis negatively impacts all areas of daily life

- Patient voice allergy survey

3. Uncontrolled AR negatively impacts patients’ QoL

Table 5: WPAI questionnaires results in AR, depression, hypertension, and DM

<table>
<thead>
<tr>
<th>WPAI Score (%)</th>
<th>AR (n = 223)</th>
<th>Depression (n = 58)</th>
<th>Hypertension (n = 163)</th>
<th>DM (n = 149)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstention</td>
<td>14.6 (11.1)</td>
<td>31.3 (20.6)</td>
<td>21.8 (15.2)</td>
<td>4.2 (1.7)</td>
</tr>
<tr>
<td>Lost of productivity</td>
<td>23.5 (1.6)*$</td>
<td>48.4 (4.1)**</td>
<td>73.2 (2.1)**</td>
<td>15.4 (2.6)</td>
</tr>
<tr>
<td>Global loss of productivity</td>
<td>26.8 (1.3)*$</td>
<td>59.5 (4.1)**</td>
<td>8.8 (1.5)*$</td>
<td>16.7 (2.8)</td>
</tr>
<tr>
<td>Restriction on daily activities</td>
<td>27.8 (1.3)*$</td>
<td>59.4 (2.6)**</td>
<td>19.8 (2.5)**</td>
<td>25.7 (1.6)</td>
</tr>
</tbody>
</table>

Note: Only patients with all items correctly filled out were included.

Analysis of covariance. Adjusted by age, sex, comorbidities, and number of prescribed drugs. Mean and standard error (SE).

*p < 0.05, AR vs depression.

#p < 0.05, AR vs hypertension.

$#p < 0.05, AR vs diabetes.

$p < 0.05, depression vs hypertension.

$p < 0.05, depression vs diabetes.

**p < 0.05, hypertension vs diabetes.

AR = allergic rhinitis; DM = diabetes mellitus; WPAI = Work Productivity and Activity Impairment.

- Negative impact on daily activities greater for AR patients than those with diabetes mellitus or hypertension.
Presenteeism and absenteeism

- 44% of respondents reported absenteeism, presenteeism or both
- Productivity impaired by an average of 23% when symptoms are at their worst

Katelaris et al, Am J Rhinol Allergy 2012
4. Uncontrolled AR reduces work productivity...

- Survey of 1000 SAR patients in UK
- Over 90% of patients experience a negative impact on work when symptomatic
7. Allergic rhinitis carries a high socioeconomic burden

Allergic rhinitis
- Unproductivity for 2.3 h per work day when symptomatic at a cost of $593/person/year
  - Greater than that for heart disease, asthma, diabetes, hypertension and respiratory illnesses combined!

4. ...and negatively impacts school performance

- Children with SAR more likely than non-allergic individuals to unexpectedly drop a grade during summer examinations if they are:
  - Symptomatic (OR: 1.4)
  - Taking AR medication (OR: 1.4)
  - Taking sedating anti-histamine (OR: 1.7)

Walker et al, JACI 2007;120:381-7
SAR: seasonal allergic rhinitis; OR: odds ratio
5. Uncontrolled AR carries a high social burden

**Social exclusion/embarrassment**
- Socially embarrassing to be seen sneezing, sniffing, or nose-blowing\(^1\)

**Psychological disturbance**
- A risk factor for depressive mood in pre-adolescents.\(^2\)

**Practical issues**
- Untreated AR can impair driving ability\(^3\)

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Increase of air pollution significantly associated with AR visits

- Single pollutant model
  - Increased rate of AR occurrence and ambient concentration of
    - PM$_{10}$
    - SO$_2$
    - NO$_2$
    - CO
    - O$_3$

Chen et al, J Toxicol Environ Health A 2016

AR: allergic rhinitis; PM: particulate matter; SO$_2$: sulphur dioxide; NO$_2$: nitrogen dioxide; CO: carbon monoxide; O$_3$: ozone
Rhinitis comorbidities
Rhinitis –allergic and non- allergic precedes asthma

Cumulative incidence rate of asthma

Shaaban R. Et al., The Lancet, 2008
And the impact of that co-morbidity?
Uncontrolled rhinitis negatively impacts asthma control to the same degree as smoking

Multiple logistic regression: predicting poor control (ACQ score >1.25)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Compared with no rhinitis:</th>
<th>OR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinitis</td>
<td>Significant rhinitis</td>
<td>4.62</td>
<td>3.71–5.77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Mild rhinitis</td>
<td>2.09</td>
<td>1.72–2.54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>Compared with never smoking:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Current smoker</td>
<td>4.33</td>
<td>3.58–5.23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Ex smoker</td>
<td>1.59</td>
<td>1.36–1.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adherence</td>
<td>Compared to high adherers:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low adherers</td>
<td>1.35</td>
<td>1.18–1.55</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Based on a survey of 4,429 patients prescribed ICS in 83 UK general practices

Gaining control of AR in asthma patients with an AR co-morbidity is essential

ACQ: Asthma Control Questionnaire; OR: odds ratio; CI: confidence interval; ICS: inhaled corticosteroid; AR: allergic rhinitis
Implications of comorbid rhinitis: paediatric asthma – Brazil

- Children and adolescents with acute asthma on ICS therapy (n=126)
- 
  - Allergic rhinitis prevalence: 74.6% (95%CI 65.9–81.7)
  - Allergic rhinitis combined with asthma severity represented the greatest risk factor for use of emergency care

<table>
<thead>
<tr>
<th>Factors</th>
<th>Crude OR (95%CI)</th>
<th>Adjusted OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe persistent asthma</td>
<td>2.17 (1.03–4.54)</td>
<td>2.09 (1.05–4.44)</td>
</tr>
<tr>
<td>Presence of allergic rhinitis</td>
<td>2.76 (1.09–7.02)</td>
<td>2.98 (1.10–8.06)</td>
</tr>
</tbody>
</table>

95%CI = 95% confidence interval; OR = odds ratio.
## Symptomatic coverage of AR treatments

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Nasal Anticholinergic</th>
<th>Decongestant</th>
<th>Mast cell stabilizer</th>
<th>Leukotriene Antagonist</th>
<th>Oral antihistamine</th>
<th>Intranasal antihistamine</th>
<th>Intranasal corticosteroid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal congestion</td>
<td>-</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Nasal pruritis</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Sneezing</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Ocular itching</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Ocular watering</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Ocular redness</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
</tbody>
</table>

No single medication class provides optimal relief from all symptoms.
1. Symptom burden is high for allergic rhinitis; even when treated

- 1000 patients with SAR from the UK
- Moderate severe disease
  - 96.2% treated
  - 70.5% on multiple therapy
- Most patients remained symptomatic
  - Significant nasal and ocular symptoms remaining

SAR: seasonal allergic rhinitis; rTNSS: reflective total nasal symptom score; rTOSS: reflective total ocular symptom score
2. Most patients use multiple therapies in an effort to control their symptoms...

% moderate/severe patients on ≥ 2 AR medications

The need for faster and more effective treatment was the primary reason for co-medicating

Data from a UK survey including 1000 SAR patients

Price et al, Clin Transl Allergy, 2015
AR: allergic rhinitis
...but and are dissatisfied with therapy

- N=21 Allergy centres in Italy (n=301 patients with AR and/or asthma)

Ciprandi et al., Curr Med Res Opin, 2011

AR: allergic rhinitis; M/S: moderate/severe; OR: odds ratio; INS: intranasal corticosteroid; INAH: intranasal anti-histamine; OC: oral corticosteroid; IM cort.: intramuscular corticosteroid; LTRA: leukotriene receptor antagonist

Factors associated with AR therapy dissatisfaction

- **Rhinitis severity** (OR: 1.39; p<0.05)
- **Co-morbidity** (OR: 2.39; p<0.05)
- **Anti-histamine use** (OR 2.53; p<0.05)


AR: allergic rhinitis; M/S: moderate/severe; OR: odds ratio; INS: intranasal corticosteroid; INAH: intranasal anti-histamine; OC: oral corticosteroid; IM cort.: intramuscular corticosteroid; LTRA: leukotriene receptor antagonist
Perception and satisfaction with AR treatments

- Overall 55% belief there is no truly effective AR treatment (some regional variation)
- Satisfaction with INS is low – 0% to 50% are v. satisfied

Katelaris et al, Am J Rhinol Allergy 2012
INS: intranasal corticosteroid; AR: allergic rhinitis
What do Allergic Rhinitis patients want?

Introduction to the world of Discrete Choice Experiments

• Discrete choice experiments are based on the premise that any good or service can be described by its characteristics (or attributes)

• Secondly, the extent to which an individual values a good or service can be described in terms of the levels of these characteristics

• The technique involves presenting individuals with choices of scenarios described in terms of attributes and associated levels

• Participants are asked to choose their preferred scenario
What do Allergic Rhinitis patients want?

We asked them using a Discrete Choice Experiment (DCE)

- Patients were presented with 7 product characteristics:
  1. Maximum symptom relief (mild, moderate, complete)
  2. Time to maximum relief (3, 7, 14 days)
  3. Time to first dose benefit (0.5, 3, 8 hours)
  4. Risk of side effects (2%, 5%, 10%)
  5. Administration method (tablet, nasal spray, both)
  6. Frequency of medication (once, twice, three times/day)
  7. Monthly out-of-pocket cost (£15, £30, £45). Patients were asked to imagine that they paid the full cost of this prescription medication

- Patients were presented with 19 pairs of ‘potential Allergic Rhinitis products’ (based on the above characteristics) and asked to choose between them

Acaster et al, EAACI 2012
An Example Choice Set

Patients were presented with 19 of these and asked to pick ‘A’ or ‘B’

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Treatment A</th>
<th>Treatment B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum treatment symptom relief</td>
<td>Complete relief</td>
<td>Mild improvement</td>
</tr>
<tr>
<td>Time to achieve maximum treatment symptom relief</td>
<td>7 days</td>
<td>14 days</td>
</tr>
<tr>
<td>Time to feel a benefit after first dose</td>
<td>3 hours</td>
<td>8 hours</td>
</tr>
<tr>
<td>Side effects</td>
<td>10 in 100</td>
<td>2 in 100</td>
</tr>
<tr>
<td>Administration method</td>
<td>Tablet</td>
<td>Nasal spray</td>
</tr>
<tr>
<td>Frequency of medication</td>
<td>Twice a day</td>
<td>Three times a day</td>
</tr>
<tr>
<td>Cost per month</td>
<td>£15</td>
<td>£30</td>
</tr>
</tbody>
</table>

Which treatment do you prefer? A. □ B. □

Acaster et al, EAACI 2012
What AR patients want
DCE results: moderate to severe SAR patients

I want a treatment for my allergic rhinitis which works quickly and provides complete symptom relief

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Odds Ratio</th>
<th>P Value</th>
<th>WTP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment relief: complete vs. mild</td>
<td>6.63</td>
<td>&lt;0.01</td>
<td>£43.81</td>
</tr>
<tr>
<td>Treatment relief: moderate vs. mild</td>
<td>2.31</td>
<td>&lt;0.01</td>
<td>£19.37</td>
</tr>
<tr>
<td>Time to maximum relief: per day</td>
<td>0.97</td>
<td>&lt;0.01</td>
<td>-£0.62</td>
</tr>
<tr>
<td>Time to first dose benefit: per hour</td>
<td>0.96</td>
<td>&lt;0.01</td>
<td>-£0.98</td>
</tr>
<tr>
<td>Side effects: per 1%</td>
<td>0.98</td>
<td>&lt;0.01</td>
<td>-£0.40</td>
</tr>
<tr>
<td>Administration: tablets vs. nasal spray</td>
<td>1.08</td>
<td>0.04</td>
<td>£1.80</td>
</tr>
<tr>
<td>Administration: tablets &amp; nasal spray vs. nasal spray</td>
<td>1.07</td>
<td>&lt;0.01</td>
<td>£1.64</td>
</tr>
<tr>
<td>Frequency of medication: times/day</td>
<td>0.87</td>
<td>&lt;0.01</td>
<td>-£3.18</td>
</tr>
<tr>
<td>Cost: £1 / month increase</td>
<td>0.96</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

Results from a survey conducted in the UK including 746 SAR patients

Willing to pay £43.81 for complete relief vs mild relief
£0.62 less for day to max symptom relief
£0.98 less for each hour slower to onset
Key Message

- Rhinitis is common
- affects the nose & its connections
- reduces work/school ability and QOL
- worsens asthma
- deserves effective and safe treatment
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- Rhinitis is common
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- worsens asthma
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Burden

1. Symptoms & daily life
2. Polypharmacy
3. QoL
4. Productivity
5. Social
6. Comorbidity
7. Cost
8. Sleep