Research in Real-Life

The burden of rhinitis in Australia

Protocol for MEDA Pharmaceuticals

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Study 1: Rhinitis treatment patterns in Australia

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2 BACKGROUND

Allergic rhinitis is a chronic respiratory disease with a major impact on quality of life. In a study looking at the burden of rhinitis amongst UK patients, 75% reported some impact of their rhinitis symptoms on health-related quality of life[1]. Rhinitis currently affects 10-30% of the world's population[2], with prevalence and impact continuing to increase. In Australia, the prevalence is estimated at 19% of the population[3]. In addition, asthma and rhinitis often co-exist,[4] and it has been proposed that respiratory diseases including rhinitis account for 8% of total healthcare costs in Australia[5]. Therefore Australia suffers substantial economic costs from both prescription medication for rhinitis and time taken off work by both patients and carers as a result of the disease[6]. In view of this, there may be a need for improved therapy or management of rhinitis to facilitate improved quality of life for patients and reduced economic costs for the country.

Seasonal rhinitis, intermittent rhinitis or hay fever, is caused by an inflammatory response to seasonal airborne allergens, such as grass or tree pollen[7]. Perennial rhinitis occurs in some patients who suffer from rhinitis symptoms outside the pollen season, possibly with a seasonal flare[8]. In Australia, the onset and duration of the pollen season varies in different regions of the country depending on local climate, winds and flora. The principal allergenic grasses in the subtropical area (Northern territory and Queensland) tend to pollinate from January to March. In the southern part of Australia temperate grasses flower from October to December[9]. Therefore for the purpose of this study the following areas will be studied separately: Queensland & Northern Territory (NT); Victoria, South Australia (SA), Tasmania; New South Wales (NSW) & Australian Capital Territory (ACT); Western Australia (WA).

Physicians recognise that rhinitis can be very challenging to treat[10]. The Allergic rhinitis and its Impact on Asthma (ARIA) guidelines[11] classify rhinitis as either intermittent (symptoms <4 days per week or <4 consecutive weeks) or persistent (symptoms >4 days per week and >4 consecutive weeks), and both types can be either mild, or moderate-severe depending on the effect of symptoms on the patient's life. For mild-intermittent allergic rhinitis, an H1-antihistamine (either oral or nasal) along with a short-term decongestant or Leukotriene Receptor Antagonist (LTRA) (if concomitant asthma) is recommended. For moderate-severe intermittent or mild-persistent rhinitis, intranasal corticosteroids with or without the added H1-antihistamine or LTRA are suggested, with step-up treatment recommended in persistent patients if symptoms are not managed within 2-4 weeks [10]. For persistent patients with moderate-severe rhinitis, intranasal corticosteroids are preferred over antihistamine or LTRA treatment[10]. Step-up options include increasing the corticosteroid dose and adding antihistamine for itch or sneeze, ipratropium for rhinorrhoea and a decongestant or short-term oral corticosteroid for congestion. In addition, whilst oral and nasal therapy can improve allergic conjunctivitis, some patients may require additional topical ocular therapy.

The use of multiple therapies to manage rhinitis symptoms is extremely frequent, as illustrated by a recent study in the UK[12] that demonstrated physicians frequently prescribe more than one medication to their patients. This co-prescribing behaviour becomes more frequent as the hay fever season (March-June in the UK) advances, bringing dissatisfied patients with uncontrolled symptoms

back to their physician. This suggests that initial antihistamine or intra-nasal corticosteroid monotherapy provides insufficient symptom control for many rhinitis patients.

Data from the above UK study did not include OTC medication, suggesting that the use of multiple therapies might be even more widespread as patients may purchase additional medications on top of their prescription drugs. Indeed, a 2002 survey of allergy sufferers in Australia suggests that nearly two-thirds of respondents did not consult their doctor about their current rhinitis treatment[13]. Therefore it is important to carry out further investigations that include OTC medications in order to better understand the real-life treatment of rhinitis in Australia. The proposed study will evaluate the unmet clinical need in rhinitis by examining the use of multiple therapies to control rhinitis symptoms, and the proportion of prescription and OTC medications.

3 STUDY AIM & RESEARCH QUESTIONS

Primary aim: rhinitis treatment patterns in Australia *(split by geographic area[i])*

1) To assess the number of therapies (single vs. multiple drugs) used to treat rhinitis in Australia

2) To describe the combination of therapies used to treat rhinitis in Australia

3) To investigate the influence of OTC medications on the count and combination of therapies used to treat rhinitis in Australia

Secondary aims

4) To investigate the seasonality of rhinitis treatment patterns

5) To estimate the cost of rhinitis treatment in Australia

6) To investigate the relationship between rhinitis treatment patterns and co-morbid asthma treatment

[i] Queensland & NT; Victoria, SA, Tasmania; NSW & ACT; WA

4 DATABASE

Data source: NostraData

This study will be completed using data from NostraData, Australia. NostraData collects data on pharmacy purchases throughout Australia from 2011 to present. The data include:

A) Doctor prescription data: These data are available for about 50% of pharmacies in the country, providing excellent geographic coverage of the territory. The information is available when a patient purchases a drug with a doctor prescription. Data include date of prescription, date of purchase, drug purchased, price, instructions on the label and postcode of the purchase. Demographic data are available for 10% of patients only, as pharmacies have to add it themselves and not all pharmacies do; however, the same patients can be tracked when purchasing at different pharmacies. There is no information on patient diagnosis, however PBS codes will be provided where available

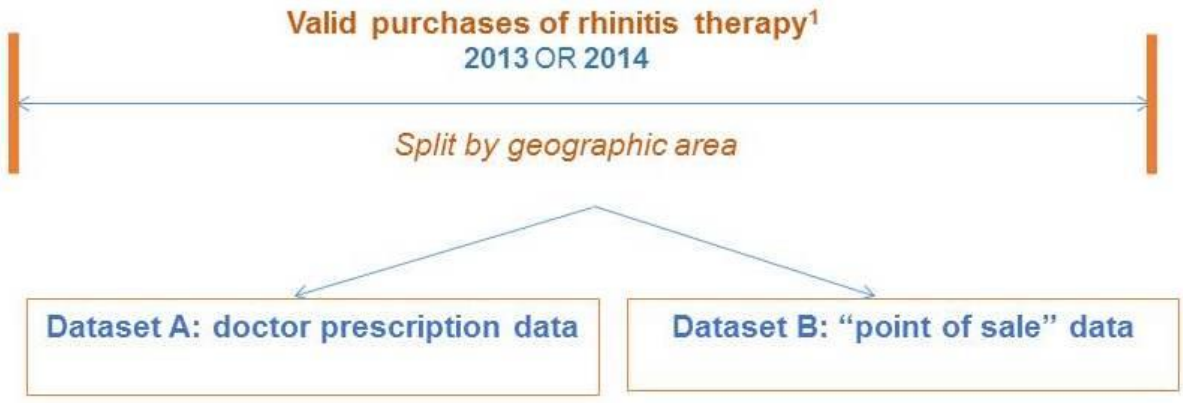
B) Point of sale data: These data include linked doctor prescription of OTC purchases and are available for about 20% of the pharmacies in the country. The data include information on the "basket" of a pharmacy customer, so can include both prescription drugs and OTC drugs. For instance, it is possible to find data relating to a specific prescription drug (e.g.: Antihistamines) and see what else was in the "basket" of the pharmacy customers who purchased that prescription drug. However, there is no other information (e.g. demographics) attached to these data, and it is not possible to track the same patients purchasing at different pharmacies or on different occasions using this dataset. Geographic coverage needs to be confirmed but we anticipate will be fairly representative of the territory.

Drug categories

Drug lists using UK drug codes have been developed by the research team, including advice from clinical specialists. These have been developed and refined over the last five years, through the RiRL's own research and in collaboration with other academic partners, in a large number of primary care database studies. A list of the rhinitis drugs that will be included in the study can be found in the appendix.

5 STUDY DESIGN

The study is a retrospective database study of pharmacy-related claims between 1st January 2013 – 31st December 2014 using data from NostraData (www.nostradata.com.au). Annual treatment patterns of patients with rhinitis will be documented separately for each 12-month period in each geographic area[ii].



[1]Rhinitis therapy = Antihistamines, Nasal steroids, Non-steroidal nasal spray, Leukotriene receptor antagonist, Eye drops

Figure 1. Study design

Note. For patients prescribed antihistamines alone, only 60% are likely to have a diagnosis of rhinitis[iii]

[ii] Queensland & NT; Victoria, SA, Tasmania; NSW & ACT; WA

[iii] Smith et. al. (2015), submitted to REG online

6 STUDY POPULATION

The study will include two datasets. Dataset A will include doctor prescription data, and dataset B will include "point of sale" data (see section 4 for details). The patient criteria for each dataset will be as follows:

6.1 DATASET A: DOCTOR PRESCRIPTION DATA

Inclusion criteria

- Purchased prescription rhinitis therapy[iv]

Exclusion criteria

- Patients were prescribed LTRA ALONE will be excluded (as LTRA alone is likely to have been prescribed/purchased for the treatment of asthma rather than rhinitis)
- The distribution of oral steroid use in the study population will be examined and if possible patients prescribed long term oral will be excluded (as long term oral steroids may blunt rhinitis symptoms)

6.2 DATASET B: POINT OF SALE DATA

Inclusion criterion

- Purchased OTC rhinitis therapy [iv] (with or without additional prescription rhinitis therapy [iv])

7 OUTCOMES

All analyses will be conducted separately for each study year (1st January 2013 – 31st December 2013 or 1st January 2014 – 31st December 2014) in each geographic area.

A subgroup analysis of demographic variables will be conducted in patients from Dataset A (doctor prescription data) that have demographic data available (approximately 10% of the population of Dataset A). This analysis will aim to characterise patients according to basic demographic information (gender, age).

[iv] Rhinitis therapy : Antihistamines, Nasal steroids, Non-steroidal nasal spray, Leukotriene receptor antagonist, Eye drops

7.1 PRIMARY OUTCOMES: RHINITIS TREATMENT PATTERNS

The following outcomes will be analysed separately for Dataset A and Dataset B for each calendar year (2013 and 2014) in each geographic area

1. **Count of therapies**: To assess the frequency of single vs. multiple therapies use

2. **Combination of therapies**: For multiple therapy patients, to describe the combinations of different drugs used

For patients in Dataset B ("point of sale" data), with purchased OTC AND prescription rhinitis therapy only:

3. **Proportion of prescribed and OTC medications**

7.2 SECONDARY OUTCOMES

The following outcomes will be analysed separately for Dataset A and Dataset B for each calendar year (2013 and 2014) in each geographic area. Secondary outcomes will be analysed in relation to the primary outcomes rhinitis treatment patterns (i.e. count of therapies, combination of therapies and where appropriate proportion of prescribed and OTC medications)

4. To assess the **seasonality of rhinitis treatment patterns**. If possible treatment patterns will be documented for a subgroup of perennial patients[v] (Dataset A only)

5. To estimate the **cost of rhinitis treatment** in Australia

6. To investigate the relationship between rhinitis treatment patterns and **co-morbid asthma treatment**

8 STATISTICS

- Statistical analyses will be undertaken using SPSS version 22 and R[14]
- Count of therapies will be reported as means and standard deviation [SD], and/or median and inter-quartile range (25th and 75th percentiles) along with minimum and maximum values. Moreover, count of therapies will be presented as single, multiple and total number of therapies.

[v] Perennial patients will be defined as those who purchased rhinitis therapy outside the pollen season in their geographic area

- Within the multiple therapy patients group, the combination of different drug will be reported as absolute numbers as well as proportions and percentages.
- Prescribed and over-the-counter medications will be reported as absolute numbers as well as proportions and percentages.
- Time series analysis will be used to explore seasonality of rhinitis treatment patterns over the study period
- The cost of rhinitis treatment will be reported as mean and median purchase (in Austrian dollars) along with their inter-quartile range and minimum and maximum values of purchases. This will be reported by different groups (single therapies, multiple therapies, geographical areas, prescribed and over-the-counter medications)
- Poisson regression analyses will be used to investigate a) the relationship between rhinitis treatment patterns and co-morbid asthma treatment and b) the relationship between rhinitis treatment patterns and demographic characteristics for patients with prescribed medications (Dataset A).

9 RESEARCH TEAM

Chief Investigator

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11 TIMELINES

Action	Timeline
Test data	31st January 2015
Feedback from RiRL	7th February 2015
Data extraction	14th February 2015
Initial analysis	22nd April 2015
Abstract 1 for submission as a late breaker	30th April 2015
Final Study report and slide set	31st May 2015
Manuscript	21st September 2015

12 APPENDIX : RHINITIS DRUG CATEGORIES

Antihistamine	Nasal steroid	Nasal spray	Eye drops	LTRA
Acrivastine	Beclomethasone	Azelastine	Nedocromil	Montelukast
Cetirizine	Betamethasone sodium	Ipratropium bromide	Lodoximide	Zafirlukast
Desloratadine	Budesonide	Oxymetazoline	Olopatadineatadin	
Fexofenadine	Ciclesonide	Chromolyn	Sodium	
Levocetrizine	Flunisolide	Antimuscarinic		
Loratadine	Flucticasone propionate	Ephedrine		
Mizolastine	Fluticasone furoate	Xylometazoline		
Alimemazine tartrate	Mometasone furoate	Sodium Cromoglycate		
Chlorphenamine	Triamcinolone acetonide	Oxymetazoline		
Cyproheptadine		Levocabastine		
Hydroxyzine				
Promethazine				

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