British Journal of Medicine & Medical Research
2(2): 157-171, 2012

SCIENCEDOMAIN *international*
www.sciencedomain.org

Discrepancies in Guidelines for Allergy Management in Asia-Pacific

Weiling Soon[1], Jia-Li Kwek[1], Sock-Yuen Kwek[1], Xiang-Xuan Tan[1], Peiting Xie[1], Zihui Yang[1] and De-Yun Wang[2*]

[1]Yong Loo Lin School of Medicine, National University of Singapore, NUHS Tower Block, 1E Kent Ridge Road, Singapore119228, Singapore.
[2]Department of Otolaryngology, Yong Loo Lin School of Medicine, National University of Singapore, NUHS Tower Block, 1E Kent Ridge Road, Singapore 119228, Singapore.

STATEMENT OF CONTRIBUTION

All co-authors have contributed to the study design, data search and analysis, and write-up of the manuscript.

Research Article

Received 20th August 2011
Accepted 29th October 2011
Online Ready 6th December 2011

ABSTRACT

Objectives: We have conducted this study to assess (1) the existence of prevention programmes for AR as developed by professional and health care organizations in Asia-Pacific countries; (2) any discrepancies in local guidelines in comparison to ARIA, or within and across these countries.
Study design: Web search study.
Methodology: We have conducted a study using Web search in accordance with the perspective of physicians or patients for the relevant prevention and pharmacotherapy guidelines in the management of AR as developed by professional and health care organizations in Asia-Pacific countries/regions.
Results: National allergy (AR and/or asthma) preventive programs are found in only 6 out of 17 (22.2%) countries (excluding Japan and South Korea). There exist several aspects of discrepancies in existing educational programs such as in (1) allergic disease (asthma or AR) that the guidelines focus on; (2) targeted age groups (children or adults); and (3) breadth and depth of coverage, such as for particular inhalant allergens or food allergies only. Based on the information provided by MIMS website (updated in 2011 by

**Corresponding author: Email: entwdy@nus.edu.sg;*

UBM Medica, London, United Kingdom) and the MIMS proven by the country's local health authority, controversies exist in recommended minimum age, doses and potential side-effects of many commonly used 2nd-generation antihistamines and intranasal corticosteroids.

Conclusion: This is the first study that demonstrates discrepancies and a lack of public education programmes for AR prevention and management in Asia-Pacific countries/regions.

Keywords: Allergic rhinitis; international guidelines; public education programmes; pharmacotherapy; allergen avoidance; Asia-Pacific countries/regions.

1. INTRODUCTION

Allergic rhinitis (AR) is an extremely common disease worldwide, constituting one of the commonest conditions encountered in medical practice and possibly, presenting to a wide range of medical practitioners (Bousquet et al., 2001, 2008). Successful treatment of AR relies on appropriate patient and physician education, which provides efficacious evidence-based treatment with long-term efficacy, safety and a good cost-benefit ratio. To date, international guidelines and consensus statements for the management of rhinitis have been developed to enhance its effectiveness and quality (Bousquet et al., 2001, 2008; Brozek et al., 2010). The Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines (Bousquet et al., 2001, 2008), for example, recommended allergen avoidance, pharmacotherapy and immunotherapy as the three main steps in management. However, the impact of these guidelines on physician management and on public education programmes managed by professional and healthcare organizations of individual countries has not been assessed.

The usefulness of these guidelines is questionable given that there are discrepancies across countries and even between administrators and organizations within the same country. Such uncertainties plaguing the treatment of AR and other allergic diseases often leave patients highly dissatisfied with the standard of care they receive from healthcare workers. Only when such discrepancies are addressed can there be a standardized clinical practice guideline for the treatment and management of patients with allergic disease.

We have conducted this study to assess (1) the existence of prevention programmes for AR as developed by professional and health care organizations in Asia-Pacific countries; (2) any discrepancies in local guidelines in comparison to ARIA, or within and across the Asia-pacific countries. We aimed to identify major controversial areas in allergy practice, namely allergen avoidance and pharmacotherapy. Immunotherapy was not included in the study as this method of treatment is not commonly employed in Asia-Pacific countries.

2. MATERALS AND METHODS

2.1 Web Search for the Relevant Prevention Guidelines in the Management of AR

Information obtained for this study is based on following inclusion and exclusion criteria:

- Web search using search engines (Google and Yahoo), or web links from the World Allergy Organization (WAO) website (Johansson and Haahtela, 2007). This route of access is in accordance with the perspective of physicians or patients, who are likely to use common search engines to retrieve information.
- From Asia-Pacific countries only.
- The search keywords are 'allergic rhinitis', 'allergy', 'prevention' and '(name of country)'.
- Availability of information provided by governmental or professional organizations. Countries are shortlisted if there are relevant links in the top 20 results.
- It is restricted to relevant information provided in English or Chinese.

Based on the inclusion criteria, guidelines for management of AR are available from 6 Asia-Pacific countries. The 6 countries (in alphabetical order) are Australia & New Zealand (Australasia) (World Allergy Organization, 2010), China (Haodf, 2010), Malaysia (Malaysian Society of Allergy and Immunology, 2010), Philippines (Philippine Society of Allergy, Asthma and Immunology, 2010) and Thailand (Asthma, Allergy and Immunology Society of Thailand, 2010). In addition, countries such as USA (National Institute of Environment Health Science, 2010), UK (British Allergy Foundation, 2010) and South Africa (Allergy Society of South Africa, 2010) are included as there are well established allergy management guidelines in these countries. Information provided by the WAO (Johansson and Haahtela, 2007) is used as a basis for comparison. Table 1 shows the different guidelines used as well as the range of topics they cover.

Table 1: Guidelines and the topics covered by each guideline

Topics	WAO	ASIA-PACIFIC COUNTRIES					OTHERS		
		AUS	CHI	MAL	PHI	THA	S AFR	UK	USA
House dust mite	√		√	√	√	√	√	√	√
Pets	√	√	√	√	√	√	√	√	√
Pollen	√		√				√	√	√
Mould	√	√	√		√	√	√	√	√
Cockroach	√				√	√			√
Total	**5**	**2**	**4**	**2**	**4**	**4**	**4**	**4**	**5**

WAO – World Allergy Organization; AUS – Australasia (Australia and New Zealand); CHI – China; MAL – Malaysia; PHI – Philippines; THA – Thailand ; S AFR – South Africa; UK – United Kingdom; USA – United States of America (NIEHS)

The following countries/regions are excluded based on a lack of professional guidelines (e.g. Singapore, North Korea, Indonesia, Cambodia, Vietnam, Brunei, Laos, Myanmar, Taiwan, Hong Kong, India), or a lack of translation (e.g. Japan, South Korea).

2.2 Information on Pharmacotherapy (2nd-Generation Antihistamines and Intranasal Corticosteroids)

Information on the recommendations of the use of 2nd-generation antihistamines and intranasal corticosteroids was taken from the Monthly Index of Medical Specialities (MIMS) website, updated in 2011 (2011 UBM Medica, London, United Kingdom) (MIMS, 2011; MIMS UK, 2011). The information present in MIMS is provided by the country's local health authority based on the approved prescription information in that country. The website offers quick access to information on the increasing number of drugs in the market, especially

regarding drug indications, dosage and side effects, and is thus commonly used by healthcare professionals. This includes general practitioners (or family physicians) among the front-line in treating AR patients, and as such, gives a good idea of the possible problems that they may encounter when faced with the information in MIMS.

Countries (or regions) with drug information available from the MIMS website were included. The 12 of them are (in alphabetical order): China, Hong Kong, India, Indonesia, Malaysia, Philippines, Singapore, Taiwan, Thailand, UK, US and Vietnam. Countries without information available for free were excluded (e.g., New Zealand and Australia).

The US Food and Drug Administration (FDA) recommendations were included in the study to provide a baseline comparison for both 2nd-generation antihistamines and intranasal corticosteroids (USFDA, 2011). The Australia Therapeutic Goods Administration (TGA) (TGA, 2011) recommendations were also included, where available but only for corticosteroids.

3. RESULTS

3.1 Prevention of AR

Among 19 Asia-Pacific countries/regions, 11 (57.9%) do not provide prevention recommendation guidelines for the management of AR.

Table 2 shows the information obtained on the different methods in the avoidance and reduction of allergen exposure for the prevention of AR. Data was categorized by types of allergen – house dust mite (HDM), pets, pollen, mould, cockroaches and irritant (i.e., cigarette smoke). Of these topics, we narrowed down to focus on the prevention of HDM and pet allergies as these two allergens are common and most relevant to the Asia-Pacific setting. We compared the effectiveness of prevention of allergy to HDM and pets to that recommended by ARIA (Bousquet et al., 2008; Brozek et al., 2010), regarded as the referent standard.

The results show that none of the 17 preventive methods have been recommended by all 9 countries/organizations. The regular use of chemical sprays/acaricides is only recommended by 1 country (South Africa). However, some recommendations are agreeable among the majority, such as keeping animals away from home to avoid pet allergens (8 out of 9), and ensuring that soft toys are dust-free (7 out of 9).

3.2 Pharmacotherapy – 2nd-Generation Antihistamines

The recommendations for the minimum age and somnolence as the most common side effect of the use of 2nd-generation antihistamines are shown in Tables 3 and 4 respectively. A specific brand of drug was chosen for each generic form so as to standardise across countries and provide a more suitable comparison. Countries not carrying that particular brand of drug are indicated accordingly in both Tables 3 and 4. The most updated FDA drug labels (USFDA, 2011) available for viewing on the FDA website are used as reference for each drug. Specific drug names are indicated in italics in both tables under the FDA column.

Table 2: Recommended methods for the avoidance and reduction of pet & house dust mite (HDM) allergen exposure

Category	Recommendation	Effectiveness (ARIA 2008 Update)*		WAO	ASIA-PACIFIC					OTHERS			Total
		Allergen level	Clinical benefit		AUS	CHI	MAL	PHI	THA	S AFR	UK	USA	
House dust mite				√	–	√	√	√	√	√	√	√	8
Avoidance	Soft toys should be washed/dust-free	N/A	N/A	√	–	√	√	√	–	√	√	√	7
	Mite proof encasing	Some	None (adults) Some (children)	√	–	√	–	√	√	–	√	√	6
	Use vacuum fitted with HEPA filter	Weak	None	√	–	√	–	–	√	–	√	√	5
	Remove/reduce curtains and soft furnishings	N/A	N/A	√	–	√	–	–	√	–	√	√	5
	Replace carpet with hard flooring	Some	None	√	–	√	–	–	√	–	√	√	5
	Dust surfaces with damp cloth	N/A	N/A	√	–	–	–	–	√	√	√	√	5
	Reduce humidity to below 50% by ventilation or dehumidifier	N/A	N/A	√	–	√	–	–	√	–	√	√	5
	Minimize objects that collect dust	None	None	–	–	–	–	–	√	√	–	–	2
Elimination	Wash bedding at 55-60℃	Some	None	√	–	√	–	–	√	√	√	√	6
	Freeze bedding overnight	N/A	N/A	–	–	–	–	–	√	–	–	√	2
	Expose bedding to strong direct sunlight for 5 hours	N/A	N/A	√	–	–	–	–	√	–	–	–	2
	Use chemical sprays/acaricides regularly	Weak	None	–	–	–	–	–	√	–	–	–	1
Pets				√	√	√	√	√	√	√	√	√	9
Avoidance	Do not keep animals at home/remove pets from home	Weak	None	√	√	√	√	–	√	√	√	√	8
	Keep pets outdoors, away from bedroom	Weak	None	√	–	–	√	√	√	–	√	√	6
	Clean/wash/vacuum regularly	N/A	N/A	√	–	–	–	–	√	–	√	√	4
	Change clothes after playing with pet	N/A	N/A	√	–	–	–	–	√	–	√	√	4
	Wash pets weekly	Weak	None	–	–	√	–	–	√	–	√	√	4

√ *Positive recommendation; – No information; N/A Not Available; * (Bousquet et al., 2011)*

The abbreviation for each country is same to Table 1

Table 3: Minimum age (in years) recommendations of 2nd Generation Antihistamines for treatment of AR across countries

Drug		FDA	MIMS										
Generic	**Specific**		**CHI**	**HK**	**INDIA**	**INDO**	**MAL**	**PHI**	**SIN**	**TWN**	**THA**	**UK**	**USA**	**VIET**
Acrivastine	Semprex	N/A	12*	N/A	N/A	N/A	N/A	12*	12*	N/A	N/A	N/A	N/A	12*
Cetirizine	Zyrtec	2 (SAR); 0.5 (PAR)*	1*	0.5*	0.5*	0.5* *[Ryzen]*	1*	1*	1*	3*	2*	2* *[Zirtek]*	0.5*	2*
Desloratadine	Aerius	2 (SAR); 0.5 (PAR)* *[Clarinex]*	12	0.5*	0.5* *[Rodera]*	1*	1*	0.5*	2*	12	0.5*	1* *[NeoClarityn]*	2 (SAR); 0.5 (PAR)* *[Clarinex]*	0.5
Ebastine	Kestine	N/A	2	N/A	6 *[Ebast]*	N/A	N/A	6* *[Aleva]*	Not stated	12 *[Ebastin]*	N/A	N/A	N/A	12
Fexofenadine	Telfast	2* *[Allegra]*	6 *[Raltiva]*	12	6* *[Allegra]*	12	12	12	6	6 * *[Allegra]*	6	6	6 *[Fexofenadine HCl]*	12
Levocetirizine	Xyzal	2 (SAR); 0.5 (PAR)*	6	2*	6*	6	6	2*	6	6	6	2*	6*	6
Loratadine	Clarityne	2* *[Claritin]*	2*	2*	2 *[Claridin]*	2* *[Claritin]*	2*	2* *[Claritin]*	2*	2*	2*	2* *[Loratadine]*	N/A	2*
Mizolastine	Mizollen	N/A	12	N/A	12 *[Elina]*	N/A	N/A	N/A	N/A	13	N/A	12	N/A	13

SAR: Seasonal Allergic Rhinitis; PAR: Perennial Allergic Rhinitis
** - available in syrup/solution form as well*
N/A - drug not available in country
FDA – US Food and Drug Administration; CHI – China; HK – Hong Kong; INDIA – India; INDO – Indonesia ;MAL – Malaysia; PHI – Philippines; SIN – Singapore
TWN – Taiwan ;THA – Thailand ; UK – United Kingdom; USA – United States of America; VIET – Vietnam

Table 4: Indication of somnolence[#] as side effect of drugs across countries

Drug		FDA	MIMS											
Generic	**Specific**		**CHI**	**HK**	**INDIA**	**INDO**	**MAL**	**PHI**	**SIN**	**TWN**	**THA**	**UK**	**USA**	**VIET**
Acrivastine	Semprex	N/A	Yes	N/A	N/A	N/A	N/A	Yes	Yes	N/A	N/A	N/A	N/A	N/I
Cetirizine	Zyrtec	Yes	N/I	Yes	Yes	Yes *[Ryzen]*	Yes	N/I	Yes	Yes	Yes	N/I	Yes	N/I
Desloratadine	Aerius	Yes *[Clarinex]*	N/I	N/I	Yes *[Rodera]*	Yes	N/I	N/I	N/I	N/I	N/I	N/I *[NeoClarityn]*	Yes *[Clarinex]*	N/I
Ebastine	Kestine	N/A	Yes	N/A	Yes *[Ebast]*	N/A	N/A	Yes *[Aleva]*	N/I	Yes *[Ebastin]*	N/A	N/A	N/A	Yes
Fexofenadine	Telfast	Yes *[Allegra]*	Yes *[Raltiva]*	N/I	Yes *[Allegra]*	Yes	Yes	Yes	Yes	Yes *[Allegra]*	Yes	Yes	Yes *[Fexofenadine HCl]*	Yes
Levocetirizine	Xyzal	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Loratadine	Clarityne	Yes *[Claritin]*	Yes	Yes	Yes *[Claridin]*	Yes *[Claritin]*	Yes	Yes *[Claritin]*	Yes	Yes	N/I	N/I *[Loratadine]*	N/A	Yes
Mizolastine	Mizollen	N/A	N/I	N/A	Yes *[Elina]*	N/A	N/A	N/A	N/A	Yes	N/A	Yes	N/A	Yes

N/A – Drug not available in country
N/I – Not indicated
 # – Occurring in greater than or equal to 1- 3% of patients who receive the recommended daily dose of the drug and more commonly than placebo
The abbreviation for each country is same to Table 3

3.2.1 Recommendations for the minimum age and dose

Three commonly prescribed 2nd-generation antihistamines such as cetirizine, levocetirizine and desloratadine have shown different recommended minimal ages in different countries. For cetirizine, the minimum age varies between 6 months to 3 years.

Hong Kong, Philippines, Thailand and Vietnam have their minimum age stipulated as 6 months. In China, Malaysia, Philippines and Singapore, the minimum approved age is 1 year. In Thailand and Vietnam, it is 2 years, while in Taiwan, it is only approved for children aged 3 and above. For fexofenadine, the ages of approval vary between 6 and 12 years. China, India, Singapore, Taiwan, Thailand, UK and USA approves them for children above 6 years, while in Hong Kong, Indonesia, Malaysia, Philippines and Vietnam, it is approved only in patients aged 12 and above. On the other hand, there is a common agreeable recommended minimum age of 2 years for loratadine for all countries.

The dose recommended for children also varies in different countries. Different parameters are used in recommendations for dosage in different countries. For example, in case of loratadine, the recommended dose by FDA, India and UK is 5 mg for children aged 2 to 5 years and 10 mg for children 6 years and older, whereas most of the other countries/regions (eg. China, Hong Kong, India) make recommendations based on the child's age and weight, where in children aged 2 to 12, those weighing below 30 kg should take 5 mg while those above 30 kg should take 10 mg.

Variations in recommendations exist not only in children, but in adults as well. For fexofenadine, adult dosage (≥ 12 years) may be either 120 mg or 180 mg, depending on the country. Hong Kong, Indonesia, Thailand and Vietnam allow for 120 mg or 180 mg, while Philippines and UK recommend 120 mg only, and Malaysia and Singapore 180 mg only. For levocetirizine, USA, India and Indonesia allows for total dose of 5 mg a day only in adults/children 12 years and above, whereas the rest of the countries approve the use of 5 mg of levocetirizine daily in children from 6-years old on.

3.2.2 Somnolence as a side effect

2nd-generation antihistamines are known for their non-sedating properties. However, a check on MIMS shows that most 2nd generation antihistamines report somnolence as one of its adverse side effects. Side effects are reported when it occurs in greater than or equal to 1-3% of patients who receive the recommended daily dose of the drug and occur more commonly than placebo (MIMS, 2011). Levocetirizine has been reported in all countries/regions to cause somnolence. For the same drug, some countries/regions report it as causing somnolence whereas in others, this side effect is not mentioned. For example for desloratadine, 9 out of 12 (75%) countries/regions do not indicate that it causes somnolence. For fexofenadine, 11 out of 12 (91.7%) countries/regions indicate it as causing somnolence. It is important to note that in Table 4, "not indicated (N/I)" does not necessarily indicate that there is no somnolence, but that it is not reported on MIMS to cause somnolence.

3.2.3 Pregnancy safety profile

By FDA classification (USFDA, 2011), all 2nd generation antihistamines have not been proven to be completely safe in pregnant women. Acrivastine, cetirizine, levocetirizine and loratadine have been classified under Category B, desloratadine and fexofenadine are under Category C, while ebastine and mizolastine were unavailable (MIMS, 2011).

According to FDA, a Category B classification would mean "either animal-reproduction studies have not demonstrated a foetal risk but there are no controlled studies in pregnant women or animal-reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the 1st trimester (and there is no evidence of a risk in later trimesters)", while Category C would mean "either studies in animals have revealed adverse effects on the foetus (teratogenic or embryocidal or other) and there are no controlled studies in women or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the foetus." Drugs in both categories are not proven to be definitely safe in pregnant women.

3.3 Pharmacotherapy - Intranasal Corticosteroids

A total of eight available intranasal corticosteroids were selected. The recommendations for the minimum age and daily dose are shown in Tables 5 and 6 respectively.

3.3.1 Recommendations for the minimum age and dose

Triamcinolone acetonide has four different recommendations in minimal age, ranging from ≥2 years (US, Thailand) to 12 years (Indonesia). It is followed by mometasone furoate (n=3, ranging from ≥2 to 6 years), then fluticasone furoate (n=2, ranging from ≥2 to 6 years) and budesonide (n=2, ranging from ≥6 years to "not for children"). Mometasone furoate can be used for children aged ≥2 years (Hong Kong, India, Indonesia, Philippines, Singapore, US, Vietnam), ≥3 years (Australia, China, Malaysia, Taiwan, Thailand) and ≥6 years (UK). Budesonide is approved for children aged ≥6 years in all countries except UK (not recommended for children), while fluticasone furoate is approved for children aged ≥2 years in all countries except Singapore and UK (≥6 years). In a few instances, recommendations for the minimum age are not even stated at all.

There are differences in total daily dose, especially in children, as recommended in different countries (Table 6). Doses approved for beclomethasone dipropionate in China, Hong Kong, Malaysia and Thailand (300-400 µg) are significantly larger than that approved by FDA (168-336 µg). The dose approved for budesonide in most countries is 256 µg (the maximum total daily dose recommended by FDA) for use in adults and children ≥6 years although FDA recommends an initial daily dose of 64 µg. Additionally, while most countries allow adult dosing for the paediatric population, FDA is more conservative (64-128 µg for children aged 6-11). The UK does not approve it for use in children at all. India and Indonesia also allow higher daily doses (400 µg).

3.3.2 Pregnancy safety profile

Budesonide is the only intranasal corticosteroid under Category B, while beclomethasone dipropionate, ciclesonide, fluticasone propionate, fluticasone furoate, mometasone furoate and triamcinolone acetonide are classified under Category C. FDA pregnancy safety data for flunisolide was unavailable.

4. DISCUSSION

It is shocking to find in our study that national allergy (AR and/or asthma) preventive programmes are found in only 6 out of 17 (22.2%) Asia-Pacific countries/regions (excluding Japan and South Korea).

Table 5: Minimum age (in years) recommendations of Intranasal Corticosteroids across countries for treating AR

SAR: Seasonal Allergic Rhinitis; PAR: Perennial Allergic Rhinitis

Drug		TGA AUS	FDA	MIMS										
Generic	**Specific**			**CHI**	**HK**	**INDIA**	**INDO**	**MAL**	**PHI**	**SIN**	**TWN**	**THA**	**UK**	**US**	**VIET**
Beclomethasone dipropionate	Beconase	N/A	6	6	6	Not stated *[Beclate]*	N/A	6	N/A	Not stated *[Beclomet]*	Not stated *[Beclomet]*	6	6	N/A	6 *[Beclate]*
Budesonide	Rhinocort	6	6	6	6	Not stated	Not stated (generic)	6	6 *[Budecort]*	6	6 *[Pulmicort]*	6	Not for children	6	6
Ciclesonide	Omnaris	N/A	6 (SAR) 12 (PAR)	N/A	6 (SAR) 12 (PAR)	N/A	N/A	12	6 (SAR) 12 (PAR)	N/A	N/A	N/A	N/A	N/A	N/A
Flunisolide	Syntaris	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	5	5 *[Flunisolide]*	N/A
Fluticasone propionate	Flixonase	N/A	4 *[Flonase]*	4	4	4	4	4	4 *[Flixotide]*	4	4	4	4 *[Nasofan]*	4 *[Flonase]*	4
Fluticasone furoate	Avamys	2	2 *[Veramyst]*	N/A	2	N/A	Not stated	2	2	6	Not stated	2	6	2 *[Veramyst]*	N/A
Mometasone furoate	Nasonex	3	2	3	2	2 *[Metaspray]*	2	3	2	2	3	3	6	2	2
Triamcinolone acetonide	Nasacort	N/A	2	12 *[Xing Rui Ke]*	6	N/A	12	6	6 *[Actonaze]*	4	6	2	6	2	6

N/A – Drug not available in country or not indicated for AR
Not stated – Information not stated on MIMS website
TGA AUS – Therapeutic Goods Administration Australia
FDA – US Food and Drug Administration

The abbreviation for each country is same to Table 3

Table 6: Total daily dose (µg) recommendations of Intranasal Corticosteroids across countries for treating AR

Drug		Dose	TGA AUS	FDA	MIMS											
Generic	**Specific**				**CHI**	**HK**	**INDIA**	**INDO**	**MAL**	**PHI**	**SIN**	**TWN**	**THA**	**UK**	**US**	**VIET**
Beclomethasone dipropionate	Beclate/ Beclomet/ Beconase	A C	N/A	168-336	300-400	300-400	300-400 N/A	N/A	400	N/A	200-500 200-250 (<12)	200-500 200-250 (<12)	300-400	400	N/A	200-400 (>6)
Budesonide	Budecort/ Pulmicort/ Rhinocort	A C	256 (≥6)	64-256 64-128 (6-11)	256 (≥6)	256 (≥6)	400 N/A	400 N/A	256 (≥6)	256 (≥6)	256 (≥6)+	256 (≥6)	256 (≥6)	256 N/A	64-256 64-128 (6-11)	256 (≥6)
Ciclesonide	Omnaris	A C	N/A	200	N/A	200	N/A	N/A	200	200	N/A	N/A	N/A	N/A	N/A	N/A
Flunisolide	Flunisolide /Syntaris	A C	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	200-300 Up to 150	200-300 Up to 150	N/A
Fluticasone propionate	Flixonase/ Flixotide/ Flonase/ Nasofan	A C	N/A	200 100-200 (4-11)	200-400 100-200 (4-11)	200-400 100-200 (4-11)	200-400 100-200 (>4)	200-400 100-200 (4-11)	200-400 100-200 (4-11)	200-400 100-200 (4-11)	200-400 100-200 (4-11)	200-400 100-200 (4-11)	200-400 100-200 (4-11)	200-400 100-200 (4-11)	200 100-200 (4-11)	200-400 100-200 (>4)
Fluticasone furoate	Avamys/ Veramyst	A C	110 55-110 (2-11)	110 55-110 (2-11)	N/A	110 55-110 (2-11)	N/A	Not stated	110 55-110 (2-11)	110 55-110 (2-11)	110 55-110 (6-11)	Not stated	110 55-110 (2-11)	110 55-110 (6-11)	110 55-110 (2-11)	N/A
Mometasone furoate	Nasonex	A C	200 100 (3-11)	200 100 (2-11)	200-400 100 (3-11)	200 100 (2-11)	200-400 100 (2-11)	200-400 100 (2-11)	200-400 100 (3-11)	200-400 100 (2-11)	200-400 100 (2-11)	200-400 100 (3-11)	200-400 100 (3-11)	200-400 100 (6-11)	200 100 (2-11)	200 100 (2-11)
Triamcinolone acetonide	Actonaze/ Nasacort/ Xing Rui Ke	A C	N/A	220 110-220 (6-12) 110 (2-5)	440 N/A	220 110 (6-12)	N/A	220 N/A	220 110-220 (6-12)*	220 110-220 (6-11)	220 110-220 (4-12)	220 110-220 (6-12)	220 110-220 (6-12) 110 (2-5)	220 110 (6-11)*	220 110-220 (6-12) 110 (2-5)	220 110-220 (6-12)*

A: Adult; C: Child
SAR – Seasonal Allergic Rhinitis; PAR – Perennial Allergic Rhinitis
+ - 32, 64µg/ dose
N/A – drug not available in country or not indicated for AR
** - continuous use beyond 3 months is not recommended for children <12 years*
Data presented in parenthesis in table indicates age

TGA AUS – Therapeutic Goods Administration Australia

The abbreviation for each country is same to Table 3.

What is perhaps more alarming is that there exist several aspects of discrepancies across these different guidelines. Firstly, there are mixed indications for these guidelines. Malaysia and Thailand guidelines are indicated for broad allergic diseases, whereas guidelines by Philippines focus on asthma.

This causes confusion as to whether the guidelines can be applied to a scope of conditions. Secondly, the targeted age group varies. For instance, Malaysia and Australasia both have recommendations targeted only at children, whereas other countries do not specify the target group. Again, this questions whether prevention methods should be generalized or catered specifically to the needs of different age groups. Thirdly, the different guidelines vary in breadth and depth for various topics of recommendations (Tables 1, 2). For example, guidelines from USA and WAO have a comprehensive coverage of all topics. In contrast, Australasia's guidelines focus more on food allergy, emphasizing less on common airborne allergies, and omitting recommendations for HDM. Given the various levels of discrepancies as highlighted above, there is perhaps a need to devise a set of centralized guideline to avoid confusion.

So far, several practical recommendations have been implemented by professional and health care educational organizations (Table 1) in Asia-Pacific countries although there are differences recommendation details among countries. One method is the use of a vacuum fitted with a HEPA filter, where it is recommended by 5 out of 9 guidelines. However, this method may not be practical in terms of cost, as a HEPA filter costs approximately USD100 per set, and requires replacement every few months, compounding the cost. This recommendation is thus unfeasible, especially in Asia where there are many patients in developing countries who might be unable to afford the high cost. Moreover, based on ARIA 2008 update and 2010 revision, all current available single chemical or physical preventive methods, or in combination, have not been well confirmed to be effective in reducing HDM exposure (Bousquet et al., 2008; Brozek et al., 2010).

The minimum age of 2nd-generation antihistamine recommendations differ across countries largely based on availability of forms of the medication. If the drug is available in paediatric drops or syrup/solution form, the minimum age tends to be lower in that country. For example, desloratadine is approved for children of lower ages in countries where the solution/syrup preparation of desloratadine is available. However, we also noticed that even with the same forms of drug available, there were still some variations in recommendations of minimum age. These differences in minimum age are not caused by availability of the form of the drug, as all countries carry the same form of the drug. For example, fexofenadine is available only in capsule/tablet form in all the countries mentioned in Table 3 but yet differences in minimal age recommendations across countries still exist. This difference in minimum age should not be present as it is illogical, for example, for a 2-year-old not to be allowed to take a certain drug should he travel to another country with a different minimum age requirement.

There also seems to be a discrepancy between FDA recommendations and what is provided under US MIMS. The minimum age for Fexofenadine and Xyzal (levocetirizine) differ between FDA and US MIMS. We compared 2 different brands of Fexofenadine – Allegra (FDA) and Fexofenadine hydrochloride (US MIMS), as Allegra was absent from the US MIMS database. Though they are marketed as different brands, they are essentially the same drug with the same amount of active ingredient, so this discrepancy in minimum age should be further elucidated as differences in guidelines within a country can potentially mislead healthcare practitioners. Discrepancies in dose recommendations arise from many

aspects, such as different parameters being used as reported earlier. The reasons should be elucidate, as this can cause confusion and result in vastly different dosages being prescribed for patients. There are also discrepancies in whether the drug causes somnolence across countries. This could be due to differing standards across countries in determining severity or importance of a side effect to be listed. It is important to find out the cause of the discrepancies in order to give a more accurate picture of the kind of adverse drug effects on the patient.

Recommendations for intranasal corticosteroids provided are based on the approval of relevant authorities in individual countries, not prescribed in the ARIA guidelines. Lack of standardisation may be surprising given that some drugs have already been in the market for years. The recommended use of triamcinolone acetonide for children varies within Singapore itself, with MIMS Singapore stating its suitability for children ≥4 years old, while local Ministry of Health (MOH) Clinical Practice Guidelines recommended it for children ≥6 years old (MOH, Singapore, 2010). It is possible that such discrepancies may also exist within other countries and calls for greater cooperation between governmental bodies and local drug approval authorities in reaching a consensus on prescribing drug use recommendations in the local setting. For dosage recommendations, most drugs show similarity across countries while maximum total daily dose may vary (eg. beclomethasone dipropionate, fluticasone propionate and momethasone furoate). India and Indonesia's higher daily dose (400 µg) for budesonide could be attributed to the use of generically approved drug information. Another issue identified is dosage recommendation in MOH Singapore's CPG in terms of number of spray, despite local availability of budesonide in 2 dosage volumes: 32 µg/spray and 64 µg/spray (Health Sciences Authority, Singapore, 2010). Hence, careless prescription based on MOH CPG (2-8 sprays) without reference to the dosage volume may actually exceed recommended total daily dose (256 µg).

Bone growth suppression in children from the use of intranasal corticosteroids remains inconclusive at the moment. Labels provide conflicting information across countries, with most mentioning it as a possible side effect, some even including reports of such findings (e.g. budesonide and triamcinolone acetonide) whereas others (e.g. for fluticasone furoate and mometasone furoate), show no significant short-term impact within one year. Yet, most also carry the disclaimer that long-term effects are not fully studied and advise caution in growth velocity monitoring for chronic, high-dose use in children. Epistaxis is commonly mentioned as a side-effect in most countries but not for budesonide (UK), fluticasone propionate (India, Indonesia) and fluticasone furoate (Indonesia, Taiwan).

FDA no longer uses the old Pharmaceutical Pregnancy Categories (A, B, C, D and X) to indicate the safety of drugs in pregnant women (USFDA, 2009). In November 2009, FDA issued a statement regarding the revision of the above-mentioned Pharmaceutical Pregnancy Categories (A, B, C, D and X) as they "do not always distinguish between risks based on human versus animal data findings or between differences in frequency, severity, and type of foetal developmental toxicities". Under the new proposed rule, the pregnancy subsection in drug labels should carry 3 components – a foetal risk summary, clinical considerations and a data section. However, pregnancy safety information on the MIMS website is still based on the outdated pregnancy category risk system. Current FDA-approved drug labels available on the FDA website have not yet been revised with the updated pregnancy subsection. For example, the current label for fluticasone propionate has been in use since 2004. This may cause confusion among physicians and patients.

Some limitations were faced while conducting the analysis. During our research, we found that some countries carry many brands of the same drug. India, for example, tends to carry easily 30 brands of the same antihistamine. While this gives the consumer a wider choice, this can be troubling to both the patient and the doctor. Such practices should be reviewed. For intranasal corticosteroids, the same active component in a drug may be marketed under different names under different companies, complicating the comparison so the most common drug is selected for each active component for comparison within the countries where it is approved for use. As a result of this selection, we may be unable to capture the true picture of differences in drug dosage and minimum age for drug use.

5. CONCLUSION

The lack of coordination between international bodies which specialize in allergy practice and national bodies result in controversy in the recommendation guidelines for allergen avoidance and drug regulation of allergic patients. It is important for the establishment of a standardised clinical practice guideline for health care professionals to provide the best form of management and treatment to their patients. As such, there needs to be extensive collaboration between the international bodies (who harbours the knowledge and expertise in allergy practice) and governmental administration (who sets the nation's clinical practice guidelines), in order to achieve a consensus in the management of allergic patients. The reason behind the differences in recommendations across countries and within specific countries itself should be elucidated and improvements on reducing these discrepancies made to reduce confusion for the benefit of the physician prescribing these medications and ultimately for the benefit of our patients.

ACKNOWLEDGEMENT

We would like to thank our other member, Tai Beishan Sarah, for her contributions.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

Asthma, Allergy and Immunology Society of Thailand (AIST). Retrieved 26 September, 2010, from http://www.immunologythai.org/index.php?name=people_publication&file=Allergy06

Bousquet, J., Khaltaev, N., et al. (2008). Allergic rhinitis and its Impact on Asthma (ARIA) 2008 Update. Allergy., 63 (Suppl 86), 1-160.

Bousquet, J., Van Cauwenberge, P., Khaltaev, N., et al. (2001). Allergic rhinitis and its Impact on Asthma (ARIA) (ARIA Workshop Report). J Allergy Clin Immunol., 108 (5 Suppl), S147-334.

British Allergy Foundation (Aug 2008). Avoiding Indoor Allergens Allergy UK. Retrieved 26 September, 2010, from http://www.allergyuk.org/fs_indoor.aspx.

Brozek, J.L., Bousquet, J., Baena-Cagnani C.E., Sergio Bonini, Canonica, G.W. et al. (2010). Allergic Rhinitis and its Impact on Asthma (ARIA) 2010 revision. J Allergy Clin Immuno., 126, 466-476.

Dr. Adrian Morris (date) General - The Control Measures of House dust Mites. Allergy Society of South Africa. Retrieved 26 September, 2010. from http://www.allergysa.org/C_OL_General.asp

Drugs@FDA. *U.S. Food and Drug Administration*. Retrieved 18 June, 2011, from http://www.accessdata.fda.gov/scripts/cder/drugsatfda/

Health Sciences Authority, Singapore. Retrieved 25 August, 2010, from http://eservice.hsa.gov.sg/prism/common/enquirepublic/SearchDRBProduct.do?action=load

Johansson, S.G.O., Haahtela, T., (2007). World Allergy Organization Guidelines for Prevention of Allergy and Allergic Asthma. World Allergy Organisation. Retrieved from http://www.worldallergy.org/wad2007/infosheet.pdf

Malaysian Society of Allergy and Immunology (MSAI) (2005-2007). Prevention of Allergy in Children XYZofAllergy.org. Retrieved August, 2010, from http://www.xyzofallergy.org/index.php?mode=articleRead&id=78.

MIMS (2011). Retrieved 18 June, 2011, from www.mims.com.

MIMS UK (2011). Retrieved 18 June, 2011, from www.mims.co.uk.

Ministry of Health, Singapore. (2010). *Management of Rhinosinusitis and Allergic Rhinitis. MOH Clinical Practice Guidelines 2/2010.* Retrieved 25 August, 2010, from https://www.moh.gov.sg/mohcorp/publications.aspx?id=24046

National Institute of Environment Health Science(NIEHS) (December 15 2010 last reviewed) Allergens and Irritants. National Institute of Environment Health Science(NIEHS). Retrieved August 2010, from http://www.niehs.nih.gov/health/topics/conditions/asthma/allergens/index.cfm

Philippine Society of Allergy, Asthma and Immunology (PSAAI). Asthma Triggers in your Home. Retrieved 26 September, 2010, from http://www.psaai.org/articles/asthma-triggers-in-your-home

Summary of Proposed Rule on Pregnancy and Lactation Labeling. (2009, November 12). *U.S. Food and Drug Administration*. Retrieved 2 January, 2011 from http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093310.htm.

Therapeutic Goods Administration, Australia. Retrieved 2 Jan 2011 from http://www.tga.gov.au/

World Allergy Organization. Retrieved August, 2010, from http://www.worldallergy.org/index.php

过敏反应科. Haodf. Retrieved September, 2010, from http://guomin123.haodf.com//