Cost of therapy for allergic rhinitis

Francois Wessels, Robin Green, David Luyt

Objective. To describe the cost of medicines used in the treatment of allergic rhinitis in South Africa.

Design. MIMS was used as the reference for the list of drugs, drug formulation and size, and recommended dosage. These figures were then checked against the package insert of each agent. The cost of each agent was originally derived from the same source, but for standardisation purposes the blue book price was used. Measure of effectiveness was derived from the International Consensus Report on the Diagnosis and Management of Rhinitis. Costs per treatment periods of 10 days (course) and 30 days (month) were calculated. The 'cost' differs from the 'price' in that it takes efficacy into account.

Main outcome measures. Cost of drugs used in the treatment of allergic rhinitis.

Results. The least costly treatments for allergic rhinitis are the intranasal corticosteroids. Sodium cromoglycate was the most costly, being nearly 20 times more expensive than the nasal steroids. Anticholinergic sprays and topical decongestants were also more costly than nasal steroids, as were the antihistamines. The older-generation antihistamine, ketotifen, was not only more costly than the four oral newer-generation agents in this class but has the added disadvantage of greater sedative side-effects. All oral antihistamines were outclassed by the topical antihistamine, levocabastine.

Conclusions. This study in no way aims to recommend treatment for allergic rhinitis. However, it highlights the need to consider efficacy of a drug before unit price in the selection of treatment regimens. It is therefore a comment on practical issues in drug selection in the treatment of allergic rhinitis.

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Cost is an integral consideration of the management of any disease. It is now well recognised that for South Africa to continue to afford quality health services, providers of medical care will have to look critically at the therapy they prescribe.[1] This is particularly true in chronic conditions such as asthma and allergic rhinitis. To consider prices in

Johannesburg

Francois Wessels, MSc (Pharmaco-economist)

Parklane Clinic, Johannesburg

Robin Green, FC Paed (SA)

David Luyt, FC Paed (SA)

isolation, though, results in component management, and can lead to escalating health care costs.[2] In order to succeed, a disease management approach should be followed and the underlying basis should include a clinical consensus statement, e.g. the asthma consensus statements.[3-6] Only in this way can we persuade the medical community to consider these guidelines their own and adopt them as a standard to guide the management of a disease.[7]

Allergic rhinitis is a very common condition with significant potential morbidity. The prevalence of allergic rhinitis has been reported to be as high as 24%[8] and there is evidence that this prevalence is increasing.[9] It is now no longer regarded as a trivial disease. Rhinitis *per se* has significant effects on the quality of life of the patient.[10,11] Patients frequently suffer from headaches, impaired concentration and poor sleep. Furthermore, rhinitis is also associated with significant complications that demand an ever-increasing share of the health budget. Examples include grommets for serous otitis media, investigations and surgical procedures for chronic sinusitis and surgical correction of dental malocclusion. Unlike in most northern climes, in South Africa allergic rhinitis sufferers face one additional problem — the condition is usually perennial (possibly with seasonal exacerbations) and not typically restricted to a short pollen season. Clearly our long pollen seasons[12] and common perennial triggers such as house-dust mite[13] are responsible for this scenario.

Therefore, if we wish to de-trivialise allergic rhinitis and thus manage it better, with prophylactic and regular therapy much like that for asthma, we need to look to cost-effective therapy. It is difficult, if not impossible, to make didactic recommendations about cost-effective therapy for every patient and every eventuality in the case of a chronic, often variable, condition. However, what can be done is to look at the rand value of a therapy in association with its documented efficacy in this condition and produce an 'adjusted' cost per treatment period. In this way the relative cost of two agents can be compared, and the doctor facing the decision to treat this condition can make an informed selection.

In this paper we evaluated the cost of each drug registered for allergic rhinitis in South Africa and, using documented efficacy, evaluated the cost of each agent. The paper aims to guide doctors to use cost rather than price to select agents when prescribing.

Methods

Assumptions

In developing the measures of cost-effectiveness, assumptions in respect of duration of a course of treatment and effectiveness of drug categories have to be made. Drugs registered for allergic rhinitis that were evaluated are listed in Table I.

Dosage

The recommended dosage of each agent was sourced from *MIMS Medical Specialities*.[14] These figures were then checked against the package insert of each agent.

Table I. Treatment of allergic rhinitis in adults[15]

Drug category	Itch/ sneezing	Discharge	Blockage	Impaired smell
Sodium cromoglycate	+	+	±	–
Oral antihistamines	+++	++	±	–
Ipratropium bromide	–	+++	–	–
Topical decongestants	–	–	+++	–
Topical corticosteroids	+++	+++	++	+
Oral corticosteroids	+++	+++	+++	++

Duration of a course of treatment

The average course of treatment was assumed to last 10 days. Figures representing the price for medication were thus calculated for two periods, viz. a course (10 days) and a month (30 days). Many of these drugs, e.g. topical corticosteroids, are not used over as short a period of time as 10 days; however, for comparative purposes, calculations were made for all agents for both treatment periods.

Measure of effectiveness

The measures of effectiveness in the treatment of three of the most important (and most measurable) symptoms of rhinitis were derived from the International Consensus Statement[15] (Table I). A fourth symptom, impaired smell, was excluded from the calculation. This document indicated relative effectiveness in terms of pluses and minuses (+++ most effective, ++ less effective, + not very effective, ± rather ineffective, – not effective). These were then expressed as numbers, with 1 being the most effective and 5 the least effective (effectively penalty scores therefor!). The scores are therefore essentially weights that indicate or assess the performance of different drug categories in controlling individual symptoms or symptom complexes. This scoring system is shown in Table II.

Table II. Measures of ineffectiveness

Drug category	Itch/ sneezing	Discharge	Blockage	Total
Sodium cromoglycate	3	3	4	36
Oral antihistamines	1	2	4	8
Ipratropium bromide	5	1	5	25
Topical decongestants	5	5	1	25
Topical corticosteroids	1	1	2	2

The total score of (in)effectiveness was calculated in a multiplicative way, by determining the product of symptom-specific effectiveness scores. A multiplicative approach was adopted, given that the measure of interest was to indicate the ability successfully to treat all three symptoms combined, and not only one of them.

Formulation, unit size and unit price

Formulation indicates the strength or sometimes unit strength of the drug under consideration. Information on the formulation of the drug was derived from *MIMS*[14] and the package insert of each agent.

Unit size indicates the volume or number of doses per dispenser, bottle or inhaler. *MIMS*[14] was used as the reference work and the standard unit size reported was used in calculations. In almost all cases this was appropriate, given that a course of medication covers 10 days, and the standard unit size usually covers a similar period. The use of a bigger container or unit size is usually not justified.

The pharmaceutical listing or 'blue book' (April 1996) was used as a reference for *unit price.* These retail prices were used as a standard, given that they are published in a well-known source, which can be considered to be without commercial bias and therefore objective.

General assumptions

Where the dosage was expressed in drops, a drop was assumed to be 0.05 ml or, alternatively, that there were 20 drops per millilitre.

Rhinocort (budesonide) aqueous nasal spray presented some problems in that the number of doses per dispenser was not indicated in *MIMS*.[14] The manufacturers confirmed that the dispenser contained 200 doses. One puff daily was taken to mean one puff per nostril daily.

Methodology

The drug categories included in the cost analysis were taken from the International Report on the Diagnosis and Management of Rhinitis.[15] Within these categories, the most important drugs currently used in South Africa were identified. Unless otherwise stated, the dosage reflected is an adult dosage.

It was decided to focus on two treatment periods, here identified as a treatment course and a month of treatment. This will enable one to distinguish between acute and chronic treatment.

On the basis of the daily requirements shown in Table III, the requirement per treatment period (both *course* and *month*) was calculated as a multiple of the unit size. This was done by calculating the total volume of active ingredient or the total number of doses per container or dispenser as the product of the unit size and the strength (or formulation). The total dosage required per treatment period was 10 or 30 times the daily dosage required, respectively.

The drug requirement is expressed as the number of units per treatment period. Multiplication of this figure by the unit price determined the price per treatment period (Table III) and can be used to do a simple price comparison. This is not very meaningful, however, given that it does not take *efficacy* into consideration and is therefore only a one-dimensional comparison.

To make the transition from *price* to *cost*, a measure of efficacy was introduced. This came in the form of the total symptom control score reported in Table II. The prices previously calculated were multiplied by these scores to obtain cost-effectiveness scores or cost. Once again, this was done both for a treatment course and a month's treatment for every drug considered. The last two columns in Table IV list the respective costs. These can be used for comparison of the costs of different drugs in the control of allergic rhinitis.

Results

No attempt is made to suggest how and for how long individual agents should be used in treatment. However, as described above, most agents are to be used long term so comparisons were made for these time periods.

Drugs registered for use in allergic rhinitis are listed in Table III. The formulation and daily dosage are derived from *MIMS*.[14] The list is divided into four groups, the last reflecting two individual agents in individual classes; sodium cromoglycate and ipratropium bromide. These are the five classes of agents evaluated as allergic rhinitis in the International Consensus Report.[15] Table II shows the total ineffectiveness scores for each class of drug.

Table III. Medicines registered for allergic rhinitis that were used in analysis

Generic name	Trade name	Formulation	Daily dosage
Astemizole	Hismanal	Tablets – 10 mg	10 mg
		Syrup – 1 mg/ml	5 mg
Cetirizine	Zyrtec	Tablets – 10 mg	10 mg
Ketotifen	Zaditen	Tablets – 1 mg	2 mg
		Syrup – 0.2 mg/ml	1 mg
Loratidine	Clarityne	Tablets – 10 mg	10 mg
		Syrup – 1 mg/ml	5 mg
Terfenadine	Triludan	Tablets – 60 mg	120 mg
Levocabastine	Livostin	50 µg/puff	400 µg
Oxymetazol HCl	Drixine	Spray – 0.5 mg/ml	0.5 ml
		Drops – 0.5 mg/ml	0.5 ml
		Paed. spray pump – 0.25 mg/ml	0.5 ml
		Paed. drops – 0.25 mg/ml	0.5 ml
Oxymetazoline HCl	Iliadin	Adult meter spray – 0.5 mg/ml	0.6 ml
		Adult drops – 0.5 mg/ml	0.6 ml
		Paed. meter spray – 0.25 mg/ml	0.6 ml
		Paed. drops – 0.25 mg/ml	0.6 ml
		Nasal spray – 0.5 mg/ml	0.2 ml
Xylometazoline HCl	Otrivin	Adult drops – 1.0 mg/ml	0.6 ml
		Paed. drops – 0.5 mg/ml	0.2 ml
		Spray – 1.0 mg/ml	0.05 ml
Dimethidene	Vibrocil drops	– in adults and children + 6 yrs	1.2 ml
Phenylephrine		– in children 1 - 6 yrs	0.6 ml
Neomycin		– in infants	0.3 ml
		Nasal spray microdoser	0.3 ml
Beclomethasone	Beconase	50 µg/puff	400 µg
	Clenil	50 µg/puff	400 µg
	Viarox	50 µg/puff	400 µg
	Ventnase	50 µg/puff	400 µg
Betamethasone	Betnesol drops	1 000 µg/100 ml	0.6 ml
Budesonide	Rhinocort MDI	50 µg/puff	400 µg
	Rhinocort aqueous	1 000 µg/100 ml	400 µg
Flunisolide	Syntaris	25 µg/puff	100 µg
Fluticasone	Flixonase	50 µg/puff	200 µg
Triamcinalone	Nasacor	55 µg/puff	220 µg
Sodium cromoglycate	Rynocrom	20 mg/ml	26 mg
Ipratropium bromide	Atronase	20 µg/puff	160 µg

In Table IV the mean price per course and per month as well as the adjusted cost per course and per month are shown.

As is evident from this comparison, the older-generation antihistamine, Zaditen (ketotifen), does not compare favourably with the newer less sedative antihistamines (Hismanal (astemizole), Zyrtec (cetirizine), Clarityne (loratidine) and Triludan (terfenadine)). Livostin (levocabastine), one of the new topical antihistamines, in turn outperforms the latter group.

On average, nasal corticosteroids seem to be the least costly way of treating allergic rhinitis. Rynocrom (sodium cromoglycate) proved to be the most costly drug in the control of rhinitis. The nasal steroids typically outperformed sodium cromoglycate by a factor of close to 20. This means that Rynocrom has to be 20 times safer than nasal steroids to justify inclusion in a treatment protocol — a significant margin in any comparison.

Both anticholinergics and topical decongestants are outclassed by the nasal steroids. Topical decongestants are a costly way of treating allergic rhinitis.

Table IV. Cost analysis of drugs registered for allergic rhinitis

Drug	Unit price (R)	Daily dosage (mean)	Price per course (mean) (R)	Price per month (mean) (R)	Cost per course (mean)	Cost per month (mean)
Hismanal						
Tablets	107.65	10 mg	35.88	107.65	287.07	861.20
Syrup	51.74	5 mg	25.87	77.61	206.96	620.88
Zyrtec						
Tablets	123.93	10 mg	41.31	123.93	330.48	991.44
Zaditen						
Tablets	234.49	2 mg	78.50	235.49	627.97	1 883.92
Syrup	149.61	5 ml	37.40	112.21	299.22	897.66
Clarityne						
Tablets	109.85	10 mg	36.62	109.85	292.93	878.80
Syrup	55.36	5 mg	27.68	83.04	221.44	664.32
Triludan						
Tablets	107.05	120 mg	35.68	107.05	285.47	856.40
Livostin	62.40	400 µg	33.28	99.84	266.24	793.72
Drixine						
Spray	18.30	0.5 ml	9.15	27.45	228.75	686.25
Drops	18.30	0.5 ml	18.30	54.90	457.50	1 372.50
Paed. spray pump	27.98	0.5 ml	55.96	167.88	1 399.00	4 197.00
Paed. drops	17.61	0.5 ml	35.22	105.66	880.50	2 641.50
Iliadin						
Adult meter spray	29.48	0.5ml	29.48	88.44	737.00	2 211.00
Adult drops	22.39	0.6 ml	26.87	80.80	671.70	2 015.10
Paed. meter spray	29.48	0.6 ml	70.75	212.26	1 768.80	5 306.40
Paed. drops	22.39	0.6 ml	53.74	161.21	1 343.40	4 030.20
Nasal spray	22.71	0.2 ml	4.54	13.63	113.55	340.65
Otrivin						
Adult drops	21.50	0.6 ml	12.90	38.70	322.50	967.50
Paed. drops	19.90	0.2 ml	7.96	23.88	199.00	597.00
Spray	22.73	0.05 ml	1.14	3.41	28.41	85.24
Vibrocil						
Drops (adults)	24.25	1.2 ml	29.10	87.30	727.50	2 182.50
Drops (children)	24.25	0.6 ml	14.55	43.65	363.75	1 091.25
Drops (infants)	24.25	0.3 ml	7.28	21.93	181.88	545.63
Nasal spray	58.76	0.3 ml	11.75	35.26	293.80	881.40
Beconase	126.03	400 µg	50.41	151.24	100.82	302.47
Clenil	71.27	400 µg	28.51	85.52	57.02	171.05
Viarox	87.06	400 µg	34.82	104.47	69.65	208.94
Ventnase	71.40	400 µg	28.56	85.68	57.12	171.36
Betnesol drops	47.30	0.6 ml	56.76	170.28	113.52	340.56
Rhinocort MDI	108.21	400 µg	43.28	129.85	86.57	259.70
Rhinocort aqueous	114.54	400 µg	45.82	137.45	91.63	274.90
Syntaris	130.88	100 µg	21.81	65.44	43.63	130.88
Flixonase	138.07	200 µg	46.02	138.07	92.05	276.14
Nasacor	118.71	220 µg	47.48	142.45	94.97	284.90
Rynocrom	99.56	26 mg	49.78	149.34	1 792.08	5 376.24
Atronase	22.15	160 µg	17.72	53.16	443.00	1 329.00

Discussion

The analysis reported in this paper enables one to compare different drug categories that can be used in the treatment of allergic rhinitis. As mentioned in the methodology, we have expressed the results in terms of cost rather than price by including efficacy in the costing equation. Any cost comparison is only as sound as the underlying clinical protocol. As this comparison is based on the International Consensus Report on the Diagnosis and Management of Rhinitis,[15] the results are presented with a fair amount of confidence. Independent evaluation of the importance of these symptoms was via a survey of 700 doctors familiar with allergic rhinitis.[16] We felt that it was essential to include efficacy in these calculations, as we are comparing different classes of drug. We have assumed all drugs within each class to be equally efficacious, an assumption that has not been tested. There is insufficient information on the relative efficacy of all the different agents in the different classes to stratify individual agents in terms of efficacy although the newer agents do seem to be more efficacious.

The comparison of antihistamines included one older-generation oral drug, Zaditen, the newer-generation oral drugs, Hismanal, Zyrtec, Clarityne and Triludan, and the new topical agent, Livostin. In respect of the three drugs available in syrup form and therefore suitable for children, Hismanal and Clarityne were similarly priced but Hismanal has the potential disadvantage of cardiac side-effects.[17] Zaditen was not only the most costly agent, but also compares unfavourably with the other two agents in syrup form in this class as it also has more sedative side-effects.[17] In tablet form, Zaditen was also the most costly agent. The other four oral agents were similarly priced, but again both Hismanal and Triludan have potential disadvantages because of their cardiac side-effects. Therefore, because of these potential side-effects, Zyrtec and Clarityne would appear to be the agents to choose, with Zyrtec being marginally cheaper. However, it too is outclassed by Livostin, which is not only the cheapest antihistamine in the comparison but also, because it is used topically, has no systemic side-effects, most notably an absence of sedation.

If the topical decongestants are assumed to be equally efficacious, these drugs as a class are overall a costly form of therapy. In general, the sprays are the cheaper alternative in the adult formulation, but where available in paediatric formulations are more costly than drops.

The topical corticosteroid sprays were, as a class, the cheapest form of treatment for allergic rhinitis. Aside from Betnesol (betamethasone) drops and the generic agents of beclomethasone dipropionate, the costs per month of the remaining drugs were very comparable. Agents from the generic drug houses (Clenil and Ventnase — both beclomethasone dipropionate) were the cheapest. However, one could expect these agents to be considerably cheaper than the 'ethical' agents for three reasons: (*i*) their price of licensing is considerably less than for the ethical agents; (*ii*) the production price must have been significantly cheaper than for the ethical agents as they were not developed by these drug houses; and (*iii*) with licensing regulations not requiring clinical testing, the efficacy or safety of these drugs has not been tested as would be the case for the ethical agents. The newer ethical agents, Beconase (beclomethasone dipropionate), Rhinocort MDI and Flixonase (fluticasone propionate) are similarly priced. The once daily dosing of Flixonase and Rhinocort may be a marginal advantage when choosing between these three drugs. In addition, there is some evidence of differing efficacy between steroids, but these intra-class differences are much smaller than the differences between the different drug classes considered.[18]

Rynocrom was by far the most costly drug in this comparison. It was on average 20 times more costly than the topical nasal corticosteroids. The main expense associated with this agent was its documented lack of efficacy. Sodium cromoglycate has the advantage of no documented side-effects. Atronase is effective only for rhinorrhoea, one of three components of allergic rhinitis and possibly the least important in children. It too is costly because of its lack of efficacy.

Conclusions

Given the assumptions made, our calculations suggest that topical steroids represent the least costly option in the management of rhinitis. From the figures presented, one can infer that an antihistamine like Hismanal will have to have a side-effect profile 2 - 3 times better than that of a typical topical steroid, and that a sodium cromoglycate formulation will have to have a side-effect profile 20 times better to warrant its substitution for nasal steroids in the treatment protocol.

Some cost comparisons on combination therapy can still be done, and will be able to add interesting information to our findings.

A quality-of-life assessment study is planned to follow up the cost-effectiveness analysis. This will add another dimension to the analysis, and turn the treatment guidelines into a proper patient-directed protocol.

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