Allergic rhinitis: indicators of quality of life*
Rinite alérgica: indicadores de qualidade de vida
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Abstract
The objective of this review was to present evidence of the relationship between allergic rhinitis and impairment of quality of life. The data sources were original articles, reviews and consensus statements entered into the Medline and LILACS databases between 1997 and 2008. The following search terms were used: “allergic rhinitis”; “quality of life”; and “sleep disorders”. Quality of life is often impaired in patients with allergic rhinitis, due to the classic symptoms of the disease (sneezing, pruritus, rhinorrhea and nasal obstruction). In addition, the pathophysiology of allergic rhinitis often disrupts sleep, leading to fatigue, irritability, memory deficits, daytime sleepiness and depression. The total burden of this disease goes beyond impairment of physical and social functioning. It has also a financial impact, which becomes greater when we consider the evidence that allergic rhinitis is a possible causal factor of comorbidities, such as asthma and sinusitis. Nasal obstruction, the most prominent symptom, is associated with sleep disorders, which can have a profound effect on mental health, learning, behavior and attention. Finally, allergic rhinitis—a chronic condition that affects adults, adolescents and children—is often underdiagnosed or inadequately treated. The deleterious impact that allergic rhinitis-related sleep disorders have on patient capacity to perform activities of daily living is an important component of the morbidity of the disease. With an accurate diagnosis, there are various available treatments that can reduce the burden of allergic rhinitis.

Keywords: Rhinitis, allergic, perennial; Rhinitis, allergic, seasonal; Quality of life; Sleep disorders.

Resumo
O objetivo desta revisão foi apresentar evidências da relação entre rinite alérgica e redução da qualidade de vida. As fontes de dados foram artigos originais, revisões e consensos indexados nos bancos de dados Medline e LILACS entre 1997 e 2008. As palavras de busca foram “rinite alérgica”, “qualidade de vida” e “distúrbios do sono”. Os pacientes com rinite alérgica frequentemente têm redução na qualidade de vida causada pelos sintomas clássicos da doença (espirros, prurido, coriza e obstrução). Além disso, a fisiopatologia da rinite alérgica, com frequência, interrompe o sono, ocasionando fadiga, irritabilidade, déficits de memória, sonolência diurna e depressão. A carga total da doença recai não apenas no funcionamento social e físico prejudicados, mas também no impacto financeiro, que se torna maior quando se consideram as evidências de que a rinite alérgica é um possível fator casual de comorbidades, tais como a asma e a sinusite. A obstrução nasal, o mais proeminente dos sintomas, está associada a eventos respiratórios relacionados aos distúrbios do sono, uma condição que tem profundo efeito sobre a saúde mental, o aprendizado, o comportamento e a atenção. Finalmente, a rinite alérgica — doença crônica que afeta crianças, adolescentes e adultos — frequentemente se sobdiagnosticada ou inadequadamente tratada. O impacto deletério dos distúrbios do sono associados à rinite alérgica sobre a habilidade para realizar as atividades de vida diária dos pacientes é um importante componente da morbidade da doença. Com um diagnóstico acurado, existem vários tratamentos disponíveis que podem reduzir a carga associada à rinite alérgica.

Descritores: Rinite alérgica perene; Rinite alérgica sazonal; Qualidade de vida; Transtornos do sono.

Introduction
Allergic rhinitis (AR) is defined as a symptomatic disease of the nose, resulting from the inflammatory reaction mediated by specific IgE antibodies, and is manifested after the exposure of the mucosa of the nasal cavity to the allergen involved. The symptoms of AR—nasal obstruction, hyaline rhinorrhea, sneezing and nasal pruritus—are reversible (spontaneously or with treatment).(1,2)

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Financial support: None.
There is no universally accepted definition for rhinitis. The distinction between a normal individual and one with rhinitis is generally based on the clinical history. Reports of the occurrence of at least one of the cardinal symptoms that are characteristic, but not pathognomonic of AR, after exposure to the possible triggering or typical aggravating factors—house dust allergens, allergens of fungi of domestic animals, pollen; tobacco smoke, strong odors, pollution and environmental changes in temperature and humidity—can facilitate the identification of cases.

Although the onset of the clinical manifestations of AR occurs most commonly during childhood, up to 30% of patients present a later onset. Depending on the frequency of the symptoms, AR is classified as intermittent or persistent and, according to the intensity of the symptoms, as mild or moderate-to-severe (Chart 1).

The objective of this review was to present some of the available evidence on the relationship between AR and the impairment of quality of life.

**Importance of the evaluation of quality of life**

The evaluation of the presence and intensity of a certain disease is conducted, traditionally, through the investigation of characteristic symptoms and objective functional parameters. Similarly, the clinical evolution, with or without improvement of the symptoms and objective parameters, is typically used as the standard method to measure the efficacy of the treatment instituted. Although there are no doubts that such aspects are very important and that they should never be neglected, their capacity to determine the effects of diseases on the health of the individual is often inadequate or insufficient.

In the last decade, the evidence that patients and physicians differ in their perception of the disease has increased. This is certainly an aspect that should be considered, and the study of this aspect often provides data different than those obtained by the mere evaluation of symptoms or parameters that are considered objective. As a result, health professionals have shown to be more alert and interested in the importance of the evaluation of the quality of life and of the satisfaction of the patient, in parallel with the evaluation of other aspects related to the disease or to the treatment.

The great problem is that the concept of quality of life varies among people and depends on the degree of expectations and perceptions of the disease and life, expectations that can change over time and with the evolution of the disease.

The degree to which quality of life is impaired varies principally depending on the standards of the individual regarding “personal well-being”, perception of the surrounding world and expectations regarding treatment. We find it surprising that some studies show, for example, that the intensity of the symptoms does not necessarily correlate with the degree of quality of life impairment, an aspect that again highlights the relevance of the individuality of each patient.

**AR and quality of life**

Although it is frequently seen as a trivial and temporary disease or, yet, as a less severe disease when compared with asthma, AR is capable of markedly altering the quality of life of the patients, as well as their performance, learning and productivity.

In addition, AR is commonly associated with other respiratory diseases, and the cost resulting from these comorbidities increases even more the socioeconomic impact of the disease.
Apparently, the severity, and not the duration of the clinical profile, has a more relevant effect on the quality of life of the patients with AR, with repercussions for sleep quality and professional performance. In a study in which the severity and duration of AR were evaluated in 3,052 patients, it was concluded that 11%, 8%, 35% and 46% of the patients, respectively, presented intermittent mild forms, persistent mild forms, intermittent moderate-to-severe forms and persistent moderate-to-severe forms. The impact that AR severity had on quality of life—sleep, activities of daily living and professional performance—in those patients was more significant than was the duration of the disease. More than 80% of the patients with more severe forms reported impairment in their activities due to the disease, compared with only 40% of those with mild forms.[8]

Disease-specific questionnaires are the instruments most widely used in order to “measure the quality of life”, because they more accurately describe the problems associated with the disease and are more responsive to possible alterations in the quality of life, when compared with generic questionnaires. In the case of allergic rhinoconjunctivitis, the disease-specific questionnaire most commonly used is the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ).[12,9]

It is fundamental to highlight that AR-related physical, psychological and social impairments are experienced not only by adults but also by children and adolescents. In general, the patients feel inconvenienced by the symptoms per se, particularly by the nasal obstruction, rhinorrhea and sneezing. They are irritated by not being able to sleep well at night and often being exhausted during the day. They also experience non-nasal symptoms that cause discomfort, such as thirst, inability to concentrate and headache. They consider certain practical problems quite irritating, such as the need to carry tissues or handkerchiefs and to frequently blow their nose. They present with limitations in their activities of daily living, which leaves them frustrated and irritated.

Although adolescents experience problems similar to those of the adults, they present greater difficulty in concentrating, particularly on their school work. Younger children, however, present a slightly different profile: they feel uncomfortable with symptoms and practical problems, such as having to carry tissues or handkerchiefs and to take medicine; however, they tend to experience less limitation in their activities of daily living and do not exhibit the emotional disturbance experienced by adults and adolescents.[10,11]

**Impact on sleep**

Sleep disorders can impair the quality of life, leading to fatigue, irritability, memory deficits and daytime sleepiness.[2,11]

Evidence indicates that fragmented sleep and sleep deprivation, even when partial, cause increased daytime sleepiness and impair cognitive performance.

Sleep disorders also have a significant effect on mental health and can cause psychiatric diseases, depression and anxiety.[12]

In addition, respiratory events associated with sleep disorders, in childhood and adolescence, are associated with greater frequency of disorders related to learning, behavior and attention.[13,14]

In patients with AR, quality of life is often impaired not only due to the typical symptoms of the disease—sneezing, pruritus, nasal obstruction and rhinorrhea—but also due to the activity of the mediators that participate in its pathophysiology and can disrupt sleep.[15] Among the most commonly implicated mediators are histamine, leukotrienes (C4 and D4), interleukins (IL-1β, IL-4, IL-5 and IL-13), prostaglandin D2, substance P and bradykinin.[16]

Sleep disorders related to the inability to breathe well during the night are in fact commonly observed in patients with AR. Studies on this topic have shown not only that the impairment of the sleep has an important impact on social life, professional skills and learning of the patients but also that the treatment of AR can have a beneficial effect, improving the quality of sleep and, consequently, reducing all limitations secondary to the sleep disorders.[17,18]

Nasal obstruction and rhinorrhea are the nasal symptoms that have the greatest impact on sleep, since postnasal drip and mucosal edema obstruct the nasal cavities, increasing nasal resistance. Nasal obstruction combined with congestion is also a risk factor to respiratory events associated with sleep disorders, including apnea, hypopnea and snoring.[11,19]
In patients with AR whose sleep was evaluated by polysomnography, the obstructive apnea events were more frequent and of longer duration in those who presented nasal obstruction than in those who did not. Similarly, the occurrence of apnea or hypopnea—severe respiratory disorders related to the sleep—was 1.8 times more common among AR patients with nasal obstruction than among those without.

In a survey involving individuals with AR, 68% of those with perennial AR and 48% of those with seasonal AR reported that the disease interfered with their sleep.

**Impact on learning and social life**

Memory and learning are functional characteristics that can be impaired in patients with AR, leading to a crucial impact on their intellectual performance. In fact, patients with AR whose symptoms are not adequately controlled can have learning problems, either due to direct interference of the symptoms or due to impaired quality/quantity of nighttime sleep, resulting in daytime fatigue.

In a six-month, open, single-blind study involving 113 children with perennial AR and 33 children with non-allergic rhinitis, the authors found that rhinorrhea had less of an impact on sleep and on school attendance, as well as on the ability to concentrate on schoolwork, among the children treated with beclomethasone or ipratropium bromide.

The home life of many patients is affected by AR. Children with AR can experience feelings of total isolation, even within their families, since the presence of allergens frequently hinders their participation in family activities, such as picnics, as well as preventing them from playing with pets and going camping.

The social effect of AR is not restricted to the family sphere. In school, children with AR can present emotional disturbance caused by the learning impairment that commonly accompanies AR or by the limitations of activities imposed due to the need to avoid contact with allergens. As a result, they are unable to achieve complete and unrestricted integration with their peers, and emotional disturbances arise.

In a study involving 1,948 individuals who completed the RQLQ, the three parameters that best characterized the influence of AR on the social perspective of those individuals were the following: embarrassment (in 70%); frustration (in 72%); and practical problems, including the inconvenience of carrying tissues or handkerchiefs, the need to “wipe” the nose or the eyes, and to repeatedly blow the nose (in 98%).

**Impact on productivity and socioeconomic impairment**

Rhinitis, like asthma, is a chronic condition that has a major socioeconomic impact on patients, their families, health care systems and society as a whole.

This impact comprises direct costs, generated by the use of the health care system, and by indirect costs, associated with the loss of economic productivity. Therefore, people with rhinitis or asthma need to cope with the immediate and long-term burdens related to these diseases, which habitually affect their activities of daily living. They often have to choose how to distribute their financial resources—normally directed to daily needs, such as food and clothing—to pay for the medical care necessary to improve their health status.

The direct costs of AR include visits to medical offices, laboratory tests, medication and allergen immunotherapy.

In addition to those direct costs, designated the “evident” costs, there still are “hidden” direct costs, which include the treatments for asthma, allergic conjunctivitis, atopic dermatitis, upper respiratory tract infections and nasal polyposis—conditions that occur with considerable frequency in patients with AR. The indirect costs are also substantial and, in general, encompass absenteeism and decreased productivity, even when the patient is able to go to work every day.

There have been many fewer studies on the economic impact imposed on people with AR than on that imposed on those with asthma. It is estimated that AR results in impaired productivity or job loss in approximately half of all patients.

The degree of impairment of professional activities has been reported to be up to 60% in patients with seasonal AR and up to 40% in those with perennial AR. Patients complain of headache, fatigue, low productivity and inability to concentrate at work. It is noteworthy that conjunctivitis, commonly associated with AR,
can impair visual acuity and therefore activities requiring good vision.

It is of note that not only the disease but also the medication used for the relief of the symptoms can influence productivity. It is estimated that 50% of patients who treat the disease with first generation antihistamines (sedatives) work at only 25% of their total capacity for 14 days/year.\(^{(26)}\) With the use of new antihistamines, these problems have been significantly reduced.

In a survey of 8,267 employees working in the United States, it was concluded that 55% experienced AR symptoms, on average, for 52.5 days/year, had been absent due to AR from work for 3.6 days/year and were unproductive due to AR symptoms for 2.3 h/day of work. The total losses in productivity due to the AR were US$ 593 per employee per year.\(^{(26)}\)

It is believed that, in the United States, AR is responsible for annual losses of 3.5 million days of work and 2 million days of school.\(^{(27)}\)

It is also estimated that, regardless of the day of the week, approximately 10,000 children per day are absent from school due to AR.\(^{(6)}\) It should be noted that, depending on the age of the child, school absenteeism will also affect the productivity of the parents or will cause their absence from work.

A study on the direct medical costs of diseases among children in the United States, with and without asthma, revealed that children with asthma used the health services with substantially greater frequency than did the children who did not have asthma. However, only 26% of the difference in these costs was related to the medical care specific for asthma. A great percentage of the additional cost was associated with other conditions, principally with upper airway diseases, such as AR.\(^{(28)}\) It is certain that AR increases the costs of asthma.

In a study involving patients with asthma alone or with asthma and AR, it was shown that the mean annual expenses for medical care were 46% greater among those who had asthma and AR.\(^{(29)}\)

### Chart 2 - Evidence of the effects of intranasal corticosteroids on sleep and quality of life of patients with allergic rhinitis.

<table>
<thead>
<tr>
<th>Type of AR</th>
<th>Study design/number of participants/drug tested</th>
<th>Principal outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perennial(^{(23)})</td>
<td>Open/14/budesonide</td>
<td>Post-treatment vs. baseline:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less apnea/hypopnea (p = 0.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fewer symptoms and improved sleep quality</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Budesonide vs. placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less daytime fatigue (p = 0.03)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less daytime sleepiness (p = 0.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Improved sleep quality (p = 0.05)</td>
</tr>
<tr>
<td>Perennial(^{(22)})</td>
<td>DBPC/22/budesonide</td>
<td>Fluticasone vs. placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less nasal obstruction (p = 0.04)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less daytime sleepiness (p = 0.01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tendency toward less daytime fatigue (p = 0.08)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Improved sleep quality (p = 0.04)</td>
</tr>
<tr>
<td>Seasonal(^{(42)})</td>
<td>DBPC/285/fluticasone (furoate)</td>
<td>Fluticasone vs. placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Better scores for nasal and ocular symptoms (p &lt; 0.001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Better quality of life scores (p &lt; 0.001)</td>
</tr>
<tr>
<td>Perennial(^{(39)})</td>
<td>DBPC/32/fluticasone (propionate)</td>
<td>Fluticasone vs. placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Improved sleep quality (p &lt; 0.04)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Apnea-hypopnea index (NS)</td>
</tr>
<tr>
<td>Seasonal and perennial(^{(40)})</td>
<td>Open/651/triamcinolone</td>
<td>After treatment vs. baseline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fewer symptoms and improved sleep quality (p &lt; 0.001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fewer “practical problems”</td>
</tr>
</tbody>
</table>

AR: allergic rhinitis; DBPC: Double-blind, placebo-controlled; and NS: not significant.
In the United States, 40 million people suffer from AR, including 6 million children. Although half of the patients with AR presents symptoms for a period of 4 months per year or less, approximately 20% experience symptoms for more than 9 months per year.\(^\text{30,31}\)

In 2002, AR was responsible for 14 million visits to medical offices.\(^\text{32}\) The direct costs of medical visits and medication are approximately US$ 4.5 billion annually. The indirect costs are estimated at approximately US$ 4 billion, corresponding to approximately 4 million days missed from work and school.\(^\text{33}\) It is estimated that the total economic burden of AR in children is greater than US$ 5 billion/year.\(^\text{14}\)

It is of note that, as the incidence of allergic diseases continues to increase, their economic impact also continues to grow.

**Impact of treatment**

Any therapy that controls or relieves the symptoms of AR, particularly nasal obstruction, can be of use in improving the quality of life of the patients.

Although avoiding the contact with the allergen—environmental control—is important in therapeutic terms, it is often impracticable or insufficient to control the symptoms. In most of the cases, pharmacotherapy is the principal intervention, and, in this sense, antihistamines and intranasal corticosteroids are the first-line agents.\(^\text{1,9,35}\)

Patients with AR often attribute their daytime fatigue to side effects of the treatment instituted. However, although some medications used in the treatment of AR can have a sedative effect, AR alone can produce sleepiness.

Worldwide, H1 antihistamines are among the most commonly prescribed medications. Although all H1 antihistamines are similar in terms of their efficacy in the treatment of patients with AR, there are major differences among them in terms of their chemical structure, clinical pharmacology and potential for toxicity.

The first-generation antihistamines, when compared with those of the second generation, present an unfavorable risk-benefit relationship, since the former present low selectivity to H1 receptors and have pronounced sedative and anticholinergic effects.\(^\text{35}\)

Second generation H1 antihistamines efficiently reduce all the nasal symptoms, except for nasal obstruction\(^\text{1,9,35}\) although there is evidence that desloratadine can decrease nasal congestion.\(^\text{16}\)

Limited data suggest that some second generation H1 antihistamines, such as cetirizine and fexofenadine, can have favorable effects on the sleep of patients with AR; however, further studies are necessary in order to appropriately characterize and confirm these effects.\(^\text{5,37,38}\)

At any rate, it is recommended that, for the treatment of AR, whenever possible, preference be given to the second generation antihistamines.\(^\text{1,9,33,35}\)

The evidence indicates that intranasal corticosteroids are more efficacious than are antihistamines in the control of AR symptoms. This “superiority” is principally related to their effect on nasal obstruction.\(^\text{1,8,34}\)

Intranasal corticosteroids seem to be among the most efficacious agents for the control of nasal obstruction secondary to AR. In view of the significant impact that nasal obstruction has on sleep quality, the efficacy of intranasal corticosteroids in promoting the relief of nasal congestion suggests that these agents reduce the frequency of sleep disorders and thus the daytime sleepiness associated with such disorders. In fact, this has been demonstrated in various clinical studies, based on subjective data (symptom journals) or on validated instruments that objectively assess the quality of the sleep and the quality of life related to sleep (Chart 2).\(^\text{17,22,39-42}\)

In grouping the data of three of their placebo-controlled studies on the use of intranasal corticosteroids (budesonide, flunisolide and fluticasone) in patients with perennial AR, one group of authors showed that, in the treated patients, there was a significant reduction in nasal obstruction, sleep disorders and daytime sleepiness. It is therefore evident that the reduction in nasal obstruction obtained through the use of those compounds is correlated with improved sleep quality and reduced daytime sleepiness.\(^\text{43}\)

Decongestants, leukotriene receptor antagonists and mastocyte stabilizers are also part of the therapeutic arsenal for the treatment of AR.

Decongestants are alpha-adrenergic agents that control nasal obstruction. Topical decon-
In clinical practice, various factors, such as adherence to treatment, preference of the patient, availability of the medication and the potential adverse effects, must be considered when outlining treatment strategies for patients with AR.

Generally, patients with persistent forms, who frequently suffer from significant nasal obstruction, are usually better treated with intranasal corticosteroids. When the symptoms are mild or only intermittent, sodium cromoglycate is the drug of choice. Treatment with antihistamines is principally indicated during crises, in order to prevent the worsening of the symptoms.

The “balance” between use of nasal corticosteroids and antihistamines, isolated or associated, should be devised for each patient individually. In children with persistent symptoms, intranasal corticosteroids are an extremely efficacious therapeutic option, and the new agents have proven safe, with a major local effect and minimal systemic effects. They are the following: mometasone and fluticasone furoate (for children ≥ 2 years of age); triamcinolone and fluticasone propionate (for children ≥ 4 years of age); and budesonide and ciclesonide (for children ≥ 6 years of age).

Comorbidities

Associations among allergic diseases are frequently observed. Therefore, there are strong...
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inconvenient symptom of the disease, deeply affects the quality of life, principally by reducing the "restoring power of the sleep".

Poor quality sleep causes daytime sleepiness, fatigue and significant impairment in learning, cognition and professional performance. As a consequence, adults become ill-humored, less efficient and more subject to work-related accidents. Children tend to be shy, depressed, anxious or fearful.

The total burden of the disease goes beyond the impairment of social and physical functioning. It also has a financial impact, which becomes greater when we consider the evidence that AR is a possible causal factor of comorbidities such as asthma and sinusitis.

The deleterious impact of AR-related sleep disorders on various aspects of the daily lives of the patients is an important component of the morbidity associated with the disease. However, unfortunately, this component is rarely recognized or valued and is even more rarely addressed by health professionals who deal with AR patients.

The appropriate environmental prophylaxis, based on the sensitization and exposure of the patient, combined with the appropriate pharmacological treatment, with the use of compounds which efficiently reduce the numbers of inflammatory cells and mediators, can relieve the symptoms and, consequently, markedly improve the quality of life of patients with AR.

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