

Case report**Comprehensive therapy in united airway disease:
Evidence Based Case Report**

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ABSTRACT

Background: The concept of the united airway disease (UAD) recognises the association between allergic inflammation in the upper and lower airways. Patients with asthma and concomitant allergic rhinitis experience more asthma-related primary and secondary care visits. **Purpose:** To determine the best treatment option in the case of patients with asthma related allergic rhinitis, both in the control of nasal and pulmonary symptoms. **Case report:** A case case of 45 years old woman with asthma related to allergic rhinitis treated with combination of intranasal steroid and asthma therapy. **Clinical question:** In adult patient with allergic rhinitis related to asthma, does the combination of intranasal and inhaled steroids give better clinical improvement subjectively and objectively compared to monotherapy? **Method:** Literature search through two different databases (PubMed and Cochrane Library) and by searching the bibliography of articles to evaluate the outcome of combination therapy and monotherapy for the disease. **Result:** Two articles were found relevant with the topic fulfilled the requirements and relevant with the formulation or clinical question. **Conclusion:** Treating the inflammation associated with allergic rhinitis may have a true impact on the control of asthma, while the failure to treat rhinitis may impair asthma control.

Keywords: allergic rhinitis, asthma, pulmonary function, nasal symptoms

ABSTRAK

Latar belakang: Konsep United Airway Disease (UAD) mengenali adanya hubungan antara inflamasi alergi pada saluran napas atas dan bawah. Pasien asma yang bersamaan dengan rinitis alergi melakukan lebih banyak kunjungan ke perawatan primer dan sekunder terkait asma. **Tujuan:** Menentukan pilihan pengobatan terbaik pada pasien dengan rinitis alergi terkait asma, baik dalam pengendalian keluhan hidung maupun paru. **Laporan kasus:** Satu kasus seorang wanita berusia 45 tahun dengan asma yang berhubungan dengan rinitis alergi. **Metode:** Mengumpulkan jurnal terkait dari dua database yang berbeda (PubMed dan Cochrane Library). Pencarian artikel juga dilakukan dengan mencari pada daftar pustaka artikel untuk mengevaluasi luaran dari terapi kombinasi dan terapi tunggal untuk penyakit ini. **Pertanyaan klinis:** Apakah terapi kombinasi dengan steroid intranasal dan steroid hirup dapat memberikan perbaikan lebih signifikan secara subjektif maupun objektif dibandingkan dengan terapi tunggal pada pasien dewasa dengan rinitis alergi dan asma? **Hasil:** Didapatkan dua artikel yang relevan dengan topik, sesuai dengan pertanyaan klinis serta memiliki penilaian kritis yang baik. **Kesimpulan:** Mengobati peradangan yang terkait dengan rinitis alergi dapat berdampak nyata pada pengendalian asma, sedangkan kegagalan untuk mengobati rinitis dapat mengganggu pengendalian asma.

Kata kunci: rinitis alergi, asma, fungsi paru, gejala hidung

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INTRODUCTION

Upper and lower airways are considered a unified morphological and functional unit, also the connection existing between them has been observed for years, both in health and disease.¹⁻² Various attempts have been made to determine the impact of the presence of rhinitis on asthma-related morbidity. Rhinitis usually precedes the occurrence of asthma and may represent a risk factor for its development.³⁻⁵ The optimal therapeutic approach should focus on the simultaneous treatment of both conditions. The Allergic Rhinitis and its Impact on Asthma (ARIA) workshop stated that the concomitant treatment of rhinitis is fundamental to asthma control.^{5,6}

Allergic Rhinitis (AR) is the most common of all atopic diseases, most patients report the onset of symptoms before 30 years of age, and considered as a major public health problem, due to its prevalence and impact on patient's quality of life, work/school performance, and productivity economic burden. It is characterized by the classic symptoms of nasal itching, sneezing, rhinorrhea, and nasal obstruction. In addition, AR is associated with a variety of comorbidities, such as atopic dermatitis, sleep-disordered breathing, conjunctivitis, rhinosinusitis, otitis media, asthma, and emotional problems.^{3,5,6} AR is considered a risk factor for developing asthma. Asthma is a heterogeneous disease characterized by chronic airway inflammation and hyperresponsiveness to direct or indirect stimuli, which can persist even when symptoms are absent or lung function is normal but may normalize with treatment. Asthma is defined by the history of episodic respiratory symptoms, such as wheeze, shortness of breath, chest tightness, and cough, and is associated with variable

expiratory airflow limitation.^{1,3,7} Interactions between the lower and the upper airways are well known and have been extensively studied since 1990. Over 80% of asthmatics have rhinitis, and over 40% of patients with rhinitis have asthma, suggesting the concept of "one airway, one disease".^{2,8}

A central concept of United Airway Disease (UAD) (Figure 1) is the influence of the upper airway in the function of the lower airway, which is particularly evident and relevant in the allergic phenotype. The upper and lower respiratory tracts form a continuum, allowing the passage of air into and out of the lungs and sharing many anatomical also histological properties. However, the functions of the upper airway and their interactions with the lower airway are much broader than merely air-conditioning.^{1,2,9} The pathological interactions between the upper and lower airways are summarized in Figure 1 and can be divided into air-conditioning, inflammation, and neural reflexes.

The pharmacological options for long-term treatment of asthma divided into the following three main categories: Controller, Reliever and Add-on therapies for patients with severe asthma. For the best outcomes, Inhaled Corticosteroids (ICS) as controller treatment should be initiated as soon as possible after the diagnosis asthma is made. Concurrently, treatment of asthma has switched from systemic to local corticosteroids administration such as ICS.

Glucocorticosteroid (GC) have the inhibiting functions such as : (1) inhibits the functions of infiltrating inflammatory cells and their recruitment into the nasal mucosa. (2) inhibits the maturation, cytokine production, FcεRI expression and mediator release of mast

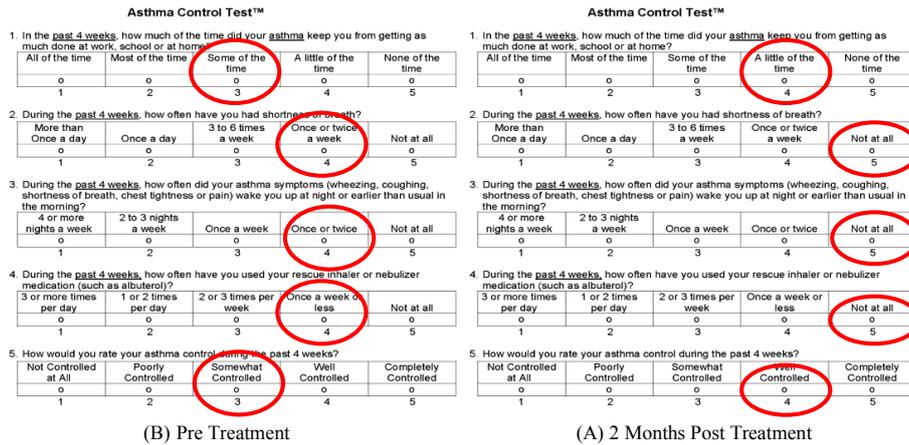


Figure 2. Pre and Post Treatment of Asthma Control Test¹¹

CLINICAL QUESTION

P: Adult patients with Allergic Rhinitis related to Asthma

I: Combination therapy of intranasal and inhaled steroid

C: Monotherapy (intranasal steroid or inhaled steroid alone)

O: Clinical improvement (e.g., symptoms, peak flow meter, spirometry)

In adult patients with allergic rhinitis related to asthma, does the combination of intranasal and inhaled steroids give better clinical improvement subjectively and objectively compared to the monotherapy?

METHOD

Clinical questions can be formulated using evidence-based medicine methods. Literature search through Pubmed and Cochrane Library databases with keywords “Allergic Rhinitis”, “Asthma”, and “Fluticasone Inhaler”. The articles were then selected based on inclusion criteria: (1) therapeutic study; (2) intranasal and inhaled steroid as treatment group; (3) nasal and asthma improvement as outcome; while the exclusion criteria: (1) children/pediatric patients; (2) non-English or Bahasa; (3) small samples and non full text (Figure 3).

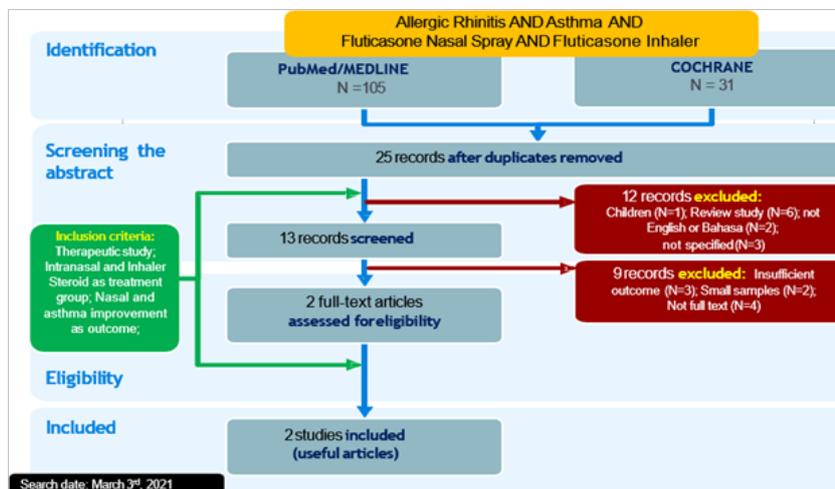


Figure 3. Literature searching

RESULT

The search was conducted on March 3rd 2021 and found 105 articles from Pubmed and 31 articles from Cochrane. After removing duplication articles and excluded studies based on inclusion and exclusion criteria, 2 articles were considered suitable and remained to be analyzed.

DISCUSSION

Several mechanisms have been postulated to support the hypothetical effects of intranasal therapy of lower airways. However, none of these have been substantiated. These include direct and indirect anti-inflammatory effects of the drug in the lung, inhibition of mediator release or cellular translocation in the nose, prevention of systemic mediator absorption with distant effects in the lung, inhibition

of nasobronchial neurogenic reflex, and also effects related to the shift from nasal to oral breathing.¹²

The successful outcome of asthma related allergic rhinitis therapy can be seen through subjective and objective assessments. Asthma is assessed by daytime and night-time wheezing and the Asthma Control Test (ACT). Classification based on ACT are uncontrolled asthma (score <20), good control asthma (score 20-24) and well controlled asthma (score of 25). Meanwhile, rhinitis is assessed using VAS for a total four nasal symptom scores (TNSS), with TNSS <5 classified as controlled rhinitis and ≥5 as uncontrolled rhinitis. Spirometry is performed for objective examination. Morning and evening Peak Expiratory Flow (PEF), Forced Expiratory Volume in first second (FEV1), bronchial responsiveness to methacholine and induced sputum are assessed.¹²

Score	Symptoms
0=None	No symptoms evident
1=Mild	Symptom present but easily tolerated
2=Moderate	Definite awareness of symptom; bothersome but tolerable
3=Severe	Symptom hard to tolerate; interferes with daily activity

The Nasal symptoms are then added for each time points to reach the TNSS.

Figure 4. Total Nasal Symptoms Scores (TNSS). Each symptom (sneezing, congestion, itching and rhinorrhea) is graded from 0-3.¹³

In this case, the outcome evaluation from combination therapy was only carried out subjectively based on improvement of symptoms, both from rhinitis and asthma symptoms. Due to pandemic situation, there was a limitation to perform aerosol generating

procedure category for safety reasons. Two-months after receiving combination therapy, patient showed significant improvement, from pretreatment TNSS of 17 to post treatment TNSS of 4, while the pretreatment ACT score was 18 and 23 after treatment (Table 1).

Table 1. Subjective evaluation pre and post treatment

	Pre Treatment (Inhaler Fluticasone Propionate only)	Two months Post Treatment (Intra Nasal Fluticasone Furoate + Inhaler Fluticasone Propionate)
TNSS	17	4
	18	23

Based on Dahl et al.¹⁴, nasal treatment with Fluticasone Propionate was effective in controlling nasal symptoms but did not influence asthmatic symptoms, bronchial responsiveness or inflammation. Treatment with Inhaled Fluticasone Propionate was effective in controlling asthmatic symptoms, bronchial responsiveness and inflammation but had no influence on the nasal symptoms. These results were in accordance with several smaller studies of comorbid allergic rhinitis and asthma, which had predominantly focused on the effects of intranasal steroid treatment in both upper and lower airways. Corren et al.¹⁵ had demonstrated that intranasal beclomethasone significantly improved rhinitis, but not asthma symptom scores or PEF in adult patients with ragweed pollen-induced rhinitis and asthma.

Lohia et al.¹⁶ reported that intranasal corticosteroid medications improved pulmonary function, bronchial reactivity, asthma symptom scores, asthma-specific quality of life, and rescue medication use in patients with both allergic rhinitis and asthma, suggesting the efficacy of local corticosteroid therapy in UAD. Nair et al.¹⁷ also supported the hypothesis that the use of combination therapy had an effect on both nasal and pulmonary symptoms. But it was contradicted by Dahl et al.¹⁴ which did not demonstrate superiority of combined intranasal and inhaled fluticasone over inhaled fluticasone alone. Their patients had mild asthma and seasonal intermittent allergic rhinitis, with well-preserved baseline lung function. They showed treatment of 500 µg of inhaled fluticasone significantly improved morning PEF (primary outcome) by only 13 l/min, but pointedly did not improve methacholine PD₂₀. Unsurprisingly, the addition of inhaled intranasal fluticasone to this dose did not result in further improvements in PEF or methacholine PD₂₀ or sputum eosinophils. This was because 500 µg/day of inhaled fluticasone was found to be on the peak dose response curve for all of these outcomes in mild asthmatics.

Dahl et al.¹⁴ had demonstrated that intranasal budesonide, intranasal beclomethasone dipropionate, and INFP also significantly protected against methacholine-induced bronchial hyperresponsiveness in patients with seasonal or perennial allergic rhinitis and asthma, when compared with placebo. Interestingly, however, protection against methacholine challenge occurred despite the lack of any significant protective effects on PEF or FEV₁ in these studies. It was demonstrated that nasal beclomethasone dipropionate and flunisolide significantly decreased seasonal asthma symptoms scores from baseline, in addition to nasal symptom scores right across the pollen season, when compared with placebo or cromolyn treatment.

The study results suggested that the failure to consider treatment of coexisting rhinitis as essential to the management of asthma might impair clinical control of the latter. The parallel and similar response to intranasal corticosteroid might indicate that mild asthma could be controlled by the exclusive use of nasal medication. Together, these findings suggested that management of allergic rhinitis should be considered an integral part of treatment for asthma according to the results presented in this case.

However, there were several limitations for this study for outcome evaluation. There were no objective examination such as spirometry to assess the FEV₁ due to pandemic outbreak. Scoring for TNSS and ACT were found to be useful for measuring symptoms improvement of UAD in this situation. In the future, we hope to be able to have more complete subjective and objective examination for evaluating outcome in single therapy versus combined therapy of UAD.

In this case report showed the outcome evaluation results were good after 2 months of using combination therapy of intranasal and inhaled steroids in controlling nasal and pulmonary symptoms as well, so it could be concluded that the strategies to treat both

diseases simultaneously and with limited burden on patients should be considered as recommended by the guidelines. We are suggesting the treatments of patients with both rhinitis and asthma should be combined and considered as an integral part of treatment for UAD, rather than treating the nasal or asthma symptoms only.

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