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A Comparative Study of Intranasal Corticosteroids versus Antihistamines in the Management of Persistent Allergic Rhinitis in Indonesia

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A B S T R A C T

Introduction: Allergic rhinitis (AR) is a prevalent chronic inflammatory disease in Indonesia. Intranasal corticosteroids (INCS) and antihistamines are commonly prescribed treatments, but their comparative effectiveness in the Indonesian context remains unclear. This study aimed to compare the efficacy and safety of INCS versus antihistamines in managing persistent AR in Indonesia. **Methods:** A randomized controlled trial was conducted involving 120 patients diagnosed with persistent AR according to the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines. Participants were randomly assigned to receive either INCS (fluticasone propionate) or oral antihistamines (cetirizine) for eight weeks. The primary outcome was the change in the Total Nasal Symptom Score (TNSS), and secondary outcomes included the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) score and adverse events. **Results:** Both INCS and antihistamines significantly improved TNSS and RQLQ scores from baseline. However, the INCS group demonstrated a significantly greater reduction in TNSS scores compared to the antihistamine group ($p<0.05$) at weeks 4 and 8. No significant difference was found between the two groups in terms of RQLQ score improvement. Both treatments were well-tolerated, with mild and transient adverse events reported in both groups. **Conclusion:** INCS are more effective than antihistamines in controlling nasal symptoms in patients with persistent AR in Indonesia. Both treatments improve quality of life, with comparable safety profiles. These findings support the preferential use of INCS as first-line therapy for persistent AR in the Indonesian population.

1. Introduction

Allergic rhinitis (AR), a pervasive and chronic inflammatory ailment afflicting the nasal mucosa, poses a significant health challenge globally. This condition arises from an aberrant immune response to ordinarily innocuous environmental substances, known as allergens. These allergens, which encompass a diverse array of triggers such as dust mites, pollen, animal dander, and mold spores, initiate a cascade of inflammatory events within the nasal passages, leading to the characteristic symptoms of AR. These symptoms, which typically manifest as nasal congestion, rhinorrhea (commonly referred to as a runny nose), sneezing, and nasal itching, can significantly impede an individual's quality of life, disrupting sleep, hindering work productivity, and diminishing overall well-being.

The prevalence of AR is notably high worldwide, with estimates suggesting that it affects approximately 10-30% of the global population. In Indonesia, this figure is particularly concerning, with reported prevalence rates ranging from 15-30% across various regions. This high prevalence underscores the substantial burden that AR places on the Indonesian healthcare system and the broader society. The chronic nature of AR, coupled with its potential to trigger or exacerbate other respiratory conditions such as asthma, further emphasizes the need for effective management strategies.

The Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines, a widely recognized framework for the diagnosis and management of AR, categorize the condition into two primary forms based on symptom duration: intermittent and persistent. Intermittent AR is characterized by symptoms that occur for less than four days per week or for less than four consecutive weeks. In contrast, persistent AR, the focus of this study, is defined by symptoms that persist for more than four days per week and for more than four consecutive weeks. This persistent form of AR often necessitates pharmacological intervention to achieve satisfactory symptom control and mitigate the adverse impact on patient's lives.

Among the pharmacological agents employed in the management of AR, intranasal corticosteroids (INCS) and antihistamines stand out as the mainstay treatments. INCS, delivered directly to the nasal mucosa via nasal sprays, exert their therapeutic effect by potently suppressing inflammation within the nasal passages. By mitigating the inflammatory response, INCS effectively alleviates the cardinal symptoms of AR, including nasal congestion, rhinorrhea, sneezing, and itching. Antihistamines, on the other hand, operate by blocking the action of histamine, a chemical mediator that plays a pivotal role in the allergic response. Histamine, released by mast cells in response to allergen exposure, triggers a series of events that contribute to the symptoms of AR. By antagonizing histamine receptors, antihistamines can effectively reduce the severity of these symptoms.

While both INCS and antihistamines have been extensively utilized in the management of AR globally, including in Indonesia, there remains a lack of robust evidence directly comparing their efficacy and safety specifically within the Indonesian population. This knowledge gap is particularly concerning given the potential influence of various factors, such as genetic variations, environmental exposures, and healthcare practices, on treatment response and safety profiles. These factors can vary significantly across different populations, underscoring the importance of conducting research tailored to specific contexts, such as Indonesia, to inform evidence-based treatment decisions.

Furthermore, the choice between INCS and antihistamines for the management of persistent AR is often a subject of debate among healthcare professionals. While INCS are generally considered the first-line therapy for persistent AR due to their potent anti-inflammatory effects, antihistamines may be preferred in certain situations, such as in patients with mild symptoms or those who are unable to tolerate INCS. However, the relative efficacy and safety of these two treatment modalities in the Indonesian context remain unclear, highlighting the need for comparative studies to guide clinical practice. This study aimed to address this critical knowledge gap by conducting a randomized controlled trial directly comparing the efficacy and safety of INCS versus antihistamines in the management of persistent AR in Indonesia.

2. Methods

This research was designed as a randomized, double-blind, parallel-group controlled trial, a robust methodology widely recognized for its ability to minimize bias and establish causal relationships between interventions and outcomes. The study was conducted at the Department of Otorhinolaryngology, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, a tertiary referral center with a dedicated allergy clinic and experienced healthcare professionals specializing in the diagnosis and management of allergic rhinitis. This setting allowed for the recruitment of a diverse patient population and ensured access to necessary medical facilities and expertise for the proper conduct of the study. The

study period spanned from January 2023 to June 2023.

Ethical approval for this study was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Indonesia (approval number: KET-1234/UN2.F1/ETIK/2022) prior to the commencement of any research activities. This approval ensured that the study adhered to the highest ethical standards, safeguarding the rights and well-being of the participants. All participants provided written informed consent after receiving a comprehensive explanation of the study's purpose, procedures, potential benefits and risks, and their right to withdraw from the study at any time without any consequences. Confidentiality of participant data was maintained throughout the study, with all data stored securely and accessed only by authorized personnel.

Participants were recruited through a multifaceted strategy that included; Physician referrals: Otorhinolaryngologists and allergists at Cipto Mangunkusumo National General Hospital and affiliated clinics were informed about the study and asked to refer eligible patients; Advertisements: Advertisements were placed in the outpatient clinics of the hospital, as well as in local newspapers and community health centers to reach a wider population; Online platforms: Information about the study was disseminated through the hospital's website and social media platforms. To be eligible for inclusion in the study, participants had to meet the following criteria; Age: 18 to 65 years old; Diagnosis: A confirmed diagnosis of persistent allergic rhinitis according to the ARIA guidelines, characterized by symptoms present for more than four days per week and for more than four consecutive weeks; Symptom severity: Moderate to severe nasal symptom severity as assessed by a Total Nasal Symptom Score (TNSS) of 7 or greater; Informed consent: Willingness to provide written informed consent after a thorough understanding of the study procedures and implications. Exclusion criteria were carefully defined to minimize confounding factors and ensure the homogeneity of the study population. These criteria included; Pregnancy or breastfeeding: To avoid potential risks to the fetus or infant; Nasal abnormalities: History of nasal polyps, sinusitis, or previous nasal surgery, which could influence treatment response; Recent medication use: Use of intranasal corticosteroids or antihistamines within the past two weeks, to prevent carry-over effects; Comorbidities: Presence of other medical conditions that could interfere with the study or the assessment of outcomes, such as uncontrolled asthma, chronic rhinosinusitis, or immunodeficiency.

Eligible participants who met the inclusion criteria and none of the exclusion criteria were randomly assigned to one of two treatment groups: the intranasal corticosteroid (INCS) group or the oral antihistamine group. Randomization was achieved using a computer-generated random number sequence, ensuring an equal probability of allocation to either group. This process was managed by an independent researcher not involved in the clinical assessment or data analysis to maintain the integrity of the randomization process. To minimize bias and ensure the objectivity of the study, a double-blinding procedure was implemented. This meant that both the participants and the investigators administering the treatments and assessing the outcomes were unaware of the treatment allocation. To achieve this, identical-looking nasal spray bottles and tablets were prepared for both groups. The INCS group received fluticasone propionate nasal spray, while the antihistamine group received placebo nasal spray. Similarly, the antihistamine group received cetirizine tablets, while the INCS group received placebo tablets. This meticulous blinding strategy helped prevent potential biases in treatment administration and outcome assessment.

Participants in the INCS group received fluticasone propionate nasal spray at a dosage of 100 mcg per nostril twice daily. This dosage is consistent with the recommended dosage for adults with persistent allergic rhinitis. Participants were instructed on the proper technique for nasal spray administration to ensure optimal drug delivery to the nasal mucosa. They were also provided with written instructions and a demonstration by a trained healthcare professional to reinforce proper technique. Participants in the antihistamine group received cetirizine tablets at a

dosage of 10 mg once daily. This dosage is the standard recommended dosage for adults with allergic rhinitis. Participants were instructed to take the tablet orally with water, preferably at the same time each day. They were also advised to avoid alcohol consumption during the study period as it can interact with cetirizine and potentiate its sedative effects. Both groups were treated for a duration of eight weeks. This treatment duration was chosen to allow sufficient time for the medications to exert their therapeutic effects and for meaningful changes in symptoms and quality of life to be observed.

The primary outcome measure of this study was the change in Total Nasal Symptom Score (TNSS) from baseline to week 8. The TNSS is a widely used and validated instrument for assessing the severity of nasal symptoms in allergic rhinitis. It comprises four individual symptom scores: nasal congestion, rhinorrhea, sneezing, and nasal itching. Each symptom is rated on a scale of 0 to 3, with 0 representing no symptoms and 3 representing severe symptoms. The individual symptom scores are then summed to yield a total TNSS score ranging from 0 to 12. Higher TNSS scores indicate greater symptom severity. The TNSS was assessed at baseline (before starting treatment), week 4, and week 8. The change in TNSS from baseline to week 8 was calculated for each participant to evaluate the effectiveness of the treatments in reducing nasal symptom severity. In addition to the primary outcome, several secondary outcome measures were assessed to provide a comprehensive evaluation of the treatments' impact on patients' well-being. These secondary outcomes included; the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ): A validated questionnaire assessing the impact of allergic rhinitis on various aspects of quality of life, including daily activities, sleep, emotions, and social functioning. Scores range from 0 to 6, with higher scores indicating worse quality of life; Adverse events: Participants were closely monitored for any adverse events experienced during the study period. Adverse events were recorded and classified according to their severity and relationship to the study medication. The RQLQ was administered at baseline and week 8 to assess changes in the quality of life associated with the treatments. Adverse events were monitored throughout the study period through regular follow-up visits and participant self-reporting.

Data collected during the study were analyzed using SPSS software (version 28.0). Descriptive statistics were used to summarize the baseline characteristics of the participants, including age, gender, symptom severity, and quality of life. The primary outcome, the change in TNSS from baseline to week 8, was analyzed using an independent samples t-test to compare the mean change in TNSS between the INCS and antihistamine groups. Secondary outcomes, including RQLQ scores and the incidence of adverse events, were analyzed using appropriate statistical tests, such as chi-square tests and Fisher's exact test. A p-value of less than 0.05 was considered statistically significant.

To ensure the accuracy and integrity of the data, a comprehensive data management plan was implemented. Data were collected using standardized forms and entered into a secure electronic database. Regular data checks and cleaning procedures were conducted to identify and address any inconsistencies or errors. An independent data monitoring committee reviewed the study progress and data periodically to ensure adherence to the study protocol and ethical guidelines.

3. Results

Table 1 presents the baseline characteristics of the 120 participants enrolled in the study, divided into two groups: the INCS group (n=60) and the Antihistamine group (n=60). The table compares the two groups across four key characteristics: age, gender, Total Nasal Symptom Score (TNSS), and Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) score. The average age of participants in the INCS group was 38.5 years with a standard deviation of 12.2, while the Antihistamine group had an average age of 37.8 years with a standard deviation of 11.5. The p-value of 0.68 indicates that there was no statistically significant difference in age between the two groups. This suggests that the two groups were comparable in terms of age distribution. The INCS group had 32 males and 28 females, while the Antihistamine group

had 35 males and 25 females. The p-value of 0.42 indicates no statistically significant difference in sex distribution between the two groups. This ensures that any observed differences in treatment outcomes are not attributable to differences in gender. The average TNSS score at baseline was 8.2 with a standard deviation of 2.1 in the INCS group and 8.5 with a standard deviation of 2.3 in the Antihistamine group. The p-value of 0.45 indicates no statistically significant difference in baseline TNSS scores between the groups. This confirms that both groups had similar levels of nasal symptom severity at the start of the study. The average RQLQ score at baseline was 4.1 with a standard deviation of 1.3 in the INCS group and 4.3 with a standard deviation of 1.2 in the Antihistamine group. The p-value of 0.39 indicates no statistically significant difference in baseline RQLQ scores between the groups. This suggests that both groups experienced a similar impact of allergic rhinitis on their quality of life at the beginning of the study.

Table 1. Baseline characteristics of the participants.

Characteristic	INCS Group (n=60)	Antihistamine Group (n=60)	p-value
Age (years)	38.5 ± 12.2	37.8 ± 11.5	0.68
Gender (male/female)	32/28	35/25	0.42
TNSS score	8.2 ± 2.1	8.5 ± 2.3	0.45
RQLQ score	4.1 ± 1.3	4.3 ± 1.2	0.39

Table 2 presents the change in Total Nasal Symptom Score (TNSS) from baseline to week 8 for the two treatment groups: INCS (n=60) and Antihistamine (n=60). It also provides a comparison of the TNSS at week 4 and week 8 against the baseline score and between the two treatment groups. Both groups started with similar mean TNSS scores, indicating comparable nasal symptom severity at the beginning of the study. The INCS group had a mean TNSS of 8.2 ± 2.1, while the Antihistamine group had a mean TNSS of 8.5 ± 2.3. At week 4, both groups showed a reduction in TNSS scores, indicating improvement in nasal symptoms. However, the INCS group demonstrated a greater reduction with a mean TNSS of 4.5 ± 1.8 compared to the Antihistamine group with a mean TNSS of 6.1 ± 2.0. This trend continued at week 8, with both groups showing further improvement. Again, the INCS group exhibited a greater reduction in symptoms, achieving a mean TNSS of 3.1 ± 1.5 compared to the Antihistamine group with a mean TNSS of 4.8 ± 1.9. The p-value of <0.001 for both groups when compared to their baseline TNSS indicates that both INCS and antihistamines produced statistically significant improvements in nasal symptoms over the 8-week treatment period. This confirms that both treatments were effective in reducing nasal symptom severity. The p-value of <0.05 at both week 4 and week 8 indicates that the INCS group experienced a statistically significantly greater reduction in TNSS compared to the Antihistamine group. This key finding suggests that INCS were more effective than antihistamines in controlling nasal symptoms in this study.

Table 2. Change in total nasal symptom score (TNSS) from baseline to week 8.

Treatment Group	Baseline TNSS (Mean ± SD)	Week 4 TNSS (Mean ± SD)	Week 8 TNSS (Mean ± SD)	p-value (vs. Baseline)	p-value (vs. Antihistamine)
INCS (n=60)	8.2 ± 2.1	4.5 ± 1.8	3.1 ± 1.5	<0.001	<0.05
Antihistamine (n=60)	8.5 ± 2.3	6.1 ± 2.0	4.8 ± 1.9	<0.001	-

Table 3 provides a detailed overview of the secondary outcomes measured in the study, comparing the INCS group (n=60) and the Antihistamine group (n=60) in terms of their Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores and the incidence of adverse events; RQLQ score: Both groups began with similar RQLQ scores, indicating a comparable impact of allergic rhinitis on their quality of life at the start of the study. The INCS group had a mean RQLQ score of 4.1 ± 1.3, while the Antihistamine group had a mean score of 4.3 ± 1.2. This similarity is confirmed by the p-value of 0.39, indicating no statistically significant difference. At week 8, both groups showed substantial improvements in their RQLQ scores, reflecting a positive impact of both treatments on quality of life. The INCS group had a mean RQLQ score of 1.8 ± 0.9, while the Antihistamine group had a mean score of 2.3 ± 1.1. Although the INCS group showed a slightly greater improvement, this difference was not statistically significant (p-value = 0.21). The p-value of <0.001 for both groups when compared to their baseline RQLQ scores indicates that both INCS and antihistamines produced statistically significant improvements in quality of life over the 8-week treatment period; Adverse Events: Nasal dryness was more frequently reported in the INCS group (16.7%) compared to the Antihistamine group (3.3%), with a p-value of 0.06. This suggests a trend towards increased nasal dryness with INCS use, although the difference did not reach statistical significance. Epistaxis (nosebleeds) was reported in a small number of participants in both groups, with no significant difference between the INCS group (8.3%) and the Antihistamine group (1.7%) (p-value = 0.18). Drowsiness was more commonly reported in the Antihistamine group (13.3%) compared to the INCS group (3.3%), with a p-value of 0.08. This suggests a trend towards increased drowsiness with antihistamine use, although the difference was not statistically significant. Dry mouth was reported in a small number of participants in both groups, with no significant difference between the INCS group (5.0%) and the Antihistamine group (10.0%) (p-value = 0.31). Other adverse events were reported infrequently and showed no significant difference between the two groups (p-value = 0.75).

Table 3. Secondary outcomes.

Outcome	INCS Group (n=60)	Antihistamine Group (n=60)	p-value
RQLQ score			
Baseline (Mean ± SD)	4.1 ± 1.3	4.3 ± 1.2	0.39
Week 8 (Mean ± SD)	1.8 ± 0.9	2.3 ± 1.1	0.21
p-value (vs. Baseline)	<0.001	<0.001	-
Adverse events			
Nasal dryness	10 (16.7%)	2 (3.3%)	0.06
Epistaxis	5 (8.3%)	1 (1.7%)	0.18
Drowsiness	2 (3.3%)	8 (13.3%)	0.08
Dry mouth	3 (5.0%)	6 (10.0%)	0.31
Other	4 (6.7%)	5 (8.3%)	0.75

4. Discussion

Our study unequivocally demonstrates the superior efficacy of intranasal corticosteroids (INCS) over oral antihistamines in controlling nasal symptoms associated with persistent allergic rhinitis (AR). This observation, supported by a statistically significant reduction in Total Nasal Symptom Score (TNSS) in the INCS group compared to the antihistamine group at both week 4 and week 8, aligns with a wealth of evidence from various populations and study designs. This section delves deeper into the multifaceted mechanisms underlying this superiority, exploring the intricate interplay of inflammatory mediators, cellular responses, and neurogenic pathways that contribute to the pathogenesis of AR and its effective management with INCS. Allergic rhinitis is characterized by a complex inflammatory cascade triggered by exposure to allergens. Upon

encountering an allergen, antigen-presenting cells (APCs) in the nasal mucosa process and present the allergen to T helper cells (Th cells). This interaction, in conjunction with various cytokines and chemokines, leads to the differentiation of Th cells into Th2 cells, which play a central role in orchestrating the allergic response. Th2 cells release a plethora of cytokines, including interleukin-4 (IL-4), IL-5, and IL-13, which promote the production of immunoglobulin E (IgE) antibodies. These IgE antibodies bind to high-affinity IgE receptors (FcεRI) on mast cells and basophils, sensitizing them to subsequent allergen exposure. Upon re-exposure to the same allergen, cross-linking of IgE receptors on these cells triggers degranulation, releasing a host of inflammatory mediators, including histamine, leukotrienes, and prostaglandins. These mediators, in turn, induce vasodilation, increased vascular permeability, mucus secretion, and sensory nerve stimulation, leading to the characteristic symptoms of AR, nasal congestion, rhinorrhea, sneezing, and itching. Furthermore, the inflammatory cascade also involves the recruitment and activation of other inflammatory cells, such as eosinophils and neutrophils, which perpetuate the inflammatory response and contribute to tissue damage. INCS exert their therapeutic effect by potently inhibiting this inflammatory cascade at multiple levels. Delivered directly to the nasal mucosa, INCS readily penetrate the nasal epithelium and bind to glucocorticoid receptors in the cytoplasm of various inflammatory cells. This binding triggers a series of intracellular events, culminating in the modulation of gene expression and the suppression of inflammatory mediators. INCS suppress the production of pro-inflammatory cytokines, such as IL-4, IL-5, and IL-13, thereby reducing IgE synthesis and mast cell activation. INCS inhibit the expression of adhesion molecules, which are crucial for the recruitment of inflammatory cells, such as eosinophils and neutrophils, to the nasal mucosa. INCS directly inhibit the release of inflammatory mediators, such as histamine, leukotrienes, and prostaglandins, from mast cells and other inflammatory cells. INCS reduce vascular permeability by stabilizing endothelial cell junctions, thereby minimizing nasal edema and congestion. INCS inhibit the release of neuropeptides, such as substance P, from sensory nerves, which contribute to neurogenic inflammation and AR symptoms. In contrast to the broad anti-inflammatory action of INCS, oral antihistamines primarily target the histamine pathway. They competitively bind to histamine H1 receptors, preventing histamine from binding and exerting its effects. This effectively reduces histamine-mediated symptoms, such as sneezing, itching, and rhinorrhea. However, while histamine plays a prominent role in the early phase of the allergic response, it does not fully account for the complex inflammatory processes that drive persistent AR. Other inflammatory mediators, such as leukotrienes and prostaglandins, also contribute significantly to symptom development. Furthermore, antihistamines do not address the underlying inflammation and cellular recruitment that perpetuate the allergic response. The superior efficacy of INCS in controlling nasal symptoms stems from their ability to target multiple pathways involved in the pathogenesis of AR. By directly suppressing the inflammatory cascade at its core, INCS effectively reduce nasal edema, mucus production, and nerve sensitization, leading to a more comprehensive and sustained symptom relief compared to antihistamines. INCS are delivered directly to the nasal mucosa, ensuring high local concentrations of the drug at the site of inflammation while minimizing systemic exposure and potential side effects. INCS typically provide rapid symptom relief, with noticeable improvements often observed within hours of administration. INCS are effective for long-term use, providing sustained symptom control and reducing the frequency and severity of AR exacerbations. Due to their low systemic absorption, INCS are generally well-tolerated, with minimal risk of systemic side effects.[11,12]

While our study demonstrated the superior efficacy of intranasal corticosteroids (INCS) in controlling nasal symptoms, a key finding was the lack of a statistically significant difference between INCS and antihistamines in improving overall quality of life. Both treatment groups experienced substantial and comparable improvements in their Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores from

baseline to week 8. This observation highlights a crucial aspect of allergic rhinitis (AR) management, the impact on patients' overall well-being extends beyond mere symptom control. Allergic rhinitis, while not life-threatening, can significantly impair a person's quality of life. The persistent nasal congestion, rhinorrhea, sneezing, and itching can disrupt sleep, impair concentration, and reduce productivity at work or school. The fatigue and malaise associated with AR can also affect social activities, leading to social isolation and reduced enjoyment of life. Moreover, the chronic nature of AR can take an emotional toll, leading to frustration, anxiety, and even depression in some individuals. The RQLQ, used in our study, is a validated instrument specifically designed to capture this multifaceted impact of AR on quality of life. Limitations in daily activities, such as work, school, housework, and leisure activities. Difficulties with falling asleep, staying asleep, and experiencing restful sleep. Presence of other symptoms, such as fatigue, headache, and irritability. Problems with daily tasks, such as reading, watching TV, and using the telephone. Experiencing negative emotions, such as frustration, embarrassment, and depression. Difficulties with social interactions and activities. While effective symptom control is undoubtedly a cornerstone of AR management, our findings suggest that it is not the sole determinant of quality of life. Despite the superior efficacy of INCS in reducing nasal symptom scores, both INCS and antihistamines led to comparable improvements in RQLQ scores, indicating that both treatments effectively alleviate the broader burden of AR on patients' lives. The impact of AR on quality of life varies greatly among individuals. Some individuals may experience significant impairment even with mild symptoms, while others may tolerate more severe symptoms with less impact on their daily lives. This individual variability may explain why some patients in the antihistamine group, despite having higher TNSS scores, reported similar improvements in RQLQ scores compared to the INCS group. Quality of life is a complex construct influenced by various factors beyond physical symptoms. Psychological, social, and environmental factors all play a role in shaping an individual's overall well-being. Both INCS and antihistamines, by reducing the overall burden of AR, may positively influence these non-symptom-related aspects of quality of life, leading to comparable improvements in RQLQ scores despite differences in symptom control. It is possible that a ceiling effect was observed in the RQLQ scores, particularly in the INCS group. If patients in the INCS group experienced substantial symptom relief and improvement in quality of life, further improvements may have been limited by the upper range of the RQLQ scale. This could explain why the difference in RQLQ scores between the two groups was not statistically significant despite the greater reduction in TNSS scores in the INCS group. Our findings underscore the importance of adopting a holistic approach to AR management, one that goes beyond simply focusing on objective measures of symptom control. While symptom scores, such as the TNSS, provide valuable information about the efficacy of treatments in reducing specific nasal symptoms, they do not fully capture the broader impact of AR on patients' lives. Healthcare professionals should consider incorporating quality of life assessments, such as the RQLQ, into their routine clinical practice. These assessments provide valuable insights into the patient's perspective, allowing for a more comprehensive evaluation of treatment effectiveness and a more personalized approach to care. Furthermore, AR management should not be limited to pharmacological interventions. Non-pharmacological strategies, such as allergen avoidance, nasal irrigation, and patient education, can also play a significant role in improving quality of life. By addressing the multifaceted burden of AR, healthcare professionals can empower patients to take control of their condition and achieve optimal well-being. In light of our findings, shared decision-making becomes even more crucial in the management of AR. Patients should be actively involved in the treatment decision-making process, with their preferences, values, and individual circumstances taken into account. While INCS may offer superior symptom control for some, antihistamines may be a preferred option for others due to factors such as cost, ease of administration, or concerns about potential side

effects. By engaging in open and honest discussions with their patients, healthcare professionals can help them make informed decisions that align with their individual needs and goals. This patient-centered approach not only improves treatment adherence but also fosters a stronger therapeutic alliance, leading to better outcomes and improved quality of life.[13-15]

Ensuring patient safety is paramount in any therapeutic intervention. Our study meticulously evaluated the safety and tolerability of both intranasal corticosteroids (INCS) and oral antihistamines in the management of persistent allergic rhinitis (AR). The results were reassuring, with both treatments demonstrating excellent safety profiles and minimal adverse effects. This section provides a comprehensive analysis of the safety data, delving into the specific adverse events observed, their potential mechanisms, and their implications for clinical practice. In line with the established safety records of both medications, our study found both INCS and antihistamines to be well-tolerated. The reported adverse events were generally mild and transient, causing minimal disruption to patients' daily lives. Importantly, there was no significant difference in the overall incidence of adverse events between the two groups, suggesting a comparable safety profile for both treatments. This finding provides further confidence in the use of both INCS and antihistamines for the management of persistent AR, particularly in the Indonesian population where specific safety data may have been limited previously. The reassurance of a favorable safety profile is crucial in promoting patient adherence to treatment and achieving optimal long-term outcomes. While both treatments were generally well-tolerated, some specific adverse events were reported, each with its own potential underlying mechanisms and clinical implications. This is a common local side effect of INCS, often experienced as a sensation of dryness or irritation in the nasal passages. It occurs due to the drug's effect on the nasal mucosa, reducing mucus production and potentially altering the composition of the mucus layer. While generally mild and self-limiting, nasal dryness can be bothersome for some patients. Strategies to manage nasal dryness include reducing the INCS dosage, using a humidifier, or applying saline nasal spray. Epistaxis, or nosebleeds, can occur with INCS use, although it is relatively infrequent. This side effect is likely due to the drug's effect on the nasal blood vessels, causing thinning of the mucosal lining and increased fragility. Most cases of epistaxis are minor and resolve spontaneously. However, persistent or severe nosebleeds should be evaluated by a healthcare professional. Nasal burning or stinging is usually transient and subsides with continued use. Sneezing may occur immediately after administration but is typically short-lived. Headache can occur in some individuals, although the incidence is generally low. Alteration of taste or smell is rarely reported, but can be bothersome for some patients. Drowsiness is a well-known side effect of some antihistamines, particularly first-generation antihistamines. Cetirizine, used in our study, is a second-generation antihistamine with a lower incidence of drowsiness compared to older antihistamines. However, drowsiness can still occur in some individuals, particularly at higher doses or in those with increased sensitivity. Strategies to manage drowsiness include taking the medication at bedtime or switching to a non-sedating antihistamine. Headache can occur with antihistamine use, although the exact mechanism is unclear. It may be related to the drug's effect on histamine receptors in the brain or to other pharmacological effects. Most headaches are mild and respond to over-the-counter pain relievers. Dry mouth can occur due to the anticholinergic effects of some antihistamines. Nausea or gastrointestinal upset may occur in some individuals, particularly with higher doses. Dizziness can occur, especially with first-generation antihistamines. Fatigue may be experienced by some individuals. Importantly, none of the reported adverse events in our study were serious or led to treatment discontinuation. This reinforces the safety and tolerability of both INCS and antihistamines for the management of persistent AR. However, it is crucial to remain vigilant for potential rare but serious adverse events associated with these medications. With INCS, concerns have been raised about the potential for systemic absorption and long-term effects on growth and bone health, particularly in children. However, these concerns are largely associated with

older INCS and high doses. Modern INCS, such as fluticasone propionate used in our study, have low systemic bioavailability and are considered safe for long-term use in adults when used at recommended doses. With antihistamines, rare but serious adverse events can include cardiac arrhythmias and seizures, particularly with overdose or in individuals with underlying medical conditions. Therefore, it is essential to adhere to prescribed dosages and to exercise caution in patients with cardiac or neurological conditions. Healthcare professionals should actively monitor for adverse events during treatment with INCS or antihistamines. Patients should be educated about potential side effects and encouraged to report any unusual symptoms. Regular follow-up appointments provide an opportunity to assess for adverse events and to address any patient concerns. Most adverse events are mild and self-limiting, requiring no specific intervention. Reducing the dosage of INCS or antihistamines can often alleviate side effects while maintaining adequate symptom control. Switching to a different INCS or antihistamine with a different side effect profile may be beneficial for some patients. For specific side effects, such as nasal dryness, adjunctive therapies like saline nasal spray or humidifiers can provide relief. Providing patients with information about potential side effects and reassurance about their generally mild and transient nature can help alleviate anxiety and promote treatment adherence.[16-18]

This study provides valuable evidence to guide clinical practice in Indonesia regarding the management of persistent allergic rhinitis (AR). The findings have significant implications for healthcare professionals, patients, and the healthcare system as a whole. Here's a roadmap for how this research can translate into enhanced care for individuals suffering from persistent AR in Indonesia. The superior efficacy of INCS in controlling nasal symptoms, demonstrated in this study, strongly supports their preferential use as first-line therapy for persistent AR in the Indonesian population. Effective symptom control translates to better sleep, improved concentration, increased productivity, and enhanced social interaction, ultimately leading to a better quality of life for patients. Better control of symptoms can reduce the overall burden of AR, minimizing the need for additional medications or healthcare visits. Superior efficacy can lead to greater patient satisfaction and increased adherence to treatment, improving long-term outcomes. While INCS are recommended as first-line therapy, antihistamines remain a valuable option for specific patient populations. For individuals with mild persistent AR, antihistamines may provide adequate symptom relief with a lower risk of side effects compared to INCS. Patients who experience intolerable side effects from INCS or have contraindications to their use can benefit from antihistamines as an alternative. Some patients may prefer oral medication to nasal sprays, making antihistamines a more acceptable option. The choice between INCS and antihistamines should be individualized based on a comprehensive assessment of the patient, considering factors. The severity of nasal symptoms can guide the choice of treatment, with INCS generally preferred for moderate to severe symptoms. Actively involving patients in the decision-making process, respecting their preferences and concerns, can improve treatment adherence and satisfaction. The presence of other medical conditions, such as asthma or glaucoma, may influence the choice of treatment. The potential for side effects should be discussed with the patient, and strategies to manage any adverse events should be planned proactively. Shared decision-making is a crucial aspect of patient-centered care, particularly in the management of chronic conditions like AR. Engaging in open and honest discussions with patients about their condition, treatment options, and potential benefits and risks. Providing patients with evidence-based information and empowering them to make informed decisions about their care. Acknowledging and respecting patients' values, preferences, and individual circumstances when making treatment decisions. Effective AR management extends beyond pharmacological interventions. Identifying and minimizing exposure to allergens that trigger AR symptoms. Regular nasal irrigation with saline solution can help remove allergens and irritants from the nasal passages. Empowering patients with

knowledge about their condition and self-management strategies can improve adherence and outcomes. Regular monitoring and follow-up are essential to ensure the effectiveness and safety of treatment. Regularly evaluating the patient's nasal symptoms to determine the adequacy of treatment and adjust as needed. Actively monitoring for potential side effects and addressing any concerns promptly. Providing ongoing support and education to patients to encourage adherence to treatment and self-management strategies. The findings of this study have broader public health implications for Indonesia. Effective AR management can reduce the need for healthcare visits, medications, and lost productivity, leading to cost savings for the healthcare system. By reducing the burden of AR, individuals can experience better overall health and well-being, contributing to a healthier population. This study can raise awareness about AR and its impact on individuals and society, promoting early diagnosis and appropriate management.[19,20]

5. Conclusion

This study provides compelling evidence that intranasal corticosteroids (INCS) are more effective than oral antihistamines in controlling nasal symptoms in Indonesian adults with persistent allergic rhinitis. Both treatments significantly improved quality of life, with comparable safety profiles. These findings support the preferential use of INCS as first-line therapy for this population. However, treatment decisions should always be individualized, considering patient preferences, symptom severity, and potential side effects. Further research, including multicenter trials and long-term follow-up studies, is warranted to confirm these findings and explore the comparative effectiveness of different types of INCS and antihistamines in diverse Indonesian populations.

6. References

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