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Changes in total nasal symptoms score and quality of life after supplementation of Habbatussauda (Nigella sativa) in persistent Allergic Rhinitis

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ABSTRACT

Introduction: Allergic Rhinitis (AR) is health problem that can influence a patient's quality of life, affecting them through various nasal symptoms. Habbatussauda (*Nigella sativa*) can alleviate the nasal symptoms due to its component *Thymoquinone,* which acts as a bioactive substance possessing anti-inflammatory, anti-oxidant, and anti-microorganism properties.
Objective: This study aims to evaluate the change in total nasal symptom scores and the enhanced quality of life in persistent AR patients after supplementation with habbatussauda.
Methods: Experimental study with parallel design was conducted in two subject groups, group H (habbatussauda) and group P (Placebo). Both groups were given standard therapy. Group H was given additional supplementation of habatussauda 2 gr for 28 days. Nasal symptoms score were measured using Total Nasal Symptoms Score (TNSS) and quality of life was measured using Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). Data were analyzed using *Mann-Whitney U test.*
Results: A total of 42 AR patients were involved which are divided into 21 subjects in each group. An average age of 31 years in the habatussauda group and 34 years in the control group which were dominated by men. In group H, the mean change in TNSS was 3.45 and RQLQ score was 17.67. Meanwhile in group P, the mean change in TNSS was 1 and RQLQ score was 8. From these results, the change in TNSS in group H was better than group P(p=0.001), likewise the RQLQ score showed a better change in group H(p=0.001).
Conclusion: Supplementation of habbatussauda for 28 days can decrease the degree of TNSS and increase quality life on AR patients.

INTRODUCTION

Allergic Rhinitis (AR) is a chronic inflammation of the nasal mucosa mediated by immunoglobulin E (IgE) with symptoms felt in the form of itchy sensation in the nose, runny nose, blocked nose and repeated sneezing. Based on the duration of time or duration of symptoms, AR is divided into intermittent and persistent. Meanwhile, based on the severity of the symptoms, AR is divided into mild, moderate and severe degrees (Kalmarzi et al., 2017). The incidence of AR can be experienced by every age group. AR is more common in children with a prevalence of 40%, while it ranges from 10% to 30% in adults. AR can occur in all races and its prevalence varies in every country(Kakli & Riley, 2016) (Rapiejko et al., 2018). *Kakli HA* reported that the global incidence

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of AR was found in 10% to 40% of the world's total population . The United States reported that as many as 600 million people experienced AR every year (Kakli & Riley, 2016). AR was experienced by 17% to 29% of the total European population (Rapiejko et al., 2018). *An SY, et al* reported that AR was experienced by 27% of the total Asian population (An et al., 2015). *Soegiarto G, et al* reported that the incidence of AR in Indonesia was found in 5% of the total population. In 2019 – 2020, there was a record number of AR patients who sought treatment at the ORL-HNS (Otorhinolaryngology – Head and Neck Surgery) polyclinic at the Regional General Hospital, Dr. Zainoel Abidin as many as 99 patients recorded (Soegiarto et al., 2019)(Chong & Chew, 2018).

The symptoms caused by AR are the body's response to the exposure to allergens, which are generally overlooked by patients. This is the basic principle in treating AR, avoiding exposure to allergens such as; dust, pollen, and animal dander. If AR patients are not treated appropriately with the therapy, they experienced disruption in their activity, rest and social function which can affect the patient's life quality and become a socio-economic burden. The disorders that arise in persistent AR patients with moderate to severe symptoms tend to be more severe than in AR patients with mild intermittent symptoms (Linneberg et al., 2016). This condition is the reason for the need of more attention to AR, emphasizing appropriate management and good education to improve the quality of life of AR patients(Meltzer, 2016)(Bernstein et al., 2016).

AR therapy could take a long time and the drugs used have side effects on patients. These are the reasons for the development of alternative therapies to treat AR. Therapeutic options include acupuncture, homeopathy and phytopharmaceuticals (AB Naafs, 2018). Phytopharmaceutical modality is a treatment using herbal plants which contain bioactive substances effective in treating the symptoms felt by patients. This therapeutic method has been used to treat AR in various countries include Europe and Asia (Hoang et al., 2021).

One of the herbal plants that is often used and has been researched to have inflammatory response is Nigella sativa or commonly known as black seed (Saadat et al., 2021). This plant is known to contain various ingredients, among which is thymoquinone. Thymoquinone is a bioactive ingredient which has effects such as anti-inflammatory, anti-oxidant, immunomodulator, anti-microorganism and various other health benefits (Ayşenur Koç et al., 2019). A study by *Nikakhlagh S et al* showed that giving black seed for two weeks succeeded in reducing symptoms experienced by AR patients. This study states that black seed can be an alternative therapy for AR patients, especially for patients who wish to avoid the side effects of medical therapy (Nikakhlagh et al., 2011).

Linear improvement in symptoms will improve the patient's life quality. If nasal symptoms in severe persistent AR are not well-treated, it can result in a decrease in the patient's life quality (Kalmarzi et al., 2017). Therefore, researchers are interested in conducting this research to evaluate the improvements in nasal symptoms and quality of life for AR patients after giving habbatussauda supplementation.

METHODS & MATERIALS

This research was an unpaired numerical comparative analytical study of two groups with a clinical trial design (parallel trial) which was conducted at the ORL-HNS Polyclinic RSUDZA Banda Aceh for 9 months, starting from February to October 2022 until the minimum number of subjects was fulfilled. The study has been approved by the Health Research Ethics Committee of the Medicine Faculty at Universitas Syiah Kuala with an ethical expedited approval number: 162/EA/FK-RSUDZA/2022.

The accessible population is persistent AR patients who seek treatment at the ORL-HNS RSUDZA polyclinic. The subjects of this research were all accessible populations who fulfilled the research inclusion and exclusion criteria. Research inclusion criteria included; Subjects aged 18-55 years, AR diagnosis based on history, physical examination and supporting examination using the Skin Print Test (SPT) with positive results, not currently undergoing other clinical tests simultaneously, patients are willing to take part in the research. Exclusion criteria for the study included a history of consuming other herbal medicines, experiencing malignancy or other systemic diseases, experiencing disorders of the anatomical structure of the nose, suffering from upper respiratory tract infections and sinusitis. The criteria for dropping out of the study were the appearance of a systemic allergic reaction, the patient deciding to withdraw as a research subject, the condition worsening during the intervention, and the AR patients not attending the final evaluation.

The number of subjects in each research group was 21 patients. Subjects who fulfilled the inclusion and exclusion criteria will be randomized with the aim of determining the group of subjects that will be included. The type of randomization used was block randomization of two groups with a computerized system (*Computer generated blocks of two*) using OpenEpi™ software. The Total Nasal Symptom Score Questionnaire (TNSS) is a measuring tool for assessing nasal symptoms. In assessing quality of life, this study used the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). Patients who have symptoms and physical examination lead to AR which needed to conduct a SPT using allergens such as; dust mites (*D. pteronyssinus*), cats (*Pingere*), cockroaches (*Cockroach B. Germanic*), cottonwood (*C. Pentranda*) and grass (*Bermuda grass*).

Patients with positive SPT results were included as research samples. Then, randomization was carried out to determine the research group in the form of group H (using black seed supplementation) and group P (placebo) with the help of an enumerator using a computerized system. Group H was given 2 grams of black seed per day (habbatussauda ajwa™ stamp) produced by CV. Vicomas International, meanwhile group P was given sugar powder. Both types of intervention will placed in capsules of the same shape and size. The interventions were carried out for 28 days. In this research, the dosage of habatussauda referred to a systematic review conducted by Gholamnezhad et al (2019) who reported that giving Habatussauda 2 grams for 30 days acts as an anti-allergic and is proven can improve allergy symptoms and increase cell activity polymorphonuclear in phagocytic and intracellular killing. Both research groups will receive standard AR therapy based on the *Allergic Rhinitis and Its Impact on Asthma* (ARIA) *classification 2016*. TNSS and RQLQ examinations will be carried out twice on D-0 and D-29. All data will be analyzed systematically.

The data obtained in this research will be assessed for statistical significance using the *paired sample t-test* and the *independent sample t-test*. If the data was not normally distributed based on data normality test *Shapiro Wilk test*, then alternative tests, the *Wilcoxon rank test* and the *Mann Whitney U test* CI 95%, will be used.

RESULTS

After conducting the data collection procedures, there were 42 research subjects with a total of 21 patients in each group. Characteristics of research subjects based on age and gender are presented in Table 1.

Table 1. Characteristics of research subjects

Characteristic of Research Subjects	Habbatussauda (+)		Placebo (+)	
	N	%	N	%
Age (year), mean mean ± SD	31 ± 10.41		34.52 ± 11.44	
Gender, n (%)				
Male	10	47.6	12	57.1
Female	11	52.4	9	42.9
Characteristic: History of Atopy				
Yes	13	61.9	15	71.4
No	8	38.1	6	28.6
Characteristic: Nasal Symptoms				
Sneeze	2	9,5	1	4.75
Runny Nose	3	14.2	2	9.5
Nasal Congestion	11	52.3	13	61.9
Itchy Nose	5	23.8	5	23.8
Itchy and Red Eyes	0	0	0	0
Itchy Palatum, Ears, and Throat	0	0	0	0
Characteristic: Types of Allergens from SPT				
Dust Mite	16	76.1	12	57.1
Grass	13	61.9	11	52.3
Cat	6	28.5	10	47.6
Cockroach	4	19	4	19
Cottonwood	2	9.4	1	4.7

Based on gender, the group which was given habbatussauda showed a higher number of female (52.4%) was higher in H group. Meanwhile, the number of male was higher (57.1%) in the placebo group. The group of subjects who received habbatussauda supplementation showed an average age of 31 years while the placebo group was 34.5 years old. In both groups the study showed the same results, the number of AR patients with a history of atopy was greater than AR patients without a history of atopy with respective percentages of 61.9% in group H and 71.4% in group p. The nasal congestion was the main complaint being the most disturbing symptom, about 11 patients (52.3%) in the H group and 13 patients (61.9%) in the P group. Statistically, this data showed that there was no significant difference between the two treatment groups in terms of the main complaints experienced by AR patients. Dust mites were the allergen that caused the most positive results from the SPT examination, about 16 patients (76.1%) in the H group and 12 patients (57.1%) in the P group. The changes in the total nasal symptom score and the quality of life of patients with persistent allergic rhinitis in the group given habbatussauda and placebo are presented in Table 2.

In the H group, the average of TNSS on D-0 was 12.21 and changed to 8.76 after supplementation for 28 days. While the average of TNSS in the P group on D-0 was 10.8 and changed to 9.8 after supplementation for 28 days. Statistically, using a *paired sample t-test*, showed a significant difference changes in total nasal symptom scores of persistent AR patients who received habbatussauda compared to the placebo group for 28 days ($p < 0.05$). Table 2 also presented the changes RQLQ scores in the H group and P group over 28 days. The H group showed a mean score of 108.4 in D-0, then changed to 90.7 after giving habbatussauda. Meanwhile, the average RQLQ score in the P group showed a score of 106 in D-0 and changed to 98 after placebo administration. Statistically, these data showed that there was a significant change quality of life in patients with persistent AR between two groups ($p<0.05$). The mean of TNSS in the H group

and the P group respectively were 3 and 1 with a difference of 2 points. This can be seen in Table 3.

Table 2. Changes in the total nasal symptom scores and the quality of life in patients with persistent allergic rhinitis in the groups given habbatussauda and placebo

Changes in Total Nasal Symptom Scores	Habbatussauda		Placebo		P value*
	N	Min/Max	N	Min/Max	
Before Therapy, mean mean ± SD	12.1 ± 2.62	6/16	10.8 ± 2.9	6/15	< 0,001
After Therapy, mean mean ± SD	8.76 ± 1.94	4/12	9,8 ± 2,78	5/14	< 0,001
Changes in Quality of Life	**Habbatussauda**		**Placebo**		**P value***
	N	**Min/Max**	**N**	**Min/Max**	
Before Therapy, mean mean ± SD	108,4 ± 18,9	64/141	106 ± 23,2	66/138	< 0,001
After Therapy, mean mean ± SD	90,7 ± 15,4	62/116	98 ± 21,6	60/128	< 0,001

** Paired sample t – test*

Table 3. The comparison of changes total nasal symptom scores in patients with persistent allergic rhinitis with habbatussauda and placebo administration

Groups	N	Median	Min	Max	p-value*
Habbatussauda	21	3	2	6	< 0,001
Placebo	21	1	1	3	

* *Independent sample t-test*

Statistically, based on the *independent sample t-test*, showed that there was a significant difference changes quality of life in persistent AR patients who were given habbatussauda supplementation compared to placebo (p<0.001).

DISCUSSION

Based on Table 1 there was no significant difference of age between H and P groups. This is in accordance with research conducted by *Passali et al* reporting the prevalence of AR has increased from the childhood group until the fourth decade. The patients have high activity in open environments on the second to fourth decade of life, so the risk of exposure to allergens is high, and the clinical symptoms of AR begin to persist and become more severe. This age group is more likely to seek treatment at a health facility (Passali et al., 2018)(Czapski, 2024). Table 1 also showed that there was no significant comparison between the genders of the two groups. This is in accordance with a systematic study and meta-analysis by *Carr* reporting that the prevalence of AR in male and female did not show a significant difference in adolescence (11-18 years) patients. Researchers argue that men and women have the same risk of exposure to allergens, especially during reproductive age. Apart from that, the nasal mucosa in both gender has the same structure, so gender did not influence the emergence of hypersensitivity reactions in the nasal mucosa (Carr & Saltoun, 2012).

Table 1 showed that the number of AR patients with a history of atopy was greater than AR patients without a history of atopy. This is in line with research by *Linneberg et al* which reported

that the amount of AR patients who had a family history of atopy were higher than AR patients without a family history of atopy (Linneberg et al., 2016). Research by *Anandan* (2011) reported around 50% of babies had the risk of allergies if one parent had a history of allergies and 75% of babies had a risk of allergies if both parents have a history of allergies. Meanwhile, according to *Koning* (2010), 40% to 60% of babies are at risk of developing allergies if both parents had a history of allergies. If both parents had the same allergic manifestations then the risk will increase to 60% to 80%. The genetic component that is passed to children through their parents is the ability to react to an inherited allergen. The genes involved in the AR reaction include 3q21, 5q31-q33, 7p1-p15, 14q24 which increase the risk of AR (Sarumpaet, 2001). Based on the results above, researchers believed that a history of atopy is a very influential factor in AR patients.

Based on Table 1, nasal congestion was the most serious complaint experienced by AR patients. This is in line with survey conducted by *Roper* (2004) which reported that 85% out of 2355 AR sufferers had nasal congestion as the main complaint. Histamine production in allergic reactions causes vasodilation reactions in blood vessels, interstitial transudation causes edema in the nasal mucosa resulting in nasal congestion in AR patients (Guyton, Arthur C. and Hall, 2011)(Resi Utomo et al., 2018). Table 1 showed that dust mites (D.pteronyssinus) was the allergens that cause the most positive results in SPT examinations. This is in line with research by (Ansari et al., 2006), reporting that the most inhalant allergens that gave positive test results on the SPT were dust mites and cockroaches. Based on research by *Muhammad Rafi et al* (2015) , reported the prevalence of the most common aeroallergens caused AR reactions were D.farinae (63.51%) followed by D.pteronyssinus (60.81%) and Blomia tropicalis (58.10%), because dust mites such as D. pteronyssinus and D. farinae live and develop in both tropical and subtropical areas and often found around the community (Ansari et al., 2006).

Based on Table 3, the results of the Mann-Whitney U test show a significant comparison of the TNSS mean in the two groups with a p value <0.001. This is in line with research by (Nikakhlagh et al., 2011) which showed that habbatussauda can reduce histamine released. This is known due to thymoquinone, the active ingredient in habbatussauda, inhibits the release of IL-4, IL-5, IL-13 and ovalbumin (OVA) IgE which is a mediator in allergic reactions that cause mast cell degranulation. (Nikakhlagh et al., 2011) reported a significant decrease after habbatussauda supplementation for 2 weeks. This is evidence that the use of habbatussauda can be considered as an additional therapy for AR patients. Research conducted by Gholamnezhad (2019) showed that habbatussauda can significantly improve the clinical symptoms of AR patients by inhibiting the release of histamine, lipoxygenase pathway metabolites like leukotrienes by blocking histamine receptors non-selective. This explains the therapeutic benefits of using habbatussauda in allergy cases (Boskabady et al., 2022). Based on Table 4, the results of the independent sample t-test show a significant difference changes in quality of life in persistent AR patients who were given habbatussauda compared to the placebo group (p<0.001). This research is in line with the findings of (Zhang & Wang, 2022) that the clinical efficacy of tuomin zhiti decoction in AR patients reduced AR symptoms and the RQLQ value decreased significantly after four weeks of treatment in both groups (Zhang & Wang, 2022). Another study also reported that the RQLQ score decreased significantly among the group given ginger extract (zingiber offinale roscoe) compared to loratadine (Yamprasert et al., 2020)).

The severity of the patient's symptoms, indicated by a high TNSS value, will affect the patient's quality of life based on the results of the RQLQ assessment (*Chawla D et al*, 2014). Patients will experience disruption at work such as reduced productive hours and decreased performance at work. Studies showed that AR patients experienced a decrease in working hours (3.6%) and a

decrease in performance at work (35.9%). This is influenced by the severity of the symptoms experienced by patients and their impact on sleep hours and daily activities (Bousquet et al., 2007). According to *Juniper* (1996), AR treatment can significantly cause changes to the quality of life of AR patients. Changes in quality of life have an impact on achievement, learning processes and work productivity. Treatment using appropriate and effective drugs will reduce inflammatory cells and various mediators in order to reduce AR symptoms (Juniper et al., 1996).

CONCLUSION

In the study, there was a significant change in the total nasal symptom score of persistent AR patients who were given habbatussauda supplementation compared to those who were given placebo. Notably, persistent AR patients who were given habbatussauda had a more significant improvement in quality of life compared to those who were given a placebo. This indicates that habatussauda supplementation can be used as additional therapy for AR due to its anti-inflammatory and immunomodulatory effects in reducing the symptoms of persistent AR.

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