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Research Article

Is there a Relationship between Social Support and High Histamine in Allergic-Non Allergic Rhinitis?

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Abstract

Background: The histaminergic system has been shown to be important for emotional state, anxiety, allergy, and the brain arousal system. In this study, we aimed to investigate the relationship between social support and high histamine in patients with Allergic-Non allergic Rhinitis (AR-NAR).

Methods: Diagnosis of AR was made using the findings of physical and nasal endoscopic examination and the results of the skin prick test. Of 131 patients, 90 were diagnosed as having AR, and 41 as having NAR. Competence of social support of all patients was assessed using the Multidimensional Scale of Perceived Social Support.

Results: Allergic patients aged less than 40 years and women who were allergic had higher scores in the "Perceived Family Support Subscale" (PFSS) than patients with NAR. We also found increased scores of PFSS, special and social support total scores in male patients with NAR than in female patients with NAR.

Conclusion: Although patients with AR and NAR have similar symptoms, our results show that patients who are allergic have increased social ability. These results can explain which allergic patients have high histamine. In accordance with our results, we found that patients who were depressive and/or anxious had social introversion, and increased histamine in the brain reduced social introversion, as well as depressive and anxiety symptoms.

Keywords: Allergic rhinitis; Social support; Family support; Skin prick test; Multidimensional scale of perceived social support

Introduction

Rhinitis is defined as an inflammation of the nasal mucosa. A high number of patients experience Allergic Rhinitis (AR) between the ages of 20-40 years [1,2]. It has clinical symptoms such as excessive mucus production, watery eyes, congestion, paroxysmal sneezing, and nasal and ocular pruritus. AR is considered a systemic disease and may be associated with constitutional symptoms such as fatigue, malaise, and headache. The most common diagnostic test for AR is the Skin Prick Test (SPT) [3]. The diagnosis of Non-Allergic Rhinitis (NAR) is made with no determining allergic or IgE-mediated causes. Acute viral infection is the most common cause of NAR. Less common chronic causes include vasomotor rhinitis, hormonal rhinitis, and NAR with eosinophilia syndrome. The epidemiology and diagnostic criteria of NAR are confusing [4]. Patients with NAR can have local production of IgE antibodies and are therefore considered allergic. This concept has been defined as "entopy" or "local AR" [5,6].

The symptoms of AR have negative effects on emotional, physical, and social functioning, and lead to concentration difficulties at home, school and work, in addition to reduced productivity. This may result in decreased health-related quality of life [7]. Although the symptoms of the patients with AR and NAR are similar, it was found that patients with NAR have higher depressive, fatigue, social introversion, and decreased life activity than patients with AR [4]. These differences may be related with some immune mediators such as histamine. The aim of this study was to investigate the relationship between social support and high histamine in patients with AR-NAR.

Materials and Methods

Patients with a pre-diagnosis of AR who had been followed up with an allergy test in the department of otorhinolaryngology were included into the study. The protocol for the research project was conducted in accordance with the principles of the Helsinki Declaration and approved by the Local Institutional Review Board and Ethics Committee. The files of 1700 patients who underwent an allergy test with a pre-diagnosis of AR were reviewed, and 131 files in which the Multidimensional Scale of Perceived Social Support (MSPSS) was completed were retrospectively analyzed.

The diagnosis of AR was made using the findings of physical and nasal endoscopic examinations and the results of the SPT. Runny and itchy nose, sneezing, nasal obstruction, presence of serous secretion in the nasal cavity, pale nasal mucosa, edema, and pale or purplish conchae were considered as AR. Patients were evaluated in regards of dermatologic signs such as urticaria, eruption, itching, and erythema. Pulmonary symptoms such as cough, wheezing and dyspnea, and ocular symptoms such as redness, itching, and edema were also questioned.

Instruments

Skin Prick test: Alyostal ST-IR (Stallergenes S.A., Antony

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Table 1: Demographic Variables.

		Allergic Rhinitis (n=90)	Non-allergic Rhinitis (n=41)
		n (%)	n (%)
Age	≤40	65 (72.2)	29 (70.7)
	>40	25 (27.8)	12 (29.3)
Gender	Female	70 (77.8)	22 (53.7)
	Male	20 (22.2)	19 (46.3)

Cedex,. France) standard allergen extracts were used for the SPT. Before the test, antihistaminic drugs were withdrawn for 10 days, antidepressants for 20 days, and H2 receptor blockers were withdrawn for 24 h. Allergen extracts were taken in standard doses in quick test applicators with 8 distinct edges were applied onto the skin after having cleaned the ventral part of the forearm with alcohol. The results were checked 15 min later. Histamine-HCl was used as positive control and isotonic NaCl was used as negative control. The validity criteria for the test were accepted as >3 mm for the positive control and <3 mm for the negative control. A skin reaction against the allergen with an induration of >3 mm in diameter was accepted as a positive reaction [8].

The most common 30 allergen extracts and positive and negative controls were applied using a total of 4 applicators onto the skin of the forearm for the SPT. Fifteen pollens, 6 food allergens, 3 animal epithelia, 3 fungal spores, 2 house dust mites, and 1 insect were used.

The SPT was not applied to patients who were under treatment for asthma, those who were suspected of having asthma, or patients being treated with beta-blocker drugs.

The Multidimensional Scale of Perceived Social Support (MSPSS): This scale is a short, practical scale that subjectively assesses the competence of social support. With the recommended subscale structure, the MSPSS scale contains a total of 12 questions about the support accepted from family, friends or specific persons. Each item is rated using a scale with seven intervals. Higher scores mean that the perceived social support is high [9]. The MSPSS is used to determine the perception of individuals' social support sufficiency. Factor analysis of MSPSS showed three subscales: family, friends, and significant others. The response format is based on a 7-point Likert scale ranging from 1 (very strongly disagree) to 7 (very strongly agree). Scores from individual items are averaged in each scale and the total scale. The range is 12-84. Cronbach's coefficient alpha ranged from 0.85 to 0.91 on individual and total scales. This scale was adapted into Turkish by Eker et al. (2001) showing good reliability and validity in Turkish samples [9]. The overall Cronbach alpha reliability of the scale was found as 0.83. Test-retest reliability for the total scale was 0.85, ranging from 0.72 to 0.85 on the subscales [10].

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences for Windows version 15.0 (SPSS Inc., Chicago, IL). After conducting factor analyses for the MSPSS, a correlation matrix was created to examine the correlations between variables and to determine which variables would be used as independent variables in the regression analyses. Student's t-test was used to assess relationships among the demographic variables and perceived social support scores. Two-way ANOVA and post-hoc analysis were used for comparisons between intergroup variables (sex, age, allergic and non-allergic groups). A p value of < 0.05 was accepted as statistically significant for all tests.

Results

The mean age of the patients was 33.2±12.3 years (range, 16-61 years); 92 (70.2%) were female and 39 (29.8%) were male. The mean age of the females was 32.3±11.7 years and mean age of the males was 35.3±13.5 years; there was no significant difference between the sexes ($p>0.05$). Of the 131 patients, 90 were diagnosed as having AR, and 41 as having NAR using SPT results. The distribution of patients with AR and NAR according to age and sex is shown in Table 1.

When Student's t-test was used to assess the patients who presented with symptoms of rhinitis, no significant difference was found between patients with positive and negative SPT results and sexes in terms of MSPSS and subscales ($p>0.05$) is shown in Table 2.

The MSPSS scores of patients with negative and positive SPT results are presented in Table 3. When the decades of patient's age with AR and NAR groups were compared, a significant difference was found between patients aged under and over 40 years in parameters of the MSPSS (Table 3). These results indicated that scores of Perceived Family Support Subscale (PFSS) of patients with AR aged under 40 years were significantly higher than those of patients with NAR aged under 40 years ($p=0.007$). Further, scores of PFSS ($p=0.005$) and social support total scores (SSTS) ($p=0.05$) were higher in patients with AR aged under 40 years than those of patients aged over 40 years in the AR group. In male patients with NAR, scores of SSTS, PFSS, and the special subscale were found statistically significantly higher than in females with NAR ($p=0.040$, $p=0.043$, and $p=0.043$, respectively). Moreover, scores of PFSS were significantly higher in female patients with AR than in female patients who were non-allergic ($p=0.013$).

Discussion

In this study, we examined the relationships between social ability and patients with AR-NAR in terms of high histamine. The results

Table 2: The Multidimensional Scale of Perceived Social Support results of groups.

	Sex			Prick test		
	Female (n=92) *Mean±SD*	Male (n=39) *Mean±SD*	*p**	Positive (n=90) *Mean±SD*	Negative (n=41) *Mean±SD*	*p**
Significant others	19.8±8.7	22.6±7.2	<0.08	20.5±8.3	20.7±8.6	<0.90
Family	22.6±7.1	22.6±7.4	<0.97	23.1±6.4	21.4±8.7	<0.20
Friends	19.5±8.1	20.1±7.9	<0.66	20.0±8.1	19.0±7.8	<0.50
SSTS†	62.1±20.5	65.2±18.1	<0.41	63.7±18.6	61.6±22.5	<0.57

*Student's t-test was performed. A p value of <0.05 was accepted statistically significant.
†SSTS: Social Support Total Score.

Table 3: Comparisons between the multidimensional scales of perceived social supports cores with age group, gender in allergic and non-allergic groups.

	Allergic group(AR)		Non-allergic group(NAR)					
	Female (n=70) Mean±SD	Male (n=20) Mean±SD	Female (n=22) Mean±SD	Male (n=19) Mean±SD	df	F	p	Sources of differences
Significantothers	20.2±8.6	21.6±7.1	18.3±9.1	23.6±7.3	1	1.57	<0.213	
Family	23.7±6.1	21.4±7.3	19.3±9.2	23.8±7.4	1	9.08	<0.003*	F†AR-FNAR, FNAR-M‡NAR
Friends	20.3±7.9	19.0±8.9	16.9±8.4	21.4±6.6	1	4.54	<0.035*	FNAR-MNAR
SSTS	64.1±18	62.2±17	55.7±24.3	68.5±18.5	1	5.27	<0.023*	FNAR-MNAR
	Allergic group		Non-allergic group					
	≤40 years(n=65) Mean±SD	>40years (n=25) Mean±SD	≤40 years(n=29) Mean±SD	>40years(n=12) Mean±SD	df	F	p	Sources of differences
Significantothers	20.9±8.1	9.5±8.7	20.1±9.1	22.3±6.3	1	0.83	<0.365	
Family	24.4±4.7	19.8±8.8	20.2±9.2	24.3±6.8	1	10.99	<0.001*	≤40AR-≤40NAR,≤40AR->40AR
Friends	20.9±7.7	17.6±8.7	18.7±8.3	19.6±7.0	1	2.07	<0.152	
SSTS§	66.1±16.7	57.3±21.8	59.5±24.7	66.8±15.5	1	4.60	<0.034*	≤40AR- >40AR

*A p value of <0.05 was accepted statistically significant.
†F: Female; ‡M: Male; §SSTS: Social support total score.

showed that young patients and women who were allergic had more family support than patients with NAR. Additionally, increased family support, special, and general social support were found in male than female patients with NAR. Although patients with AR and NAR had similar symptoms, family support was higher among patients who were allergic. These results may indicate that patients who are allergic have more affiliative or social behavior.

The psychiatric and social factors are important for the management of allergic diseases. Previous studies reported that patients who were allergic tended to have increased negative mood, social introversion, and anxiety than healthy controls [11]. Furthermore, Rondo´n et al. found that 64% of patients with NAR reported moderate-to-severe rhinitis affected their quality of life [12]. Few studies have investigated the relation between patients with AR and NAR. In accordance with our results, Ryden et al. reported that 53% of patients with NAR and 33% of those with AR said that their social life and family relationships were limited due to their symptoms [4]. The symptoms of patients with AR and NAR are similar before rhinitis attacks and related impairment of social ability [12]. This difference may be due to the allergic reactions.

Allergic rhinitis is an inflammatory disease related with type I hypersensitivity reaction. This IgE-mediated reaction induces mast cell degranulation and results in the development of an inflammation by release of histamine, leukotriene, prostaglandin, and platelet-activating factor [13], whereas it was explained that NAR is local inflammation and includes confuse reactions [6]. The most important difference between these two diseases seems to be the histamine mediator. A positive SPT shows higher histamine levels in patients with AR than in patients who are non-allergic [3].

This diversity can be related with high histamine or patients with productive histadelia. A high level of blood histamine is called histadelia. The sypmtoms of histadelia include high academic achievement, perfectionism, high self esteem, obsession and compulsion, less than average need for sleep, overstimulation with productivity, and frequent allergic reactions [14,15]. As a result, we speculate that high histamine is protective for patients with AR in terms of social ability and depression [14].

We found no information on the direct social effects of histamine; however, it was reported that there was a relationship between histamine and oxytocin mediators in the brain. Affiliative human behavior was associated with mediators such as oxytocin, vasopressin, and serotonin [16]. Serotonin can induce oxytocin neurons via 5-HT1A, 5-HT2A, and 5-HT2c receptors. The release of oxytocin is also regulated via histamine, glutamate, opioids, and dopamine [17]. Furthermore, histamine is also involved in the process of arousal-related systems including sex behaviors and anxiety [18]. These results show that histamine can have effects on social family bonding indirectly with oxytocin and the other social behaviors such as sex behaviors.

Previous studies reported that patients who were allergic were highly anxious and more sensitive to stress [19]. Anxiety disorders could be important in terms of a possible relationship with affiliative behavior towards family. The fact that some people have fewer social contacts than others may reflect attributes of temperament or personality that have negative emotions (e.g., anxiety, anger), or that hinder sociality, such as social anxiety or shyness. These two personality characteristics, negative affectivity and inhibited sociality, affect both quality of social support and social networks [20].

Brain histaminergic systems may be concerned with psychological state and memory processes [21,22]. Histamine receptors are classified in 4 subtypes; H1, H2, H3 and H4 [23]. The H3 receptor is a presynaptic auto-receptor that inhibits neurotransmitter release from histaminergic and non-histaminergic terminals, and reduces cell firing and histamine synthesis in histaminergic neurons [24].

Evidence supporting a role for the histaminergic system in social memory came from many studies that demonstrated that administration of histamine facilitated social memory in rats [25,26]. Social recognition includes memory retention in rats, in which an adult animal uses olfactory signs to remember a social interaction with a conspecific juvenile [27]. It is likely that the observed recovery of recognition memory with H3 receptor antagonists used in recent studies reports into improved social memory and cognition in patients [28,29,30]. Researchers showed that there was a relationship between impaired social memory and the reduction H3 receptors in

the hippocampal CA2 region (all 19). New H3R antagonists have been reported to have antidepressant-like effects and reduced anxiety-like behaviors in rats [31,32]. Further, it was found that mast cell-deficient mice had significant anxiety-like behaviors [33]. Histamine H3R antagonists can regulate the release of different neurotransmitters and have indicated both antidepressant and pro-cognitive effects in animal experiments [25,34]. Histamine regulates cognitive functions including motivation, arousal, learning and memory processes, and autonomic functions (sleep/wake cycle, thermoregulation, and food intake) [23]. Many of these processes are disrupted in depression, which is characterized by a lack of motivational drive, distractibility, deficit in episodic memory, insomnia or hypersomnia, reduced body weight or increased food intake. Impairment of histamine regulation can also cause social introversion [35]. These results support our hypothesis that high histamine increases sociability in human.

The results of this study showed that male patients with NAR had higher scores of PFSS, special subscale, and SSTS than female patients with NAR. This situation can be related with the fact that in the Turkish population men are more important for family, especially for their mothers, in terms of economic status, social position, and having the right to speak [36]. This result can also show that women with AR have relatively more social abilities than patients with NAR.

In the present study, it was also observed that scores of PFSS and SSTS were increased in patients with AR aged less than forty years than those aged over forty. Although there are no satisfactory data about this topic, these results may suggest that strong Turkish family ties weaken as age increases. In accordance with our results, it was shown that social support decreases as age increases [37]. Contrarily, it was reported that social support levels for older patients were higher than those for young patients, and scores of the family subscale were significantly higher with obstructive sleep apnea syndrome [38]. It was explained that AR is more frequent between the ages of 20-40 years [1]. This condition can be related with more active histamine in the mentioned age ranges. In a large population a Swiss study reported that allergen-specific Ig E and allergic illness decreased by 23% and 21% with every 10-year increase in age [39]. Furthermore, the prevalence of AR showed a significant descending pattern as 26.6%, 20.6%, and 15.6% at ages of 20-44 years, 45-64 years, and 65-84 years, respectively [40]. These results support why there is high PFSS score in young adults with AR. In accordance with our results, recent researchs reported that AR incidence increased in female patients who were allergic [41,42]. On the other hand, histamine could be higher in women than in men.

The limitations of the study are as follows: no evaluation of psychiatric illness and personality properties of patients AR and NAR were conducted, and the absence of the familial history of AR was not investigated.

Conclusions

Young patients who are allergic with increased social ability caused by AR have high histamine. Patients with depressive and/or anxiety had social introversion and studies reported that increased histamine in the brain reduced social introversion, as well as depressive and anxiety symptoms. We speculate that high histamine can positively affect the social behavior of patients with AR. Our argument will be supported by further studies, which should simultaneously evaluate blood histamine and oxythosine. More studies are needed to determine the effect of the brain histaminergic system on human social behavior.

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