



RESEARCH ARTICLE

EFFECTS OF ANTIDEPRESSANT ON SYMPTOMS AND QUALITY OF LIFE IN
PATIENTS WITH ALLERGIC RHINITIS

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ARTICLE INFO

Article History:

Received 23rd March, 2017
Received in revised form
17th April, 2017
Accepted 27th May, 2017
Published online 20th June, 2017

Key words:

Allergic rhinitis,
Antidepressants,
Escitalopam,
Rhinorrhea.

ABSTRACT

Allergic rhinitis is considered to be a major health problem that impairs quality of life. Insufficient response to treatment and declining quality of life illustrate the continuing need to find new treatment modalities for allergic rhinitis (AR). Escitalopram, a newer anti-depressants of SSRI class is one of the most favoured antidepressants for the patients of mood disorder. It is a S - enantiomer of citalopram so it lacks the antihistaminic properties. The present study aims to verify the relationship between allergic rhinitis and psychological stress aiming to improve treatment of patients with allergic rhinitis and thereby improve QOL. Patients with allergic rhinitis (166) were diagnosed then analyzed using the Kessler Psychological Distress Scale. Patients with allergic rhinitis and who were positive on the Kessler scale (122) were randomly divided equally into a control group which received levocetirizine and a study group which received levocetirizine and escitalopram. Nasal symptom assessment and QOL assessment were performed in all patients after treatment. Of the 166 patients with allergic rhinitis, 122 (73.5 %) were positive on the Kessler Psychological Distress Scale. There was a marked improvement in the study group compared with the control group as regards nasal symptoms with better QOL in the study group (6.93) compared with the control group (2.13). Psychological stress has a strong impact on persistent allergic rhinitis. When stress is controlled by a combined treatment of Escitalopram and levocetirizine, allergic rhinitis symptoms improved and a better QOL was obtained.

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Citation: Jaswant Singh Matta, Arpan Jain, Shiv Shankar Kaushik, Abdul Sajid Mansoori and Nikhil Soni, 2017. "Effects of antidepressant on symptoms and quality of life in patients with allergic rhinitis", *International Journal of Current Research*, 9, (06), 52186-52190.

INTRODUCTION

Allergic rhinitis is considered to be a major health problem, affecting up to 30 % of the adult population. Its prevalence is increasing and affecting the quality of life (QOL), especially in sleep and at work (Dykewicz and Hamilos, 2010; Bourdin *et al.*, 2009). Because the old classification of allergic rhinitis into seasonal and perennial does not adequately reflect the clinical course and its burden on QOL, a new allergic rhinitis classification has recently been introduced. According to its duration, it is either intermittent or persistent, and according to its severity, it is either mild or moderate/severe (Dykewicz and Hamilos, 2010; Bousquet *et al.*, 2008). There is a strong relationship between allergic rhinitis and specific psychiatric syndromes such as anxiety and mood disorders (Sansone and Sansone, 2011; Cuffel *et al.*, 1999) found that psychological stress was 1.7 times higher in patients with allergic rhinitis, while Patten and Williams (Patten and Williams, 2007)

mentioned that a higher rate of panic disorder and social phobia with major depression symptoms was present among patients with allergic rhinitis. The correlation between allergic rhinitis and psychological disorders may be the result of several factors such as the effects of either syndrome on immunity and immune-related illnesses (Postolache *et al.*, 2005) via the presence of cytokines (Dunn *et al.*, 2005); the physiological role of nasal obstruction and its detrimental effects on sleep, with subsequent negative effects on psychiatric symptoms (Fang *et al.*, 2010; Le'ger *et al.*, 2006); allergy-related disturbances in cognitive functioning and their subsequent effect on psychological well-being (Kremer *et al.*, 2002; Wilken *et al.*, 2012) or a possible shared genetic risk between allergies and depression (Wamboldt *et al.*, 2000). Levocetirizine (5 mg/day) is a potent histamine H1-receptor antagonist with proven efficacy as a therapeutic option in persistent allergic rhinitis (PAR) as early as the first week and which might improve QOL. The present study aims to verify the relationship between PAR and psychological stress aiming to improve treatment of patients with PAR and thereby improve QOL.

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MATERIALS AND METHODS

Design, Setting and Participants

A double randomized clinical trial was performed in the ENT Department, American International Institute of Medical Sciences, Udaipur, between April 2016 to August 2016. The study protocol was approved by the local ethics committee and written informed consent was obtained from all patients.

Patient eligibility and enrolment

Patients of both sexes older than 18 years of age and attending the ENT outpatient clinic and with persistent allergic rhinitis (more than 4 days/week and for more than 4 consecutive weeks) (Mullol *et al.*, 2015) were included in the study. Patients were excluded if they had significant co morbidities such as rhinitis medicamentosa, were receiving drugs known to induce nasal obstruction (e.g., beta blockers), or had previous turbinate or nasal surgery, hormonal therapy, occupational dust exposure, allergic asthma, negative skin prick test, nasal masses, or rhino sinusitis, or were pregnant or lactating.

Study plan

All patients provided a complete medical history and were subjected to assessment of allergic rhinitis symptoms using a scale of severity of nasal allergic rhinitis symptoms. Quality of life assessment was performed for all patients using a seven-point scale for severity of allergic rhinitis on sleep pattern at night, work performance, and social and/or recreational activities (Burckhardt and Anderson, 2013). Stress was analyzed using the Kessler Psychological Distress Scale to determine the effect of stress on severity of allergic rhinitis (10 items representing five psychological distress traits were assessed with a five-point scale) (Anderson *et al.*, 2013). All patients underwent a complete ENT and nasal endoscopic examinations, a psychological examination by an expert psychologist, skin prick test and nasal and paranasal sinus CT scan (if needed). All patients were required to complete a questionnaire assessing their subjective nasal symptoms at day zero and 30 days following initiation of treatment using a visual analogue scale (VAS), with 0 indicating no symptoms and 10 indicating severe and/or constant symptoms.

Randomization

Patients with PAR were divided into two groups, either positive or negative according to the results on the Kessler Psychological Distress Scale. The negative group received levocetirizine (5 mg/day) (Mullol *et al.*, 2005), whereas the positive group was randomly divided equally into two groups: a study group and a control group using a blocked randomization scheme by computer generated random numbers. The control group received levocetirizine (5 mg/day) (Mullol *et al.*, 2005) for 30 days and the study group received levocetirizine (5 mg/day), escitalopram (10 mg/day) (Erkul and Cingi, 2012). Objective and outcome measurement assessment The objective was to verify clinically the relationship between allergic rhinitis and psychological stress aiming to improve the treatment of patients and thereby quality of life (QOL) outcome. The primary outcome was the effect of treatment on disease-specific quality of life. All patients were required to complete another questionnaire assessing their nasal symptoms 30 days after treatment initiation using the same VAS

questionnaire previously mentioned which also recorded any side effects that had occurred. Data collection, allocation concealment and blinding at study enrolment (day 0), each participant underwent a brief interview with the physician to complete a questionnaire, and provide demographic and disease-related information. Outcomes were assessed by another interview which was conducted at the end of treatment.

Statistical analysis: Data collected were processed using SPSS version 15.

Ethical considerations: Written informed consent was obtained from all patients. The local ethics committee approved the study.

RESULTS AND ANALYSIS

In the present study, 166 patients were included who fulfilled the criteria of PAR, with a mean age of 41.2 years and made up of 96 females (57.8 %) and 70 males (42.2 %). The main symptoms were sneezing in 164 patients (98.8 %), itchy nose in 156 patients (93.9 %), nasal obstruction in 145 patients (87.3 %) and watery rhinorrhea in 131 patients (78.9 %). The main finding during nasal examination was pale, congested, bluish mucosa in 147 patients (88.5 %). The skin prick test showed that 23 patients (13.8 %) were positive to one allergen (monosensitized), whereas the remaining patients were polysensitized. The most common allergens found to be positive were: 'House Dust' in 76 patients (45.8 %) followed by 'Pollens' in 68 patients (40.9 %) and finally 'Molds' in 22 patients (13.3 %). According to the Kessler Psychological Distress Scale: 122 patients (73.5 %) were positive with a mean total perceived stress score of 17.31 ± 6.06 , whereas 44 patients (26.5 %) were negative with a mean total perceived stress score of 8.22 ± 4.1 . The difference was statistically significant ($p = 0.001$; Tables 1, 2). Patients negative on the Kessler Psychological Distress Scale received levocetirizine (5 mg/day) for 30 days. The mean intensity of nasal symptoms according to the VAS was assessed before and after treatment. This showed a statistically significant improvement after treatment (Table 3).

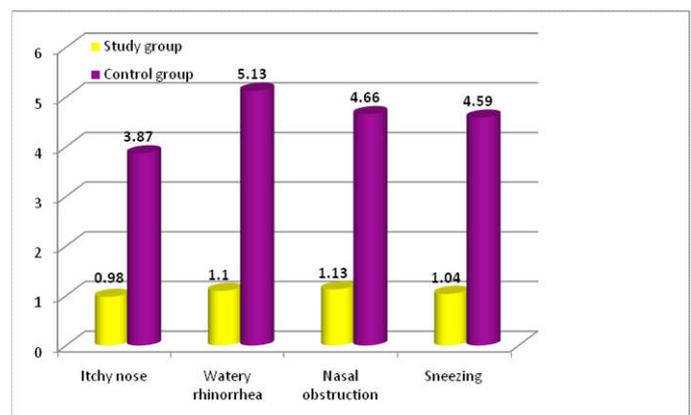


Fig. 1. Mean degree of different nasal symptoms after treatment in both groups who were positive on the Kessler Psychological Distress Scale

Patients positive on the Kessler Psychological Distress Scale were divided randomly and equally into two groups. The control group ($n = 61$) received levocetirizine (5 mg/day) for 30 days and the study group ($n = 61$) received levocetirizine (5 mg/day) and escitalopram (10 mg/day) for the same period.

Table 1. Mean scores of perceived stress symptoms

	Positive group (n = 122)		Negative group n= 44		t test	p value
	Mean	SD	Mean	SD		
Upset	1.71	0.88	1.02	0.72	2.112	0.001
Compulsive behaviors	1.67	0.64	1.01	0.65	2.636	0.0017
Nervousness	1.91	0.78	1.01	0.14	2.822	0.005
Personal problems	1.92	0.81	1.02	0.58	2.901	0.005
Loneliness	1.74	0.11	0.92	0.39	2.012	0.022
Not coping	1.77	0.21	0.14	0.47	2.498	0.006
Irritation	1.61	0.67	0.38	0.51	2.694	0.005
Difficulty concentrating	1.98	0.71	0.79	0.11	4.228	0.0001
Angered	1.65	0.59	0.98	0.27	4.401	0.0001
Difficulties	1.35	0.66	0.95	0.26	3.853	0.0001
Total perceived stress	17.31	6.06	8.22	4.1	3.096	0.003

Significant , p <0.05, Highly significant , p < 0.01

Table 2. Mean scores with Kessler Psychological Distress Scale

	Positive group (n = 122)		Negative group (n = 44)		t test	p value
	Mean	SD	Mean	SD		
Trait: anxious	4.96	2.65	3.11	0.02	4.11	0.0001
Neuroticism	3.84	1.84	2.06	0.06	4.12	0.0001
Not coping	3.77	0.16	2.11	0.43	3.92	0.0001
Uncontrollability	3.65	1.05	1.02	0.09	4.81	0.0001
Challenge difficulty	3.59	1.29	2.01	0.17	4.39	0.0001

Highly significant , p < 0.01

Table 3. Mean degree of different allergic nasal symptoms before and after treatment in patients who were negative to the Kessler Psychological Distress Scale

	Before treatment		After treatment		t test	P value
	Mean	SD	Mean	SD		
Sneezing	9.22	1.23	4.66	1.51	2.19	0.05
Nasal obstruction	8.11	1.69	4.49	1.34	2.82	0.037
Watery rhinorrhea	8.96	0.88	5.09	1.09	2.37	0.022
Itchy nose	7.98	1.04	3.76	1.04	2.02	0.019

Insignificant p < 0.05

Table 4. Mean degree of different allergic nasal symptoms before treatment in both groups who were positive on the Kessler Psychological Distress Scale

	Control group (n = 61)		Study group (n = 61)		t test	P value
	Mean	SD	Mean	SD		
Sneezing	9.06	1.89	9.11	1.93	0.16	0.931
Nasal obstruction	8.21	2.01	8.09	1.07	1.09	0.621
Watery rhinorrhea	8.45	1.55	8.37	1.43	0.43	0.594
Itchy nose	7.91	2.08	7.96	1.26	0.67	0.501

Insignificant p > 0.05

Table 5. Mean degree of different allergic nasal symptoms after treatment in both groups who were positive on the Kessler Psychological Distress Scale

	Control group (n = 61)		Study group (n = 61)		t test	P value
	Mean	SD	Mean	SD		
Sneezing	4.59	1.36	1.04	0.92	4.14	0.0001
Nasal obstruction	4.66	1.73	1.13	1.02	4.36	0.0001
Watery rhinorrhea	5.13	1.82	1.1	0.59	6.95	0.0001
Itchy nose	3.87	1.72	0.98	0.17	7.01	0.0001

Highly significant p < 0.01

The mean intensity of nasal symptoms according to VAS before treatment among the control group and study group were very similar with no statistically significant difference between the groups (Table 4). Thirty days after starting the treatment regimen, the mean intensity of nasal symptoms according to VAS among the control group and study group were compared. There was a marked improvement in nasal symptoms in the study group compared with the control group and the difference was statistically significant (Table 5; Fig. 1). Quality of life scale was calculated and assessed at the end of treatment in both groups. There was a better QOL in the study

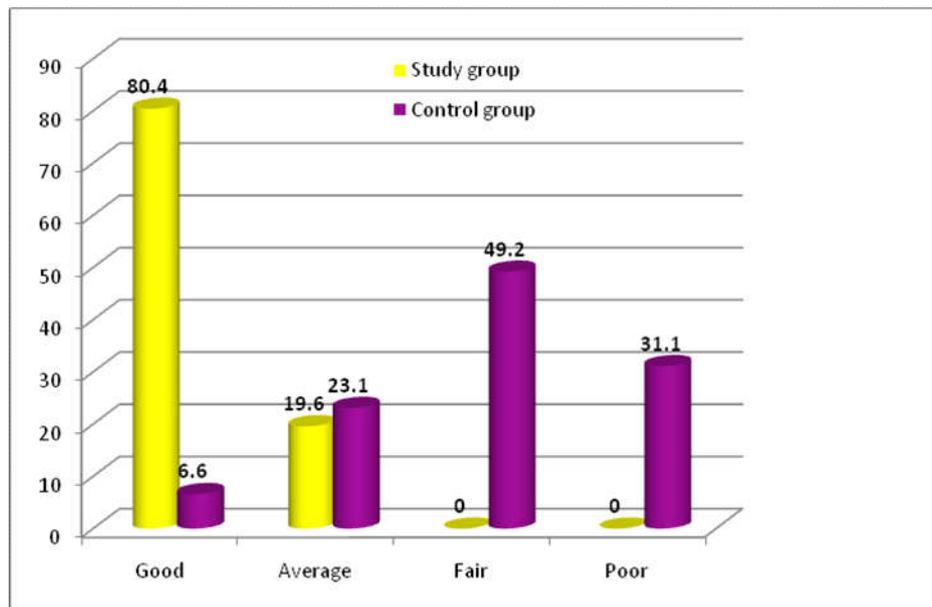
group (6.93) compared with the control group (2.13), and the difference was statistically significant (Table 6). In the study group, 80.4 % reported a good quality of life scale score compared to 6.6 % in the control group, and the difference was statistically significant (Table 7; Fig. 2). An oral dose of 10 mg/day of methylprednisolone for a duration of 5 days was given to 5 patients (11.3 %) of the group who were negative according to the Kessler Psychological Distress Scale while the same dose was given to 6 patients (9.8 %) of both the study and the control groups who showed positive evaluation using the same scale.

Table 6. Mean scores for quality of life scale after treatment in both groups who were positive on the Kessler Psychological Distress Scale

	Control group (n = 61)		Study group (n = 61)		t test	P value
	Mean	SD	Mean	SD		
Mean QOL	2.13	1.25	6.93	0.73	16.61	0.0001
Highly significant, $p < 0.01$						

Table 7. Quality of life scale assessment after treatment in both groups who were positive on the Kessler Psychological Distress Scale

	Control group (n = 61)		Study group (n = 61)		T test	P value
	n	%	n	%		
Poor	19	31.1	0	0	$X^2 = 3.12$	0.0001
Fair	30	49.2	0	0		
Average	8	13.1	12	19.6		
Good	4	6.6	49	80.4		

**Fig. 2. Quality of life scale assessment after treatment in both groups who were positive on the Kessler Psychological Distress Scale**

DISCUSSION

Allergic rhinitis is considered to be a common disease that significantly affects a patient's QOL. The traditional treatment is not always effective or tolerated (Small and Kim, 2011). PAR is the sixth most prevalent chronic condition in the world, and its prevalence has been increasing in the last few decades. If ignored, it can be complicated by chronic rhinosinusitis, secretory otitis media, nasal polyposis, or development of bronchial asthma leading to a negative impact on quality of life (Woods and Craig, 2006). Allergen avoidance is a difficult step in the treatment of allergic rhinitis because most patients are usually sensitized to many allergens (Mullol *et al.*, 2005). Effective treatment of patients with PAR must control their symptoms and improve their quality of life (Canonica *et al.*, 2006). In the present study, 73.5 % of patients with PAR proved to be positive on the Kessler Psychological Distress Scale indicating the close association between PAR and psychological stress. This was confirmed by Postolache *et al.* (Postolache *et al.*, 1968) who found a strong relationship between changes in allergy symptom scores and changes in depression scores leading to greater negative recurrent mood disorders in patients with atopy and allergic rhinitis. Many authors have investigated the mechanism of psychological stress producing persistent allergic rhinitis suggesting that

neuropeptides and hormones are released resulting in immune-mediated and neurogenic inflammatory processes with deregulation of normal haemostatic neural, endocrine systems leading to an increase in expression of disease symptoms (Wright and Cohen, 2005; Marshall and Roy, 2007). The difference in nasal symptom scores between our study group and the control group after treatment was statistically significant as shown in Tables 4 and 5, and Fig. 1. This shows that routine treatment of PAR should be revised to include antidepressants in certain cases. There was a marked improvement in QOL scale in the study group (6.93) compared with the control group (2.13) at the end of the treatment period which was statistically significant (Table 6). This supports the approach of combined therapy as in our study group rather than single therapy as in the control group. In addition, a good quality of life was reported in 80.4 % of the study group compared to only 6.6 % in the control group, and the difference was statistically significant (Table 7). Impaired QOL in patients with PAR is not only the result of typical nasal symptoms but also results from the activity of mediators such as histamine, leukotrienes (C4 and D4), interleukins (IL-1b, IL-4, IL-5 and IL-13), prostaglandin D2, substance P and bradykinin (Krouse *et al.*, 2012). The great burden associated with persistent allergic rhinitis goes beyond impairment of social and physical functioning; this component is rarely recognized or considered when treatment is usually prescribed

as it can be a possible causal factor of co morbidities such as asthma and sinusitis (Schoenwetter *et al.*, 2004). The positive effects of escitalopram on posttreatment quality of life in the Beck-positive patient group were a predictable outcome. Otolaryngologists should pay more attention to the moods of their patients with AR while they evaluate treatment during clinical follow-up visits (Erkul and Cingi, 2012). Escitalopram is composed of pure active S-enantiomer of citalopram. It removes antihistaminic properties and there are no higher dose restrictions to avoid QTc-prolongation. We did not aim to suggest a specific new treatment regimen for persistent allergic rhinitis, but our raw data showed the benefit of administering an antidepressant in resistant cases of PAR. Finally, we wanted to indicate why some patients with PAR may not respond to traditional anti-allergic treatment, as psychosocial stresses could be the underlying aetiological factor. In conclusion, psychological stress has a major impact on persistent allergic rhinitis, and when it is controlled with escitalopram and levocetirizine in a combined treatment, allergic rhinitis symptoms improved and a better QOL was obtained.

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