Desipramine plus levocetirizine as a treatment for persistent allergic rhinitis

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Received 01 January 2016
Accepted 16 February 2016

Pan Arab Journal of Rhinology
2016, 06:22–26

Background
Persistent allergic rhinitis has significant effects on the quality of life (QOL), especially on sleep and work performance, and is associated with specific psychiatric syndromes.
Aim
The aim of the present study was to verify the efficacy of combined desipramine and levocetirizine in the treatment of psychological stress related to persistent allergic rhinitis, and to thereby improve the QOL of the patient.
Patients and methods
A total of 132 psychologically stressed persistent allergic rhinitis patients (positive Kessler Psychological Distress Scale scores ≥12) were randomly divided into two groups: the control group, which received levocetirizine, and the study group, which received levocetirizine plus desipramine. QOL for all patients was assessed by using a seven-point scale after the treatment period.
Results
There was a highly statistically significant better QOL in the study group (6.79) compared with the control group (2.21) (*t*-test=15.17 and $P = 0.0001$).
Conclusion
Desipramine and levocetirizine have a better effect on the QOL outcomes in the treatment of patients with persistent allergic rhinitis, and having psychological stress disorders.
Level of evidence: 3b.

Keywords:
allergic, desipramine, levocetirizine, psychological stress, quality of life, rhinitis

Pan Arab J Rhinol 06:22–26

Introduction

Persistent allergic rhinitis has a significant effect on quality of life (QOL), especially on sleep and work performance [1].

Allergic rhinitis classification actually reflects the clinical course with its burden on QOL into: intermittent (total duration <4 weeks) or persistent (symptoms continue throughout the whole year); according to severity, it is classified as follows: either mild (patients are generally able to sleep normally and perform normal activities) or moderate/severe (significantly affects sleep and daily activities) [2].

A strong relationship between persistent allergic rhinitis and specific psychiatric syndromes has been illustrated in many studies [3].

In their studies, Katotomichelakis *et al.* [4] mentioned a 1.7 times higher psychological stress symptoms in persistent allergic rhinitis patients; in addition, Garg and Silverberg [5] found a higher rate of panic disorder with major depression symptoms among the same population.

Many theories demonstrate these relationship as either immune-related illnesses [6] through the presence of cytokines [7]; sleep disruption with subsequently negative effects on psychiatric symptoms [8]; or genetic risk between both allergies and depression [9].

Levocetirizine (5 mg/day) is a potent H_1-receptor antagonist with proven efficacy as a therapeutic option in persistent allergic rhinitis improving the nasal symptoms, and thereby improves significantly the impaired QOL [10].

Desipramine is a tricyclic antidepressant, beside its indication for the treatment of depression and improve patients mood; it has antihistaminic properties, affecting histamine H_1 receptors by regulating Treg and Th17 cells [11,12].

The present study aimed to verify the efficacy of combined dose of desipramine and levocetirizine in

the treatment of psychological stress-persistent allergic rhinitis and thereby improve QOL outcomes.

Patients and methods

Design, setting and participants

A double-blinded, randomized clinical trial was conducted in the Otolaryngology Department, Suez Canal University Hospital (Ismailia, Egypt), from December 2008 to June 2011. The study protocol was approved by the local ethics committee, and written informed consent was obtained from all patients.

Inclusion and exclusion criteria

A total of 132 psychologically stressed persistent allergic rhinitis patients (longer than 4 days/week and for >4 consecutive weeks) [13] and positive to Kessler Psychological Distress Scale scores of greater than or equal to 12 were included in our study. Kessler Psychological Distress Scale scores demonstrate the responses to the K5 questions with a minimum possible score of 5 and a maximum possible score of 25. Low scores, 5–11, indicate negative psychological distress and high scores, 12–25, indicate positive psychological distress [14].

In contrast, patients negative to Kessler Psychological Distress Scale scores (5–11), with rhinitis medicamentosa, receiving drugs known to induce nasal obstruction (e.g. β-blockers), and with previous nasal surgery, hormonal therapy, pregnancy, lactation, occupational dust exposure, nasal polyposis, or rhinosinusitis, were excluded from the study population.

Study plane

All patients were subjected to complete history taking including allergic rhinitis symptoms assessment using the visual analogue scale (VAS), which assesses subjective symptoms, with 0 indicating no symptoms and10 indicating severe and/or constant symptoms.

A complete ENT examination, with rigid nasal endoscopic examinations (Hopkins II Endoscope; Karl Storz, Tuttlingen, Germany), paranasal sinus computed tomography scan, and skin prick test, was carried out.

Psychological evaluation of Kessler Psychological Distress Scale scores demonstrates the responses to the 25 questions, with a minimum possible score of 5 and a maximum possible score of 25. Low scores, 5–11, indicate negative psychological distress (who were excluded from the study) and high scores, 12–25, indicate positive psychological distress (who were included in the study) [14].

Randomization

Patients were randomly divided into the study and the control group using a blocked randomization scheme by using computer-generated random numbers.

The control group received levocetirizine (5 mg/day) [10] for 30 days and the study group received levocetirizine (5 mg/day) plus desipramine (25 mg/day) for the same period of time [12].

Outcome measurement assessment

The primary outcome was the effect of treatment on QOL after 30 days from treatment initiation using a seven-point scale for assessing severity of allergic rhinitis on sleep pattern at night, work performance, and social and/or recreational activities [15].

Statistical analysis

Data collected were processed using SPSS (version 23; SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as means±SD, whereas qualitative data were expressed as numbers and percentages. Student's *t*-test was used to compare the significance of difference for quantitative variables that followed a normal distribution.

Ethical considerations

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

Results

Out of a total of 132 psychological stressed persistent allergic rhinitis patients, with a mean age of 41.2 ± 6.8 years [81 (61.4%) women and 51 (38.6%) men], included in the study, 113 (85.6%) patients showed the main symptoms of sneezing, followed by itchy nose in 95 (71.9%) patients, nasal obstruction in 82 (62.1%), patients and watery rhinorrhea in 79 (59.8%) patients, whereas the main finding during nasal examination was pale, congested, bluish mucosa in 115 (87.1%) patients.

Patients were divided randomly into two equal groups: the control group (n = 66) received levocetirizine (5 mg/day) for 30 days; and the study group (n = 66) received levocetirizine (5 mg/day) plus desipramine (25 mg/day) for the same period of time.

The mean intensity of nasal symptoms according to VAS before treatment in the control group was sneezing 9.35, whereas it was 9.09 in the study group: nasal obstruction was 9.13 and 8.98, respectively; watery rhinorrhea was 7.97 and 8.06, respectively; and, finally, itchy nose was 7.43 and 7.81, respectively, without any statistically significance difference between the two groups (Table 1).

After 30 days, the mean intensity of nasal symptoms according to VAS in the control group was sneezing 3.91, whereas it was 1.08 in the study group, nasal obstruction was 4.26 and 1.21, respectively; watery rhinorrhea was 4.92 and 1.01, respectively, and itchy nose was 3.24 and 1.57, respectively. There was highly statistically significant improvement in the allergic nasal symptoms of the study group (receiving levocetirizine plus desipramine) compared with the control group (only levocetirizine) (Table 2).

QOL scale was calculated, and the assessment at the end of the treatment revealed a highly significantly better life quality for the study group (6.79) compared with the control group (2.21) (*t*-test=15.17 and *P* = 0.0001), as according to the QOL scale, 1–2 means poor QOL, 3–4 fair QOL, 5–6 average QOL, and seven means good QOL. Overall, 87.9% patients in the study group reported a good QOL scale score compared with only 4.5% in the control group, with a high statistically significant difference (Table 3 and Fig. 1).

Table 1 Mean degree of different allergic nasal symptoms before treatment in both groups, for those who were positive on the Kessler Psychological Distress Scale scores

	Control group (*n*=66)		Study group (*n*=66)		*t*-test	*P* value
	Mean	SD	Mean	SD		
Sneezing	9.35	1.14	9.09	1.82	0.46	0.927
Nasal obstruction	9.13	1.97	8.98	1.81	1.05	0.672
Watery rhinorrhea	7.97	1.72	8.06	1.47	0.93	0.591
Itchy nose	7.43	1.86	7.81	1.61	0.71	0.583

Insignificant *P*>0.05

Table 2 Mean degree of different allergic nasal symptoms after treatment in both groups, for those who were positive on the Kessler Psychological Distress Scale scores

	Control group (*n*=66)		Study group (*n*=66)		*t*-test	*P* value
	Mean	SD	Mean	SD		
Sneezing	3.91	1.14	1.08	0.82	4.04	0.0001**
Nasal obstruction	4.26	1.34	1.21	1.14	4.26	0.0001**
Watery rhinorrhea	4.92	1.09	1.01	1.09	6.85	0.0001**
Itchy nose	3.24	1.71	1.57	1.01	7.12	0.0001**

**Highly significant, *P*<0.01

Table 3 Quality of life scale assessment after treatment in both groups, for those who were positive on the Kessler Psychological Distress Scale scores

	Control group (*n*=66) (*n* (%))	Study group (*n*=66) (*n* (%))	*t*-test	*P* value
Poor	24 (36.4)	0 (0)	χ^2=3.27	0.0001**
Fair	32 (48.5)	0 (0)		
Average	7 (10.6)	8 (12.1)		
Good	3 (4.5)	58 (87.9)		

**Significant

Discussion

Persistent allergic rhinitis is a common disease with significant burden on the QOL. Many treatment options directed at symptomatic relief are available, but sometimes the traditional treatment is not effective to address all aspects of the disease burden [16].

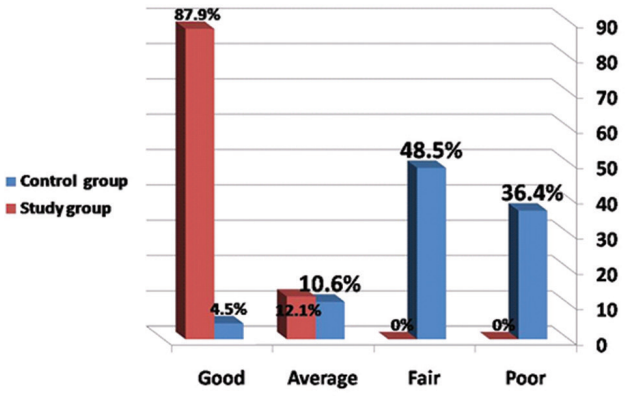
Allergic rhinitis is the sixth most prevalent chronic condition in the world, with a high risk for developing chronic rhinosinusitis, otitis media with effusion, nasal polyposis, and bronchial hyperactivity, which usually had a great burden on QOL [17].

Many authors have investigated the mechanism of psychological stress producing persistent allergic rhinitis, suggesting that neuropeptides and hormones released result in immune-mediated and neurogenic inflammatory processes, with deregulation of normal haemostatic neural, endocrine systems leading to an increase in the expression of the disease symptoms [18–21].

In their study, Tomljenovic *et al.* [22] mentioned a strong relationship between changes in allergy symptom scores and changes in depression scores leading to a larger negative recurrent mood disorders in patients with atopy and allergic rhinitis.

Lind *et al.* [23] mentioned in their study that there is an associated relationship between the psychological

Figure 1



Quality of life scale assessment after treatment in both groups, for participants who were positive on the Kessler Psychological Distress Scale scores.

and immunological state in patients with atopy as they are more depressive, and complain of anxiety, with psychosomatic symptoms.

The control group received levocetirizine for 30 days while the study group received levocetirizine plus desipramine for the same period of time. There was marked highly statistically significantly allergic nasal symptoms improvement in the study group.

Allergic rhinitis associated with depression is recognized with recommendation to treat the depression, but fortunately, desipramine has double action; beside being a tricyclic antidepressant agent, it is also attenuating to the allergic nasal symptoms by antiallergic action, as found by Zhang *et al*. [12] in a study on allergic rhinitis mice.

Rao *et al.* [11] recognized suppression of cutaneous histamine-induced wheal-and-flare with desipramine.

In addition, there was a highly significantly better life quality in the study group (6.79) compared with the control group (2.21) (t-test=15.17 and P = 0.0001) at the end of the treatment period.

Patients with persistent allergic rhinitis usually from poor QOL scores. Such poor QOL probably results from a number of symptoms like difficulty getting to sleep, waking up during the night, fatigue, mood changes irritability, memory deficits, and lack of a good night's sleep as a result of their persistent nasal symptoms. That result in forming a burden their daily life, which limits them from doing well in their work [24].

Good QOL was reported in 87.9% patients in the study group, whereas in the control group it was only in 4.5%. Meanwhile, poor QOL was not reported in the study group; it was reported by 36.4% participants in the control group.

It should be noted that the concept of QOL differs between individuals depending on the degree of expectations and perceptions of the disease. Accordingly, it varies principally depending on the standards of the individual regards 'personal well-being', perception of the surrounding world, and expectations regarding treatment [25].

The QOL of allergic rhinitis patients was often impaired, not only due to the typical symptoms of the disease (sneezing, pruritus, nasal obstruction, and rhinorrhea) but also due to the activity of the mediators such as histamine, leukotrienes (C4 and D4), interleukins (ILs) (IL-1β, IL-4, IL-5 and IL-13), prostaglandin D2, substance P, and bradykinin, which participate in its pathophysiology and can disrupt sleep [26].

Unfortunately, a great burden associated with persistent allergic rhinitis goes beyond the impairment of social and physical functioning; this component is rarely recognized or valued when the treatment is usually prescribed with a possible causal factor of comorbidities such as asthma and sinusitis [27].

We did not aim to point to a specific new treatment regimen for persistent allergic rhinitis, but our raw data showed better results for the study group, which received desipramine plus levocetirizine, compared with the control group, which received levocetirizine alone.

Finally, we want to point to the fact that persistent allergic rhinitis patients do not respond to traditional antiallergic treatment; psychosocial stresses could be a strong etiological factor. If properly treated, the patients' QOL could be improved.

Conclusion

A combination of desipramine plus levocetirizine has a better QOL outcomes in the treatment of patients with persistent allergic rhinitis having psychosocial stresses disorders.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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