

The effect of fibromyalgia syndrome to nasal mucociliary function in females

Isil Karaer Cakmak¹, Tuba Tulay Koca²

¹Malatya Research and Training Hospital, Clinic of Otorhinolaryngology, Malatya, Turkey

²Sutcu Imam University, Faculty of Medicine, Department of Physical Therapy and Rehabilitation, Kahramanmaraş, Turkey

Copyright © 2019 by authors and Annals of Medical Research Publishing Inc.

Abstract

Aim: Fibromyalgia syndrome (FM) is soft tissue rheumatism characterized by chronic widespread musculoskeletal pain. Central sensitization-related neuroaudiological symptoms are frequently seen in patients with FM. The aim of this study was to investigate the duration of nasal mucociliary clearance in FM patients and its relation with pain.

Material and Methods: A prospective case-control study was carried out in Otorhinolaryngology Clinic. Forty four (N=44) females were enrolled in the study. Twenty two (22) FM patients with age ($p=0.5$) and body mass index (BMI) ($p=0.072$) matched healthy controls were included in the study. The FM diagnosis has been determined by clinical examination according to the American College of Rheumatology (ACR) 2010 criteria. All study participants underwent measurements of nasal mucociliary clearance duration by the same individual.

Results: The mean age was 38.7 ± 1.8 years in FM group, while it was 37.05 ± 1.8 years in control. The mean duration of nasal mucociliary clearance were 8.06 ± 0.5 minutes in FM group, and 5.86 ± 0.4 minutes in control. The duration of nasal mucociliary clearance was longer in FM patients than controls ($p=0.0005$). The duration of mucociliary clearance was found positively correlated with visual analog scale (VAS) score ($r=0.423$; $p=0.005$).

Conclusion: There was a significant prolonged nasal mucociliary clearance duration in patients with FM and positively correlated with pain score. Clinically, women with FM should be followed up for possible adverse effects of prolonged mucociliary clearance duration such as sinonasal and middle ear infections.

Keywords: Fibromyalgia Syndrome; Chronic Pain; Mucociliary Function.

INTRODUCTION

Sinus health in humans is maintained by means of the mucociliary clearance mechanism. This is the main system for the nonspecific defense against the constant organic and inorganic contamination transported by air. It works by trapping particules and microorganisms in the mucus and then transporting the mucous film to the pharynx, where it is eliminated via coughing or swallowing (1). However, the change of the mucosal ultrastructural elements and the delay in the mucociliary clearance of the nasal epithelium, cause chronic rhinosinusitis and respiratory tract diseases (1,2).

The mucociliary clearance mechanism relies on the complex interaction between motile cilia, glandular secretions, and the anatomy of the sinuses and nasal environment (1). There is a general insight that physiological and hormonal changes associated with various conditions may influence rhinological functions

and disease. Several changes in the nasal mucosa during the menstrual cycle, pregnancy, oral contraceptive use, after menopause and nasal surgery, systemic diseases have been investigated in multiple studies (27).

Fibromyalgia syndrome (FM) is a chronic pain syndrome characterized by diffuse muscle pain, poor sleep and fatigue characterized by unknown etiology and limited treatment options (8). The common symptoms of FM include sleep disorders, affective disorders, chronic generalized pain, and fatigue. The pathophysiology of FM has not been elucidated yet, and no treatment is available for relieving all of the symptoms (8). The estimated prevalence of FM in the general population varies globally between approximately 2 and 11%, depending on the population (8,9). The prevalence is higher in women than men (9:1) increasing with age (10).

Neuroaudiologic complaints such as dizziness, tinnitus, hearing loss, vertigo are frequently seen in FM patients

Received: 01.10.2018 **Accepted:** 11.02.2019 **Available online:** 26.02.2019

Corresponding Author: Tuba Tulay Koca, Sutcu Imam University, Faculty of Medicine, Department of Physical Therapy and Rehabilitation, Kahramanmaraş, Turkey, **E-mail:** tuba_baglan@yahoo.com

correlated with disease severity. These symptoms are explained by central hypersensitivity, dysregulation of nervous system, which causes perception change. In a small number of studies, audiological complaints were not correlated with objective findings (11,12). The aim of this study was to investigate the duration of nasal mucociliary clearance in FM patients and its relation with pain.

MATERIAL and METHODS

Cases

A prospective case-control study was carried out in Otorhinolaryngology Clinic. Forty four (N=44) female were enrolled in the study. Twenty two (22) FM patients with age ($p=0.5$) and body mass index (BMI) ($p=0.072$) matched healthy controls were included in the study.

Fibromyalgia diagnosis and assesment

The FM diagnosis has been determined by clinical examination according to the ACR 2010 criteria, in which the patient must have pain in all of the body's four quadrants plus axial pain, and at least 11/18 predefined tender points, triggered by a pressure of a maximum of 4 kg/cm² (11,12). A visual analog scale (VAS: from 0 = no pain to 10 = the worst pain) was used to measure pain score.

Blood sampling

Sex hormones (morning) of patients; estrodiol (E2), follicule stimulating hormone (FSH) were recorded and measured by using a Centaur XP Immunoassay System (Siemens Healthcare GmbH). All participants were in premenopausal period.

Otorhinolaryngeal evaluation

The evaluation of the study involves taking a detailed history; ear, nose, and throat examinations; and nasal endoscopic evaluations done by the same trained individual. Subjects with a nasal pathology causing nasal obstruction, such as septum deviation, nasal polyposis, or concha bullosa; a history of allergy or asthma; upper respiratory tract infection during the previous 2 months; a history of nasal or paranasal operation; a history of any medication; a history of any systemic disease; and smokers were excluded from the study.

Saccharin test

The nasal mucociliary clearance duration was evaluated with the saccharin test. This is a simple, inexpensive, reproducible clinical test for determining abnormal mucociliary clearance (13). The patients were asked to blow their nose and not to consume any food or drink for 1 h before the test. A rest period of 30 minutes was allowed before the measurement. While the patient was sitting in an upright position, 1/4 of a saccharin tablet was placed at the front of the left inferior turbinate using a bayonet forceps. The patients were asked not to sneeze, sniff, or wipe their noses during the test. Until the time of experiencing a saccharin taste after the tablet placement, the patients were instructed to swallow at 30-seconds intervals and inform the investigator when they tasted saccharin. The time taken by the subjects from placement

of the tablet to the perception of the sweet taste was measured by a chronometer and recorded as minutes (14). The saccharin tests were performed by the same clinician at the Otorhinolaryngology Clinic, who was unaware of the subjects' status.

Statistical analysis

All analyses were conducted by using SPSS 15.0 (SPSS® for Windows 15.0, Chicago, USA). The normality of the distribution was assessed using the Kolmogorov-Smirnov test. Variables with a normal distribution were presented as the mean \pm standard deviation, and variables with a skewed distribution were presented as the median and interquartile range (IQR). The groups were compared with the Student t-test for parametric data and Mann-Whitney U test for nonparametric data. A p value less than 0.05 was considered statistically significant. The minimum number of subjects required in each group was determined to be 25 in order to make a significant difference between the two groups' average of 0.05 units. Type 1 error = 0.05, power of the test: 0.8. The study was approved by the Regional Committee for Ethics (protocol number: 176, 2018) in Medical Research and complied with Helsinki criteria.

RESULTS

In FM group, the mean age was 38.7 ± 1.8 years, while in control, it was 37.05 ± 1.8 years. There was no statistically significant difference regarding the age ($p=0.5$) and BMI ($p=0.072$) between the groups.

The mean nasal mucociliary clearance duration was 8.06 ± 0.5 minutes in FM group, and 5.86 ± 0.4 minutes in control. The demographic and laboratory data of the groups were shown at Table 1. The duration of nasal mucociliary clearance was longer in FM patients than controls ($p=0.0005$) (Figure 1). The duration of mucociliary clearance was found positively correlated with VAS score ($r=0.423$; $p=0.005$).

Table 1. The descriptive and analytic data of the study and control group

	FM (N=22) mean \pm std/ median, min-max	Control (N=22) mean \pm std/ median, min-max	P
Age (year)	38.7 ± 1.8	37.05 ± 1.8	0.5
BMI	28.1 ± 2.6	30.1 ± 3.4	0.072
Estradiol (E2) (pg/mL)*	21.8 (11.5-34)	16 (12-31)	0.048
FSH (mIU/mL)	68.6 (43.2-95.9)	52.2 (41.1-73.7)	0.064
Nasal mucociliary clearance duration (minutes)*	8.06 ± 0.5	5.86 ± 0.4	0.0005
VAS (0-10 cm)	7.1 ± 1.4	-	

Abbreviations: FM: Fibromyalgia; VAS: visual analog scale; BMI: body mass index; FSH: follicule stimulating hormone. * independent student t test+statistically significant difference. P<0.005

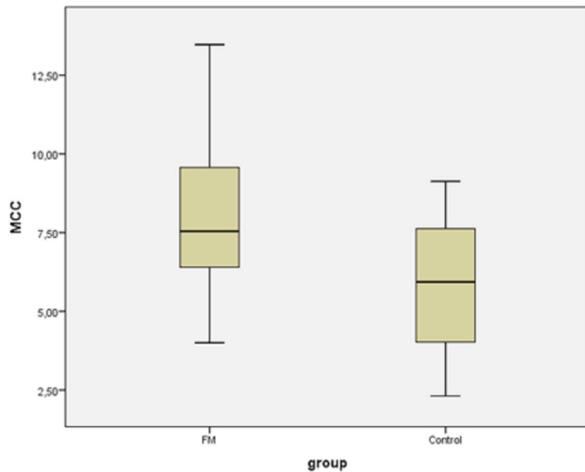


Figure 1. Boxplot of nasal mucociliary clearance (MCC) duration in the groups

DISCUSSION

In this study, we showed that women with FM has a prolonged mucociliary clearance duration in comparison with age and gender-matched healthy controls. Additionally the duration was positively correlated with VAS score. Accordingly, as the severity of the pain increases, the duration and the susceptibility to chronic infections increases.

FM is an entity with multiple concomitant disorders, rather than a single disorder. It is often accompanied by non-specific symptoms and comorbidities (15-17); such as memory and concentration problems (18), sleep disturbances, stomach ache, depressive symptoms and headache (18,19), and disorders like irritable bowel syndrome, chronic fatigue syndrome, interstitial cystitis and temporomandibular disorder (20,21). Multiple factors such as genetic factors, substance P and serotonin pathways, central sensitization, autonomous dysfunction, hypothalamic-pituitary-adrenal axis dysfunction, metabolic dysfunction, oxidative stress were found to be related to FM pathophysiology (15-21). The nervous system as well as the immune system use common signaling molecules for intra- and inter-system communications. Such signaling molecules are cytokines, neurotransmitters and neuroendocrine hormones, and their respective receptors (22).

Many neuroaudiological complaints, such as dizziness, tinnitus, hearing loss, and vertigo are frequently seen in patients with FM in correlation with the severity of the disease. These symptoms are explained by central hypersensitivity and dysregulation of the nervous system, which causes a change in perception. A small number of studies demonstrated that audiological complaints were not correlated with objective findings (23,24). These complaints develop due to an abnormal presentation of stimuli from internal or external circulation due to neural disintegration, events related to neural mediators, or systemic features of the disease (25). Gencer et al. found, the mean air conduction threshold low in FM patients at high frequencies (26). Gurbuzler et al. (27). investigated several

perceptual, acoustic and aerodynamic voice evaluation parameters in these patients. It is showed that FM impairs perceived voice quality either in patient self evaluated or in clinician evaluated rating scales. Furthermore, the results confirm that FM cause short maximum phonation time and low voice intensity (27). Soler et al. (28) observed that FM was one of the common comorbid disease in patients with chronic rhinosinusitis who underwent surgery. Patients with chronic rhinosinusitis and FM showed similar improvements in quality-of-life after endoscopic sinus surgery in comparison with healthy controls (28). Yilmaz et al. (29) assessed otoacoustic emission findings in FM. They found that although these patients generally have subjective symptoms related to ear, clinical or laboratory assessments, any objective finding related to these subjective symptoms were not found. The otologic functions seem to be spared in FM (29). Rosenhall et al. (30) showed that auditory brainstem response (ABR) was pathologic with 31% frequency in FM patients. The ABR findings indicate that a brainstem dysfunction might be present in some patients with FM. The results of the impedance audiometric tests were found generally normal in the patient group (30). The study by Doğan et al. (31) suggests the high possibility of coexistence of FM and allergic rhinitis. Neurogenic inflammation is seems to be the main common pathologic pathway of the both diseases.

The relationship between these two diseases can be explained by sympathetic and parasympathetic dysfunction. Parasympathetic reflexes and sneezing quickly clean the upper airways while protecting the lower airways. Parasympathetic dysfunction contributes to allergic, infectious and other nonallergic rhinitis and sinusitis. Sympathetic arterial vasoconstriction reduces mucosal blood flow, sinusoidal filling and mucosal thickness. Sympathetic tonus deficiency may lead to chronic, non-allergic rhinitis (32). Autonomic dysfunction known to be responsible for the etiopathogenesis of FM. The realization of autonomic dysfunction in FM has opened the possibility for therapeutic interventions. Much more research is needed to better define the role of autonomic dysfunction in the pathogenesis of FM (33,34).

In our study the negative effect of FM on mucociliary function can be explained by more than one mechanism; autonomous dysfunction, hypothalamic-pituitary-adrenal axis dysfunction, metabolic dysfunction, sympathetic hyperactivation, central sensitization, peripheral sensitization, and immunological pathways etc. It is not clear whether there is a relationship between these two diseases in terms of cause or concomitance.

It is important to keep in mind that the prolongation of the mucociliary clearance period in FM patients may predispose them to sinonasal infections.

There may be other reasons for susceptibility to sinonasal infections other than prolonged mucociliary duration in FM patients. We hope in near future we will obtain clearer information on complicated pathophysiology of FM in order to understand this relation.

Limitations of the study

The limitation of the study is small sample size. Another

limitation of the study is there is no data related with the physical examination for upper respiratory tract infection. Physical examination is required to establish a direct association between FM and chronic respiratory tract infections. We expect to find hormonal dysfunction in FM women. There was no difference between the two groups in terms of it.

The complexity of the etiopathogenesis of FM and the differences between patients cause difficulties in explaining the relationship of these diseases.

CONCLUSION

This study showed that women with FM have prolonged mucociliary clearance duration positively correlated with pain score. FM patients should be monitored for possible respiratory tract diseases such as sinonasal and middle ear infections. More detailed researches with a large number of patients are needed in order to reveal the relationship between two diseases.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports

Ethical approval: This work has been approved by the Institutional Review Board.

Isil Karaer Cakmak ORCID:0000-0002-1785-899X

Tuba Tulay Koca ORCID: 0000-0002-4596-858X

REFERENCES

- Huang HM, Cheng JJ, Liu CM, et al. Mucosal healing and mucociliary transport change after endoscopic sinus surgery in children with chronic maxillary sinusitis. *Int Jour Ped Otorhino* 2006;70:1361-7.
- Topozada H, Michaels L, Topozada M, et al. The human nasal mucosa in the menstrual cycle. *J Laryngol Otol* 1981;95:1237-47.
- Topozada H, Michaels L, Topozada M, et al. The human respiratory nasal mucosa in pregnancy. *J Laryngol Otol* 1982;96:613-26.
- Topozada H, Topozada M, El Gazzawi, et al. The human respiratory nasal mucosa in females using contraceptive pills. *J Laryngol Otol* 1984;98:43-51.
- Topozada H. The human nasal mucosa in the menopause. *J Laryngol Otol* 1988;102:314-8.
- Aroor R, Sunu Ali Z, Gangadhara Somayaji KS. Do nasal surgeries affect mucociliary clearance? *Indian J Otolaryngol Head Neck Surg* 2017;69:24-8.
- Ozbay I, Kucur C, Temizturk F, et al. Assessment of nasal mucociliary activity in patients with Behçet's disease. *J Laryngol Otol* 2016;130:348-51.
- Clauw DJ. Fibromyalgia: a clinical review. *JAMA* 2014;311:1547-55.
- Forseth KO, Gran JT. The prevalence of fibromyalgia among women aged 20-49 years in Arendal, Norway. *Scand J Rheumatol* 1992;21:74-8.
- Wolfe F, Brähler E, Hinz A, et al. Fibromyalgia prevalence, somatic symptom reporting, and the dimensionality of polysymptomatic distress: results from a survey of the general population. *Arthritis Care Res (Hoboken)* 2013;65:777-85.
- Bayazit YA, Gürsoy S, Ozer E, et al. Neurotologic manifestations of the fibromyalgia syndrome. *J Neurol Sci* 2002;196:77-80.
- Sawada F, Nomura Y, Goto F, et al. Relationship of physical distress to dizziness in patients with fibromyalgia. *Acta Otolaryngol* 2016;136:56-61.
- Stanley P, MacWilliam L, Greenstone M, et al. Efficacy of a saccharintest for screening to detect abnormal mucociliary clearance. *Br J Dis Chest* 1984;78:62-5.
- Eccles R. Physiology of the nose. In: Jones A, Phillips D, Hilgers F, editors. *Diseases of the Head and Neck, Nose and Throat*. London: Arnold 1998;675-6.
- Wessely S, Hotopf M. Is fibromyalgia a distinct clinical entity? Historical and epidemiological evidence. *Baillieres Best Pract Res Clin Rheumatol* 1999;13:427-36.
- Aaron LA, Burke MM, Buchwald D. Overlapping conditions among patients with chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder. *Arch Intern Med* 2000;160:221-7.
- Tomasdottir MO, Sigurdsson JA, Petursson H, et al. Self reported childhood difficulties, adult multimorbidity and allostatic load. a cross-sectional analysis of the norwegian HUNT study. *PLoS One* 2015;10:1371.
- Wolfe F, Clauw DJ, Fitzcharles MA, et al. The American college of rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res (Hoboken)* 2010;62:600-10.
- Ranzolin A, Duarte AL, Bredemeier M, et al. Evaluation of cytokines, oxidative stress markers and brain-derived neurotrophic factor in patients with fibromyalgia- A controlled cross-sectional study. *Cytokine* 2016;84:25-8.
- Clauw DJ. Fibromyalgia: an overview. *Am J Med* 2009;122:S3-13.
- Borchers AT, Gershwin ME. Fibromyalgia: a critical and comprehensive review. *Clin Rev Allergy Immunol* 2015;49:100-51.
- R Staud. Cytokine and immune system abnormalities in fibromyalgia and other central sensitivity syndromes *Curr Rheumatol Rev* 2015;11:109-15.
- Bayazit YA, Gürsoy S, Ozer E, et al. Neurotologic manifestations of the fibromyalgia syndrome. *J Neurol Sci* 2002;196:77-80.
- Sawada F, Nomura Y, Goto F, et al. Relationship of physical distress to dizziness in patients with fibromyalgia. *Acta Otolaryngol* 2016;136:56-61.
- Stranden M, Solvin H, Fors EA, et al. Are persons with fibromyalgia or other musculoskeletal pain more likely to report hearing loss? A HUNT study. *BMC Musculoskelet Disord* 2016;17:477.
- Gencer K, Balbaloğlu Ö, Özkırış M, et al. Does fibromyalgia have an effect on hearing loss in women? *Turk J Med Sci* 2017;47:1699-1702.
- Gurbuzler L, Inanir A, Yelken K, et al. Voice disorder in patients with Fibromyalgia. *Auris Nasus Larynx* 2013;40:554-7.
- Soler ZM, Mace J, Smith TL. Fibromyalgia and chronic rhinosinusitis: outcomes after endoscopic sinus surgery. *Am J Rhinol* 2008;22:427-32.
- Yilmaz M, Baysal E, Gunduz B, et al. Assessment of the ear and otoacoustic emission findings in fibromyalgia syndrome. *Clin Exp Rheumatol* 2005;23:701-3.
- Rosenhall U, Johansson G, Orndahl G. Neuroaudiological findings in chronic primary fibromyalgia with dysesthesia. *Scand J Rehabil Med* 1987;19:147-52.
- Doğan SC, Karadağ A, Durmuş K, et al. Evaluation of allergic rhinitis with nasal symptoms and nasal mucociliary clearance in patients with fibromyalgia syndrome. *J Back Musculoskelet Rehabil* 2018;31:917-22.
- Baraniuk JN. Neurogenic mechanisms in rhinosinusitis. *Curr Allergy and Asthma Rep* 2001;1:252-61.
- López-Solà M, Woo CW, Pujol J, et al. Towards a neurophysiological signature for fibromyalgia. *Pain* 2017;158:34-47.
- Martínez-Lavín M. Management of dysautonomia in fibromyalgia. *Rheum Dis Clin North Am* 2002;28:379-87.