

Demodex Parazytes in Schizophrenia

Şizofrenide Demodex Parazitleri

Demodex Parazytes and Schizophrenia

Mehmet Hanifi Kokaçya¹, Berna Hamamcı², Ümit Sertan Çöpoglu¹, Özlem Aycan Kaya¹ ¹Dept. of Psychiatry, Faculty of Medicine, ²Dept. of Parazitology, Faculty of Medicine, Mustafa Kemal University, Hatay, Turkey

Özet

Amaç: Demodex parazitleri tüm dünyada özellikle de insanların yüz bölgesinde yaygın olarak görülür. Demodex spp.'lerin immun sistemin kısmi olarak baskılanması ve özbakımın yetersiz olmasından dolayı şizofrenide daha yaygın olaileceği ileri sürülmektedir. Bu çalışmada şizofreni hastalarında Demodex ektoparazitinin yaygınlığının incelenmesi amaçlanmıştır. Gereç ve Yöntem: Çalışmaya katılan 31 şizofreni hastası ile herhangi bir psikiyatrik veya dermatolojik hastalığı bulunmayan 30 kontrol vakasından Demodex spp.'leri belirlemek için yüzeyel deri biyopsi tekniği ile örnek alınmıştır. Bulgular: Şizofreni grubunda dokuz, kontrol grubunda ise iki hastada Demodex spp. pozitif bulunmuştur. Demodex spp. görülme sıklığı açısından hasta ile kontrol grubu arasında istatiksel olarak anlamlı bir fark bulunmuştur (p<0.05). Tartışma: Sonuç olarak Demodex spp. şizofreni hastalarında immunsupresyon ve azalmış özbakım nedeniyle daha sık görülmektedir. Şizofreni hastalarında özellikle yüzdeki cilt lezyonlarında Demodex parazitleri akılda tutulmalı ve gerek varsa tedavi edilmelidir.

Anahtar Kelimeler

Şizofreni; İmmun Sistem; Ektoparazitik İnfestasyonlar

Abstract

Aim: Demodex parazytes are commonly present all over the world, especially in facial region of humans. Demodex spp. are assumed to be more common in schizophrenia due to partial suppression of immune system and lack of good self-care. The present study aimed to investigate the prevalence of Demodex ectoparasites in schizophrenia patients. Material and Method: In the study, 31 patients with a diagnosis of schizophrenia and 30 subjects without any psychiatric disorder or skin disease were subjected to standard superficial skin biopsy technique to determine Demodex spp. Results: Demodex spp. were found positive in nine schizophrenia patients and it was found positive in two healthy controls. Considering the prevalence of Demodex spp., a significant relationship is found between schizophrenia patients and normal controls (p<0.05). Discussion: As a result, Demodex spp. are more common in schizophrenia due conditions of reduced self-care and immunosuppression, Demodex parasites should be considered in schizophrenia patients with skin lesions, especially on the face, and should to be treated if needed.

Keywords

Schizophrenia; Immune System; Ectoparasitic Infestations

 DOI: 10.4328/JCAM.3855
 Received: 25.08.2015
 Accepted: 15.09.2015
 Printed: 01.02.2016
 J Clin Anal Med 2016;1(suppl 1): 6-9

 Corresponding Author: Mehmet Hanifi Kokacya, Department of Psychiatry, Faculty of Medicine, Mustafa Kemal University, 31100, Hatay, Turkey.
 GSM: +905052585954 F.: +90 3262294556 E-Mail: mhkokacya@mku.edu.tr

Introduction

Demodex species are commonly seen mites in the facial region of humans and widespread all over the world. Although there are numerous species of Demodex, two kinds of them can settle in the human body [1]. Demodex folliculorum and Demodex brevis live on the pilosebaceous glands and hair follicles and transmit from human to human by close contact interactions and result in infestation [2]. Demodex folliculorum is the most common ectoparasite found in humans [3]. For the diagnosis, cellophane-tape, skin scraping, punch biopsy and standard superficial skin biopsy methods are used [4]. Pathogenicity of Demodex spp. is still a debate and symptoms are very rare. It has been shown that Demodex spp. can cause severe infections only in immunesupressed and middle and older-aged people [5].

Schizophrenia is a chronic and debilitating neuropsychiatric disorder that affects approximately 1 % of world population [6]. The main clinical symptoms of schizophrenia include; delusions and hallucinations, thought, speech and behaviour disorders, social withdrawal, loss of cognitive skills. Impairment in daily life skills, reduced self-care and weak immune system are the main symptoms reported for the disease [7].

The underlying neurobiological mechanisms of this disorder remains unclear however there are growing of evidence that oxidative stress and immune sytem abnormalities play an important role in the etiology. In one third of patients with schizophrenia shows immunological abnormalities such as an altered cytokine profile in serum and cerebrospinal fluid [6].

As immun system abnormalties, lack of hygiene and self care are seen in schizophrenia, it is hyposthesized that Demodex spp. can be more prevalent in schizophrenia patients. To our knowledge, there have not been any reports focusing on the prevelance of Demodex spp. mites in patients with schizophrenia. This study aimed to identify the prevalence of Demodex spp. in patients diagnosed with schizophrenia.

Subjects and Method

Patients

Of 39 consecutive outpatients, aged 18 to 60 years, who had applied to the Mustafa Kemal University, School of Medicine, Research and Training Hospital Outpatient Psychiatry Clinic and had been diagnosed with schizophrenia according to Diagnostic and Statistical Manual of Mental Disorders IV-TR (DSM-IV-TR) between September 2013 and January 2014, 31 agreed to participate in the study. The control group included 30 healthy volunteers with no signs of skin disease.

Ethics approval for this study was obtained from local ethic committee in accordance with the Helsinki Declaration. All patients provided written informed consent for participation in this research. Exclusion criteria were to be pregnant or breastfeeding, to have a chronic disease like hypertension, diabetes mellitus etc..., to use immunsupressive agents and to have immun deficency sendroms like AIDS. The patients with any kind of comorbid dermatological or psychiatric disorder were excluded. All participants were subjected to a survey and samples were collected from participants by standard skin surface biopsy method using an adhesive band containing cyanoacrylate. Sample collection from study participants were achieved by taking samples from five different regions of their faces (nose, forehead, cheek, jaw). Before samples were taken, it was guaranteed that there was no cream or lotion on the faces of the patients and that the region where the samples would be taken was dry. Also, the region was cleaned with alcohol. To determine number of Demodex in cm2 samples were examined using Hoyer solution and observed under the light microscope at x400 and x1000 magnifications. Five of more Demodex in cm2 were accepted as positive for the Demodex.

Statistical Analysis

The SPSS 18.0 (Statistical Package for Social Sciences Chicago,IL, USA) package program was used for the statistical analysis. Descriptive and analytic statistics were performed. Chi-square test was used to compare categorical variables. Continuous variables were presented as mean \pm standard deviation p <0.05 was considered as statistically significant.

Results

Demodex spp. positivity was evaluated in terms of age and gender in patients diagnosed with schizophrenia. 14 female and 17 male schizophrenia patients aged between 18 and 60 years (mean: 36.64 ± 5.11 years) and as a control group 12 females and 18 males aged between 19 and 52 years (mean: 32.44 ± 8.58 years) were enrolled. The gender distribution of schizophrenia patients was similar to the control group (Table 1). Demodex spp. was detected on the faces of 29.03% (n=9) of patients diagnosed with schizophrenia and 9.5% (n=2) of the control group. (Table 2)

	C 1	14 . 11 . 1	C				
Table 1.	Gender	distributions	of the	schizophrenia	and	control	groups.
							0

			0 1
Gender	Schizophrenia n (%)	Control n(%)	p*
Male	17(%54,8)	18(%60)	0.797
Female	14(%45,2)	12(%40)	
Total	31(%100)	30(%100)	

* chi-square test.

Table 2. Incidence of Demodex spp. in patients with schizophrenia and control groups according to gender.

		DIAGNOSIS					
		Demodex spp. Positive		Demodex spp. Negative		Total	
		Ν	%	Ν	%	Ν	%
Schizophrenia	Male: 17	6	35.3	11	67.7	17	54.8
	Female: 14	3	21.4	11	78.6	14	45.2
Control	Male : 18	1	5.55	17	94.4	18	60
	Female: 12	1	8.33	11	91.7	12	40

The existence of Demodex spp on the faces of patients diagnosed with schizophrenia was found to be significantly higher compared to the control group (p=0.043) (Table 3). Incidence of Demodex spp. was found to be 5.7 times higher in schizophrenia as compared to control group (Table 3). Positive results were observed mostly in nose area and the second most common region was determined as forehead. In one patient, all of the regions were positive. Additionally, forehead area was determined as the region that has the highest parasite concentration (Table 4).

Table 3. Distribution of the Demodex spp. in schizophrenia and control groups.
--

		Schizophrenia n (%)	Control n (%)	p*	Odds Ratio	95% Interval Lower	Confidence Upper
Demodex spp.	Positive	9 (%29.03)	2 (%6.7)	0.043	5.72	1.12	29.25
	Negative	22 (%70.97)	28 (%93.3)				

* chi-square test.

Table 4. Distribution of Demodex spp. according to the facial area of patient and control groups.

	Schizophrenia (n=9) Demodex spp.		Control (n= Demodex s	2) pp.
	n	%	n	%
Nose + Right Cheek	5	55,6	1	50
Nose + Left Cheek	1	11,1	-	
Nose	9	100	1	50
Nose + Forehead	7	77,8	-	
Nose + Jaw	1	11,1	-	

Discussion

Demodex folliculorum and Demodex brevis are obligate parasites that only originates in human hair follicle and pilosebaceous unit. Demodex spp. normally present in intact skin, hair follicles, and sebaceous glands without any pathogenic effect. However, in conditions of poor hygiene and suppressed immune system, Demodex spp. can cause inflammatory dermatitis, keratosis and epitelioma, acne and acne rosacea [8].

The density of Demodex spp. increases with age [9]. Aycan et al.investigated the incidence of Demodex spp. in various types of disease states and age groups[4]. They used standard biopsy technique and observed 92 (%53.5) positive results among 172 patients that were 21 years old age and older. In our study, we found nine (%29.03) positive among 31 patients whose mean age was 36.64. In control group two subjects were positive (%6.7) among 30 controls whose mean age was 32.44. There was no significant relationship between the incidence of Demodex spp. and age.

There are several investigations about gender and Demodex ssp. Kokacya et al have investigated Demodex spp. Prevelance in 63 depressive patient They found four positive results in 27 male (26.7%) and 11 (34.2%) positive results in 36 female patient. They found no significance between gender and Demodex spp. prevelance [2].

In the present study, we found six (%35.3) positive among 17 males and 3 (%21.4) positive among 14 females. These results were not statistically significant (p=0.797). Although, these results were insignificant, high prevalence of Demodex spp. in schizophrenia (%35.3) in males can be associated with reduced self-care. Demodex infestation might progress heavily in elderly and immunsupressed people.

. It has been reported that Demodex spp. are widespread in patients with AIDS, leukemia, cancer, diabetes, rheumatoid arthritis, and in pregnant women and hemodialysis patients [10]. Parasite concentrations may increase due to suppressed immune system in these disease manifestations [10-13]. There are studies investigating the incidence of Demodex spp. in immunocompetent people. In a study, Ozcelik et al. identified 25.53 % positivity of D.folliculorum in patients with chronic renal failure and suppressed immune system [1]. In an another

8 I Journal of Clinical and Analytical Medicine

study, patients who were diagnosed with type 2 diabetes mellitus examined in terms of D. folliculorum ,24.6 % of patiens were positive. Also, parasite concentration were high in samples taken from cheek area compared to control group[14].

Schizophrenia is a, affecting approximately 1% population and starts before the age of

25. Schizophrenia, a complex disease with multifactorial etiology, is seen in all social classes, distorts the interpersonal and occupational capability and shows a chronic course [15]. Reduced self-care and weak immune functions are the early symptoms of schizophrenia [7,16]. Generally, schizophrenia is characterized with impartment of cell-mediated immune system, atypical lymphocytes in peripheral blood, decrease in the number and the function of lymphocytes, abnormal lymphoproliferative response to mitogens, abnormal cell-medicated and humoral response to neurons, changes in the number and the ratio of T cells [17,18]. Thus, there is a strong relationship with immune system functions and schizophrenia [19,20]. Müller et al showed that the cellular immune parameters were related to the course of the psychopathological symptoms in schizophrenia and, associated with therapeutic outcome of neuroleptic treatment [21].

Down-regulation of endogenous antioxidant and anti-inflammatory mechanisms has been identified in schizpohrenia [22]. For instance prolidase activity which is shown correlated with oxidative stress is found to be higher in schizophrenia petients [23]. Furthermore there are evidences that increased serum levels of chemokines, pro-inflammatory cytokines and, monocytosis, raised inflammatory gene expression in monocytes and altered T-cell function in schizophrenic patients [24-27].

Environmental conditions, nutrition, education level, economic status, hygiene conditions and factors such as the person's immune status is directly related to the prevalence of parasitic infections. Demodex species which are the most common types of permanent parasites of humans, leads to the formation of various dermatological problems in lesions and in skin regions that lack well cleansing. In patients with schizophrenia, especially in cases in which the negative symptoms were observed, they may neglect daily care and cleaning because the social withdrawals are at the forefront. Therefore Demodex spp. can be more prevalent in schizophrenia patients due to lack of selfcare.

In the present work, the difference was statistically significant for the positivity of Demodex spp. among patients with schizophrenia as compared with the control group (p=0,043) and incidence of these parasites in schizophrenic patients were found to be significantly higher. Although in schizophrenia, self-care is almost always being affected, high prevelance of Demodex spp. in schizophrenia patients appears to be associated with loss of functionality and self care rather than disease's direct effect.

This study has some limitations. Firstly, the sample size is small (n=31). Secondly with data being retrieved from only one hospital in Hatay, results may not be generalized for all schizophrenia patients. Thirdly as severity of schizophrenia and functionality are not measured by scales, the correlation between demodex spp presence and severity of schizophrenia could not be evalu-

ated. Despite these limitations this is the first study that evaulates Demodex spp prevelance in schizophrenia patients. To generalize these results, multicentre studies with more schizophrenia patients are needed.

Conclusion

Last of all, the weakening of the immune system, frequently impaired social behavior, especially the lack of hygienic selfcare can be risk factors for the Demodex spp. infestations in schizophrenia cases. In these patients, especially in skin lesions, Demodex spp. have to be taken into consideration by informing patients about the treat and explaining the protection-control methods and anti-parasitic treatment should be applied in parasite positive patients.

Competing interests

The authors declare that they have no competing interests.

References

1. Ozcelik S, Sumer Z, Degerli S, Ozyazici G, Hayta SB, Akyol M et al. The incidence of Demodex folliculorum in patients with chronic kidney deficiency. Turkiye Parazitol Derg 2007;31(1):66-8.

2. Kokaçya MH, Yengil E, Kaya ÖA, Şahpolat M. The Frequency of Demodex Spp in Depression Patients. Erciyes Med J 2014; 36(4): 166-169.

3. Hauswirth SG, Schachter SE, Hom MM. Symptoms Associated with the Presence of Demodex folliculorum. Invest Ophthalmol Vis Sci 2014;55(13):1996.

4. Aycan ÖM, Otlu GH, Karaman Ü, Daldal N, Atambay M. Çeşitli hasta ve yaş gruplarında Demodex sp. görülme sıklığı. Turkiye Parazitol Derg 2007;31(2):115-8. 5. Patrizi A, Neri I, Chieregato C, Misciali M. Demodicidosis in immunocompetent young children: report of eight cases. Dermatology 1997;195(3):239-42.

 Gibney SM, Drexhage HA. Evidence for a dysregulated immune system in the etiology of psychiatric disorders. J Neuroimmune Pharmacol 2013;8(4):900-20.
 Öztürk MO, Uluşahin A, editors. Ruh Sağlığı ve Bozuklukları Ankara: Tuna Matbaacılık; 2011. p. 306-7.

8. Kaya S, Selimoglu MA, Kaya OA, Ozgen U. Prevalence of Demodex folliculorum and Demodex brevis in childhood malnutrition and malignancy. Pediatr Int 2013;55(1):85-9.

9. Ekiz O BI. Acne Vulgaris and Acne Rosacea: An Update in Etiopathogenesis. Journal of Clinical and Analytical Medicine 2014. DOI: DOI: 10.4328/ICAM.2423

10. Gökçe C, Aycan-Kaya Ö, Yula E, Üstün İ, Yengil E, Sefil F et al. The effect of blood glucose regulation on the presence of opportunistic Demodex folliculorum mites in patients with type 2 diabetes mellitus. J Int Med Res 2013;41(5):1752-8. 11. Aydingöz İE, Dervent B, Güney O. Demodex folliculorum in pregnancy. Int J Dermatol 2000;39(10):743-5.

12. Damian D, Rogers M. Demodex infestation in a child with leukaemia: treatment with ivermectin and permethrin. Int J Dermatol 2003;42(9):724-6.

13. İnci M, Kaya ÖA, İnci M, Yula E, Gökçe H, Rifaioglu MM et al. Investigating Demodex folliculorum in patients with urological cancer. Turkiye Parazitol Derg 2012;36(4):208-10.

14. Akdeniz S, Bahceci M, Tuzcu AK, Harman M, Alp S, Bahceci S. Is demodex folliculorum larger in diabetic patients? J Eur Acad Dermatol Venereol 2002;16(5):539-41.

 Benros ME, Nielsen PR, Nordentoft M, Eaton WW, Dalton SO, Mortensen PB. Autoimmune diseases and severe infections as risk factors for schizophrenia: a 30-year population-based register study. Am J Psychiatry 2011;168(12):1303-10.
 Mueller N. Immunology of schizophrenia. Neuroimmunomodulation 2014;21(2-3):109-16.

17. Maes M, Bosmans E, Ranjan R, Vandoolaeghe E, Meltzer HY, De Ley M et al. Lower plasma CC16, a natural anti-inflammatory protein, and increased plasma interleukin-1 receptor antagonist in schizophrenia: effects of antipsychotic drugs. Schizophr Res 1996;21(1):39-50.

18. DeLisi LE. Is there a viral or immune dysfunction etiology to schizophrenia? Re-evaluation a decade later. Schizophr Res 1996;22(1):1-4.

19. Kirch DG. Infection and autoimmunity as etiologic factors in schizophrenia: a review and reappraisal. Schizophr Bull. 1993;19(2):355-70.

20. Pırıldar Ş, Veznedaroğlu B, Terzioğlu E, Özaşkinli S, Akdeniz F, Noyan A. Şizofrenide yıkım olan ve olmayan hastaların immunolojik özellikler bakımından karşılaştırılması. Psikiyatri Dergisi 2001;2(4):197-203.

21. Müller N, Hofschuster E, Ackenheil M, Eckstein R. T⊠cells and psychopathology in schizophrenia: relationship to the outcome of neuroleptic therapy. Acta Psychiatr Scand 1993;87(1):66-71.

 Leza JC, Bueno B, Bioque M, Arango C, Parellada M, Do K et al. Inflammation in schizophrenia: A question of balance. Neurosci Biobehav Rev 2015;55:612-26.
 Bahceci B, Bagcioglu E, Kokacya MH, Dilek AR, Bahceci I, Selek S. Prolidase activity and oxidative stress in patients with schizophrenia: A preliminary study. J

Pak Med Assoc 2015;65(2):131-5.

24. Craddock RM, Lockstone HE, Rider DA, Wayland MT, Harris L, McKenna PJ et al. Altered T-cell function in schizophrenia: a cellular model to investigate molecular disease mechanisms. PloS one 2007;2:e692-e.

25. Drexhage RC, Hoogenboezem TA, Cohen D, Versnel MA, Nolen WA, van Beveren NJ et al. An activated set point of T-cell and monocyte inflammatory networks in recent-onset schizophrenia patients involves both pro-and anti-inflammatory forces. Int J Neuropsychopharmacol 2011;14(6):746-55.

26. Weigelt K, Carvalho LA, Drexhage RC, Wijkhuijs A, de Wit H, van Beveren NJ et al. TREM-1 and DAP12 expression in monocytes of patients with severe psychiatric disorders. EGR3, ATF3 and PU. 1 as important transcription factors. Brain Behav Immun 2011;25(6):1162-9.

27. Anderson G, Berk M, Dodd S, Bechter K, Altamura AC, Dell'Osso B et al. Immuno-inflammatory, oxidative and nitrosative stress, and neuroprogressive pathways in the etiology, course and treatment of schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 2013;42:1-4.

How to cite this article:

Kokaçya MF, Hamamcı B, Çöpoglu ÜS, Kaya ÖA. Demodex Parazytes in Schizophrenia. J Clin Anal Med 2016;1(suppl 1): 6-9.