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ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

The Investigation of Olfactory Function Related Quality of Life And Psychological Symptoms In Patients With Transfusion Dependent Beta Thalassemia

Transfüzyon Bağımlı Beta Talasemi Hastalarında Koku ile İlişkili Yaşam Kalitesi ve Psikolojik Semptomların İncelenmesi

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ÖZET

Amaç: Transfüzyon bağımlı beta talasemi hastalarının kronik hastalıkları nedeniyle psikolojik rahatsızlıkları olabilmekte ve bu durum yaşam kalitelerini olumsuz etkileyebilmektedir. Ayrıca koku alma fonksiyonundaki sorunlar yaşam kalitesini ve psikolojik durumunu olumsuz yönde etkileyebilmektedir. Çalışmamızda transfüzyon bağımlı beta talasemi hastalarında koku alma işlevine bağlı yaşam kalitesi ile psikolojik bozukluk belirtileri arasındaki ilişki araştırıldı.

Gereçler ve Yöntemler: Çalışmaya İstanbul Tıp Fakültesi Talasemi Merkezi'nde takip edilen 46 transfüzyon bağımlı beta talasemi hastası katıldı. Hastanın kendi bildirdiği koku alma işlevi ve koku almayla ilişkili yaşam kalitesini (ASOF) değerlendirmek için 12 maddelik anket ve depresyon ile anksiyete semptomlarını değerlendirmek için Hastane Anksiyete ve Depresyon Ölçeği (HAD) kullanıldı. İstatistiksel analiz SPSS (v23) programı ile yapıldı.

Bulgular: Çalışmaya katılan 46 hastanın yaş ortalaması 32,5±7,3 yıl idi. Hastaların bildirilen genel koku alma kapasitesi (BKK) puanı 8,8±1,3 bildirilen belirli kokuları alma kapasitesi (BKA) puanı 4,6 ± 0,5 ve bildirilen koku duyusu ile ilişkili yaşam kalitesi (KYK) puanı 4,7 ± 0,4 idi. HAD ölçeğine göre hastaların %22'sinde anksiyete belirtileri, %65'inde depresyon belirtileri vardı. Hastaların anksiyete puanları ve depresyon puanları ile genel koku alma kapasiteleri arasında anlamlı bir negatif korelasyon bulundu (p=0.02). Depresyon semptomları ve anksiyete semptomları olan hastalar daha düşük koku alma yeteneği gösterdi (p<0.05). Depresyon semptomları olan hastalarda koku alma ile ilgili yaşam kalitesi de önemli ölçüde azaldı (p<0.05). Deferasiroks (DFX) kullanan hastalar daha iyi koku alma yeteneği gösterdi (p<0.01).

Sonuç: Transfüzyon bağımlı beta talasemi hastalarının koku alma kapasitesi ile anksiyete ve depresyon skorları arasında anlamlı bir negatif korelasyon bulundu. Depresyon semptomları olan hastalarda, koku alma işleviyle ilişkili yaşam kalitesinin daha düşük olduğunu gösterildi. Şelasyon tipi, koku alma kapasitesi ile ilişkili görünmektedir.

Anahtar Kelimeler: Anksiyete, beta talasemi, hayat kalitesi, depresyon, koku bozukluğu

ABSTRACT

Objective: Transfusion-dependent beta thalassemia (TDBT) patients may be at risk for psychological symptoms due to chronic disease, which can burden their lives. Sense of smell problems may also accompany chronic disease and lead to qualityof life problems. his study examined the relationship between olfactory function, quality of life and psychological symptoms in transfusion-dependent beta-thalassemia patients.

Materials and Methods: Forty-six TDBT patients followed up at the Thalassemia Center of Istanbul Medical Faculty were included in the study. The 12-item self-reported olfactory function and olfactory quality of life assessment questionnaire (ASOF) and the Hospital Anxiety and Depression Scale (HAD) were used to screen olfactory function capacity, olfactory-related quality of life and psychological symptoms. Statistical analysis was performed with SPSS (v23) software.

Results: The mean age of the 46 participants was 32.5±7.3 years. The overall olfactory capacity score was 8.8±1.3, the specific olfactory capacity score was 4.6±0.5 and the odor-related quality of life score was 4.7±0.4. The HAD scale showed that 22% of the patients had anxiety symptoms and 65% had depression symptoms. There was a significant negative correlation between anxiety and depression scores and general olfactory capacity (p=0.02). Patients with depression symptoms and anxiety symptoms showed lower olfactory capacity (p<0.05). Olfactory quality of life was also significantly reduced in patients with depression symptoms (p<0.05). Patients receiving deferasirox (DFX) showed better olfactory capacity (p<0.01).

Conclusion: A significant negative correlation was found between olfactory capacity and anxiety and depression scores. Patients with symptoms of depression showed a decrease in quality of life related to olfactory function. Chelation type seems to be associated with olfactory capacity.

Keywords: Anxiety, beta thalassemia, quality of life, depression, olfactory dysfunction

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INTRODUCTION

Thalassemia is a group of hemoglobinopathies resulting in mild to severe and life-threatening anemia. According to transfusion status, thalassemia syndromes are divided into Transfusion Dependent (TDT) and Non-Transfusion Dependent forms (1).

TDT patients need regular blood transfusions. TDT patients suffer from symptoms of the disease and transfusion complications such as endocrine dysfunction, heart failure and chronic liver disease (2). Psychological symptoms such as depression and anxiety are also common (3,4). Complication rate has started to decrease thanks to chelating agents (5).

Olfactory dysfunction was seen among patient with TDT (6). This sense is involved in nutrition and its deficiency results in diminishing the ability to distinguish spoiled foods, natural gas leaking, fire, and other environmental hazards (7). An intact olfactory function is necessary for a good quality of life. Moreover, olfactory dysfunction is associated with depression symptoms (8).

Studies on quality of life and psychological symptoms among patients with thalassemia are gradually increased (9). In this study, we examined the relationship between olfactory-related quality of life and symptoms of depression and anxiety in patients with TDT using questionnaires.

MATERIALS AND METHODS

Participants

A total of 46 patients (28 female and 18 male) with TDT were enrolled into study. All patients were administered regular blood transfusions. The 72% of patients received transfusions every 3 weeks. The 75% of patients used deferasirox (DFX), and 13% used deferiprone (DFP) and 10% used combination (DFX+DFP or DFO+DFP). The five patients didn't give information about trademark of chelator drug. The mean level of serum ferritin was 1559±1308.2 (median 1200 ng/mL).

Questionnaires

ASOF (The assessment of self-reported olfactory functioning and olfaction related quality of life)

The ASOF questionnaire was established by Pusswald et al. (10). ASOF includes olfactory-related quality of life scale (ORQ), self-reported functionality of perceiving specific odors scale (SRP) and subjective olfactory capability scale (SOC). It consists of 12 items of which one belongs to SOC, five items for SRP, and six items for ORQ scales.

SOC shows the smell function ability on a scale between 0 and 10 (with being 0 worst and 10 best smell score). A SOC score less than ≤3 demonstrates diminished sense of smell capabilities. SRP consists of 5 items and express the functionality of perceiving specific odors. A SRP score less than ≤2.9 reveals disorder in smelling odors. ORQ consists of six items and demonstrates smell-related quality of life. A ORQ score less than ≤3.7 are regarded as having olfactory-related issues in their quality of life. Turkish validation study was done by Saatci et al. (11). The ASOF questionnaire is easy to use and can provide information about psychological aspect of smell problem.

HAD (Hospital Anxiety and Depression Scale)

The HAD is a self-report questionnaire for screening the psychological symptoms (12). This questionnaire is used to screen the anxiety and depression symptoms of participants. It consists of 14 questions, 7 of them are related to anxiety and 7 of them are about depression. The Turkish validity trial was done by Aydemir et al. (13). The cut-off score is 7 for depression and 10 for anxiety in the Turkish validity form.

Procedure

Patients with TDT followed up at the Thalassemia Center of Istanbul Medical Faculty were asked to participate in this online survey. Patients' data were retrieved from the database and a letter containing the purpose of this study was sent. Forty-seven out of one hundred and six patients responded to the letter and completed the questionnaire. One patient did not fill out the form correctly, so the remaining 46 participants were included in the study.

Statistical Analysis

The SPSS 23.0 was performed for statistical analysis. Descriptive analysis was done. The student T test was done to make comparison between two groups of variables. Pearson analysis was performed for correlation. A value of $p<0.05$ was considered to be significant.

Ethical Approval

The ethical approval for this study was received from university ethic board (issue number 2022/2139). Study design and all procedure were done according to Helsinki Declaration.

RESULTS

Twenty-eight female and eighteen male TDT patients [mean age 32.5±7.3 years; range 15 – 47 years] were enrolled into study. The mean disease duration was 30.5±7.2 years. The median age of diagnosis was 9 months. The median age of starting regular transfusion was 12 months. The 67% of patients had splenectomy. Two of every three patients (65%) had endocrine complications (Table 1).

The SOC score of patient was 8.8 ± 1.3 (median 9). The SRP score was 4.6 ± 0.5 and ORQ score was 4.7 ± 0.4. None of patients showed hyposmia symptoms according to self-reported questionnaire (Table 2).

According to HAD (Hospital Anxiety and Depression Scale) results, the mean anxiety score was 7.6 ± 4.1 and when cut-off level 10 taken into account, 22% of patients showed anxiety symptoms. The mean depression score was 8.1 ± 4.1 and according to cut-off level of 7 score, 65% of patients demonstrated depression symptoms (Table 3).

There was negative significant correlation between subjective olfactory capability scale and depression and anxiety scores (p=0.02, r=-0.33; p=0.02, r=-0.34, respectively) (Table 4). The SOC score was significantly decreased among patients with depression signs compared to patients without depression signs (8.5 ± 1.5 vs 9.3 ± 0.8; p=0.01). The SRP score was significantly diminished in patients with depression symptoms compared to in patients without depression symptoms (4.5 ± 0.6 vs 4.8 ± 0.3, p=0.04). The ORQ score was also significantly decreased in patients with depression signs

Table 1. Sociodemographic and clinical data of participants

Characteristics	Study Group (n=46)
Gender	
Male	18 (%40)
Female	28 (%60)
Age	
mean ± SD years	32.5 ± 7.3
(median; min-max)	(31.5; 15-47)
Disease Duration	
mean ± SD years	30.5 ± 7.2
(median; min-max)	(30.5; 15-44)
Age of Diagnosis	
mean ± SD month	19.5±26.8
(median; min-max)	(9; 2-120)
Age of starting Regular Transfusion	
mean ± SD month	23.2±32.1
(median; min-max)	(12; 4-156)
Chelation Type	
DFO	1 (%2)
DFP	5 (%13)
Combination	4 (%10)
DFX-Ef	12 (%29)
DFX-Tb	19 (%46)
Splenectomy	
Yes	31 (%67)
No	15 (%33)
Ferritin Level	
mean ± SD ng/mL	1559.6±1308.2
(median; min-max)	(1200; 250-5600)
Pre-Transfusion Hgb	
mean ± SD	8.6±1.1
(median)	(8.6)
Transfusion Interval	
Every two weeks	5 (%11)
Every three weeks	33 (%72)
Every four weeks	8 (%17)
Endocrine Complications	(n=30; %65)
Osteoporosis	19 (%41)
Hypogonadism	10 (%21)
Diabetes	8 (%20)
Hypothyroidism	4 (%9)

SD: standard deviation; DFO: Deferoxamine; DFP: Deferiprone; DFX: deferasirox

Table 2. The assessment of self-reported olfactory functioning and olfaction related quality of life (ASOF) questionnaire results

Characteristics	Results (n=46)
Subjective Olfactory Capability scale (SOC) (mean ± SD)	8.8 ± 1.3
Self-Reported capability of Perceiving specific odors scale (SRP) (mean ± SD)	4.6 ± 0.5
Olfactory-Related Quality of life scale (ORQ) (mean ± SD)	4.7 ± 0.4

SD: standard deviation

Table 3. The Hospital Anxiety and Depression scale (HAD) results of participants

Characteristics	Results
Anxiety Score (mean ± SD)	7.6 ± 4.1
Anxiety Ratio (mean ± SD)	%22
Depression Score (mean ± SD)	8.1 ± 4.1
Depression Ratio (mean ± SD)	%65

SD: standard deviation

Table 4. The correlation between subjective olfactory capability scale and depression and anxiety scores of participants

Characteristics	Subjective Olfactory Capacity
Anxiety Score (7.6 ± 4.1)	r=-0.34, p=0.02
Depression Score (8.1 ± 4.1)	r=-0.33, p=0.02

Table 5. Olfactory function results of participants according to psychological symptoms

Characteristics		SOC	SRP	ORQ
Depression		p=0.01	p=0.04	p=0.02
		(mean ± SD)	(mean ± SD)	(mean ± SD)
	With	8.5 ± 1.5	4.5 ± 0.6	4.6 ± 0.5
	Without	9.3 ± 0.8	4.8 ± 0.3	4.9 ± 0.2
Anxiety		p=0.05	p=0.30	p=0.27
	With	7.9 ± 1.7	4.4 ± 0.7	4.4 ± 0.7
	Without	9.0 ± 1.1	4.7 ± 0.4	4.7 ± 0.3

Higher scores indicate better results; SOC: Subjective Olfactory Capability scale; SRP: Self-Reported capability of Perceiving specific odors scale; ORQ: Olfactory-Related Quality of life scale

Table 6. Olfactory function results of participants according to psychological symptom groups

Characteristics	Depression + Anxiety Group			
	Neither Depression nor Anxiety Mean	Either Depression or Anxiety Mean	Both Depression and Anxiety Mean	p value
SOC	9,3 ± 0.9	8,9 ± 1.2	7,6 ± 1.7	0.01
SRP	4,8 ± 0.3	4,6 ± 0.5	4,4 ± 0.8	0.13
ORQ	4,9 ± 0.2	4,7 ± 0.4	4,4 ± 0.8	0.08

SOC: Subjective Olfactory Capability scale; SRP: Self-Reported capability of Perceiving specific odors scale; ORQ: Olfactory-Related Quality of life scale

compared to in patients without depression symptoms (4.6 ± 0.5 vs 4.9 ± 0.2; p=0.02) (Table 5).

The mean SOC score was significantly decreased in patients with anxiety symptoms in comparison to in patients without anxiety symptoms (7.9 ± 1.7 vs 9.0 ± 1.1, p=0.05). The mean SRP score was 4.7± 0.4 in patients without anxiety symptoms and 4.4 ± 0.7 in patients with anxiety symptoms (p=0.30). The mean ORQ score was 4.7 ± 0.3 among patients without anxiety symptoms and 4.4 ± 0.7 in patients with anxiety symptoms (p=0.27) (Table 5).

There were 9 patients (20%) who showed both depression and anxiety symptoms and 15 patients (33%) who showed no depression or anxiety symptoms. SOC scores were gradually decreased from neither depression nor anxiety group towards both depression and anxiety group (p=0.01) (Table 6).

Olfactory function capability didn't significantly differ among patients with or without endocrine complications (9.1 w/o and 8.6 w; p=0.21). However, disease duration was associated with lower olfactory capability (r=-0.28, p=0.05).

Interestingly, patients using DFX only showed better olfactory capability compared to patients using other chelator (DFP, DFO and combination) (9.3 vs 7.5; p<0.01). Patients using DFX effervescing tablet showed tendency to have higher SRP score (specific odor capability) compared to patients using DFX film tablet (4.9 vs 4.6; p=0.09).

There was no relation between serum ferritin level, pre-transfusion level, splenectomy status and gender with olfactory capability.

DISCUSSION

In this study, we evaluated the relationship between subjective olfactory capacity and olfactory quality of life with depression and anxiety symptoms in patients with TDT. We found that a significant proportion of patients showed symptoms of depression. On the other hand, there was a very tight correlation between olfactory capacity and psychological symptoms (p=0.02, r=-0.33). Patients with both depression and anxiety symptoms had the lowest olfactory capacity. Olfactory quality of life was significantly reduced in patients with symptoms of depression. Chelation type was also associated with olfactory capacity.

Objective olfactory dysfunction was shown in patients with transfusion dependent thalassemia (6). Furthermore, olfactory impairment has been associated with difficulties in physical activities, limitations in daily life and impaired sense of general well-being. Therefore, the function of the olfactory system is closely linked to overall health.

Quality of life is one of main concern in thalassemia patients. Children with thalassemia showed lower quality of life in domains of physical, social, emotional and school (14,15). Another study also demonstrated lower quality of life in children with transfusion dependent thalassemia (16). A comprehensive study including both children and adult patients with thalassemia showed that children with thalassemia had lower quality of life compared to adults (17). Another study indicated that high ferritin level was negative predictor of quality of life in children (18).

Depression and anxiety are another main concern in thalassemia patients. Psychological symptoms are reported highly in chronic disorders and in thalassemia as well. Zolaly et al. (19) showed 60% depression rate and 50% anxiety rate in TDT patients. Adib-Hajbaghery et al. (20) also revealed high rate of depression and anxiety (60%). Maheri et al. (21) demonstrated lower depression (20%) and anxiety (25%) symptoms. Another study from Turkey (22) showed similar results (20% depression and 40% anxiety). Mohamadian et al. (23) emphasized the effect of behavioral therapy on depression and anxiety in their randomized trial.

Sense of smell is shown to be associated with quality of life and depression symptoms (8). Formerly, a tight connection between olfactory dysfunction and depression was shown in literature (24,25). Olfactory related quality of life disturbed in patients with olfactory dysfunction. On the other hand, it has been considered as a predictor of depressive symptoms in patients (8). In our study, we also showed a very close association between depression and anxiety symptoms with olfactory related quality of life. Moreover, olfactory capacity significantly decreased in patients showing depression and anxiety symptoms.

Limitation; The cross-sectional design of the study does not allow to conclude that odor-related quality of life may be a predictor of depressive symptoms in patients with thalassemia. Furthermore, the limited number of participants is also an important limitation. Another limitation is that the subjective test was not supported by an objective odor test. However, large prospective cohort studies investigating the cause-and-effect relationship between olfactory capacity, odor-related quality of life and psychological symptoms are needed to

clarify this point. The strength of this study is that we used standardized tests and questionnaires to assess psychological testing and olfactory quality of life.

CONCLUSION

This study demonstrated the relationship between olfactory function-related quality of life and psychological symptoms in patients with TDT. Although patients' subjective reports showed that olfactory capacity and olfactory-related quality of life were not affected, patients with depressive symptoms showed decreased olfactory function-related quality of life.

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