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Yazışma Adresi
Correspondence Address

Ufuk DEMİREL
Bulent Ecevit University,
Faculty of Health Science,
Nursing Department
Zonguldak, Turkey

uudemirel@gmail.com

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Zeynep ERDOGAN
Bulent Ecevit University,
Ahmet Erdoğan Vocatıonal
School of Health Services,
Nursing Department,
Zonguldak, Turkey
ORCID ID: 0000-0002-7298-7559

Mehmet Ali KURCER
Bulent Ecevit University,
Faculty of Medicine,
Public Health Department,
Zonguldak, Turkey
ORCID ID: 0000-0003-2672-1079

Ufuk DEMIREL
Bulent Ecevit University,
Faculty of Health Science,
Nursing Department
Zonguldak, Turkey
ORCID ID: 0000-0002-8630-8203

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The Use of Complementary and Integrative Health Approaches in Patients with Behcet Disease and Its Relationship with Quality of Life

Behçet Hastalığı Olan Hastalarda Tamamlayıcı ve Bütünleyici Sağlık Yaklaşımlarının Kullanımı ve Yaşam Kalitesi ile İlişkisi

ABSTRACT

Objective:

This study aims to determine the effect of common symptoms on Quality of Life (QoL) in patients with Behcet Disease (BD) and complementary and integrative health approaches used by patients to cope with these symptoms.

Methods:

The population of this descriptive study consisted of all patients with BD (n = 330) who are registered with the Behçet's Disease and Familial Mediterranean Fever Patients Association. The data were collected by the researcher and the president of the association, via an online form between 31.08.2020-06.12.2020. The sample consisted of all patients with BD who met the inclusion criteria (n=247). The data were collected using the Patient Information Form, and Behçet's Disease Quality of Life Scale (BDQoL).

Results:

Joint involvement, rectal bleeding, eye involvement, number of attacks, and disease activity are determinants of 42.5% in affecting QoL ($R2 = 0.425$, $p < 0.001$). 37.5% of patients with BD have been using CIHA for the last 1 year. They use black mulberry molasses (32%), coriander (9.3%), and thyme juice mouthwash (4%) for oral aphthous, wet cupping (24%), and St. John's wort oil (19%) for genital wounds among CIHA methods.

Conclusion:

The decisive factor in the use of CIHA in patients with BD was to have genital wounds or loss of sensation in the arm. Therefore, the results of this study are important in terms of leading to further experimental studies to determine the CIHA to be used for symptoms in patients with BD.

Key Words:

Behçet's Disease, Symptom, Complementary and integrative health approaches, Qality of life

ÖZ

Amaç:

Bu çalışma, Behçet Hastalığı (BH) olan bireylerde, sık görülen semptomların yaşam kalitesi üzerine etkilerini değerlendirmek ve hastaların bu semptomlarla baş etmek için kullandıkları tamamlayıcı ve bütünleyici sağlık yaklaşımlarını belirlemek amacıyla yapılmıştır.

Yöntem:
Tanımlayıcı olarak yapılan bu araştırmanın evrenini Behçet ve Ailevi Akdeniz Ateşi Hastaları Derneği'ne kayıtlı, Behçet Hastalığı olan tüm hastalar oluşturmuştur (n:330). Veriler, 30.08.2020- 06.12.2020 tarihleri arasında araştırmacı ve dernek başkanı tarafından online form ile toplanmıştır. Örneklem kriterlerini karşılayan tüm Behçet hastaları, araştırmanın örneklemini oluşturdu. Veriler Hasta Bilgi Formu ve Behçet Hastalığı Yaşam Kalitesi Ölçeği (BDQoL) kullanılarak toplanmıştır.

Bulgular:
Eklem tutulumu, rektal kanama, göz tutulumu, atak sayısı ve hastalık aktivitesi, yaşam kalitesini %42,5 oranında etkileyen faktörlerdir (R2=0.425, p<0.001). BH olan hastaların %37,5'i son 1 yıldır tamamlayıcı ve bütünleyici sağlık yaklaşımlarını kullanmaktadır. Tamamlayıcı ve bütünleyici sağlık yaklaşımlarında ağız yaraları için; karadut pekmezi (%32), kişniş (%9,3) ve kekik suyu gargarası (%4), genital yaralar için; yaş hacamat (%24) ve sarı kantaron yağı (%19) kullanılıyor.

Sonuç:
BH olanlarda tamamlayıcı ve bütünleyici sağlık yaklaşımları kullanımında belirleyici faktör, kolda his kaybı ya da genital yara olmasıydı. Bu nedenle, bu çalışmanın sonucu, BH olan hastalarda semptomlar için kullanılan tamamlayıcı ve bütünleyici sağlık yaklaşımlarının belirlenmesinde daha ileri deneysel çalışmalara yol göstermesi açısından önemlidir.

Anahtar Sözcükler:
Behçet Hastalığı, Semptom, Tamamlayıcı ve bütünleyici sağlık yaklaşımları, Yaşam kalitesi

INTRODUCTION

Behçet's disease (BD), which was first identified by Prof. Dr. Hulusi Behçet in 1937 and entered the world literature, is a chronic, inflammatory, multisystem health problem characterized by exacerbations and remissions, venous and arterial involvement, and classified under primary vasculitis (1-4). According to the diagnostic criteria of the International Study Group of Behçet's Disease, the diagnosis of BD is made with the concomitant of at least two of the findings of recurrent oral aphthous, genital ulceration, eye lesions, skin lesions and positive resulted pathergy test in addition to recurrent oral aphthous that cannot be explained by any other clinical reason (5). BD, which can be seen all over the world and in almost every race, is quite common in the northern hemisphere and in countries that are strikingly on the historical 'Silk Road' such as Turkey, Iran and the Far East (Japan, China, Korea). BD is most frequently seen in Turkey in the world. The prevalence ranges between 370-420 per hundred thousand in Turkey (6,7). The studies show that its prevalence is 13.5/100.000 in Japan, 1/100.000 in England, 1.67/10.000 in Iran, 1.7/10.000 in Iraq, 2/10.000 in Saudi Arabia, and 1.4/10.000 in China (8,9).

BD, due to the fact that it occurs at the age of 20-40 when life is most active, has multisystem organ involvement, and has high morbidity and mortality, besides deterioration in quality of life, it also brings workforce losses (8,10-15). Among the most important factors affecting the QoL in BD are joint involvement that causes tiredness, disability and pain, painful genital ulcers that affect body image and sexual life, recurrent oral aphthous, skin lesions, eye involvement, anxiety and depression due to immunosuppressive therapy and the disease (8,10-16). Health-related QoL evaluation helps doctors and nurses in applying clinical practices effectively, making appropriate treatment decisions for the patient, determining the patient's social, emotional and physical needs, and improving the quality of care by considering the patient holistically (8,17-19). Therefore, it is important to maintain a multidisciplinary approach in BD which is a multi-systemic disease. Since the BD is a disease of unknown etiology, there is no specific treatment. The treatment generally involves immunosuppressives, anti-inflammatory drugs, and steroid agents, but the treatment effect is not very satisfactory. For this reason, especially moderate and severe patients with BD may seek Complementary and Integrative Health Approaches (CIHA) to treat the undesirable side effects of medicinal drugs, strengthen the immune system, reduce the likelihood of recurrence of symptoms, symptom management, maintain well-being, and also treat the root causes of the disease (20-22).

The literature shows that there are many studies evaluating QoL in BD (1,8,10-13,15,16) however, there are no studies on the use of CIHA in these patients. Only one meta-analysis study was found on herbal therapy in Behçet's disease (21). Therefore, this study aims to determine the effect of common symptoms on QoL in BD and the CIHA used by BD to cope with these symptoms.

METHODS

Participants

Design, Setting, and Sample

The population of this descriptive study consisted of all Behçet patients (n = 330) who are registered with the Behçet's Disease and Familial Mediterranean Fever Patients Association. The sample consisted of all patients with BD (n = 247) over the age of 18, who agreed to participate in the study, no communication problem, and who met the diagnostic criteria proposed at the International Study Group of Behçet's Disease(International Study Group for Behçet's Disease, Criteria for diagnosis of Behçet's disease) and diagnosed with Behçet's disease by a specialist doctor. The data were collected by the researcher and the president of the association, via an online form between 31.08.2020-06.12.2020, as it coincided with the peak of the covid 19 outbreak. Each patient was informed about the study and consent was taken from the patients. Patients' personal rights and private information are protected. Volunteerism was taken as the basis for patients' participation in the study. The rate of participation in the study was 86.66%. We ran the study according to the Helsinki Declaration (World Medical Association Declaration of Helsinki Ethical Principles For Medical Research Involving Human Subjects).

Data collection

The data were collected using the Patient Information Form consisting of 20 questions including sociodemographic data (age, gender, economic status, marital status), disease-related characteristics(Presence of another chronic disease, regular drug use, duration of disease, disease attack, disease active) and the use of CIHA, CIHA methods they used to cope with the symptoms, and Behçet's Disease Quality of Life Scale (BDQoL). Gillworth et al. developed the BDQoL in 2004 in order to measure the QoL of the last month in patients with BD (23). BDQoL consists of 30 expressions with "yes" and "no" answer options. BDQoL has a negative evaluation, in other words, if the patient thinks that the statement on the scale is appropriate for their condition and marks the 'yes' option for that statement, it means that Behçet's disease affects that aspect of their life negatively. Each 'yes' answer takes 1 point, and 'no' answers take no point in the evaluation, and BDQoL total score ranges between 0-30. 0 represents the best, 30 represents the worst QoL. As the score increases, QoL decreases. Erdoğan and Pınar (2009) made the Turkish validity and reliability of the scale and the Cronbach alpha internal consistency coefficient was found to be 0.95 (17). In our study, the Cronbach alpha value of the BDQoL was found to be 0.93.

Ethical Considerations

Before the study, a permission dated 05/06/2020 with the protocol number 805 was taken from the University Human Research Board of Ethics. Each patient was informed about the study and consent was taken from the patients. We ran the study according to the Helsinki Declaration (World Medical Association Declaration of Helsinki Ethical Principles For Medical Research Involving Human Subjects, Zonguldak Bulent Ecevit University).

Statistical Analysis

Data was evaluated using the SPSS 16.0 program and after the skewness and kurtosis values exhibited the conditions of normal distribution, data was evaluated using percentages, mean values, standard deviation, chi-square test, the t test, ANOVA and linear regression analysis.

RESULTS

Table I shows the QoL scores of patients with BD according to their sociodemographic characteristics. No statistically significant difference was found between the QoL scores of the patients with a mean age of 37.4 ± 5.62 according to sociodemographic characteristics (p> 0.05).

Table I: Distribution of Quality of Life Scores According to Socio-Demographic Features (n = 247).

Socio-Demographic Features	n	%	BD-QoL (Avg ± SD)	p
Age groups	144	(58.5)	8.64 ± 3.15	0.98
18-39	103	(41.5)	8.75 ± 4.01	
40 and above			t: 0.128	
Income rate			8.96 ± 3.07	0.96
Low	31	(12.6)	9.03 ± 4.14	
Average	185	(74.9)	9.29 ± 2.42	
High	31	(12.6)	F: 0.032	
Profession			9.03 ± 4.01	p: 0.87
Housewife	35	(14.2)	10.73 ± 4.43	
Retired	18	(7.3)	8.36 ± 4.17	
Private Sector Employee	80	(32.5)	9.71 ± 4.50	
Public Employee	48	(19.5)	9.35 ± 6.45	
Self-Employed	15	(6.1)	9.07 ± 4.31	
Unemployed	26	(10.6)	8. 67 ± 4.28	
Other	25	(9.8)	F: 1.180	
Educational Background			8.63 ± 4.34	p: 0.77
Elementary School	68	(27.5)	9.31 ± 4.16	
High School	79	(32.0)	9.26 ± 5.42	
University	86	(34.8)	7.80 ± 4.73	
Postgraduate	14	(5.7)	F: 0.360	
Marital status	191	(77.3)	9.09 ± 4.14	p: 0.13
Married	56	(22.7)	8.74 ± 4.86	
Single			t: 0.376	

t: t test F:ANOVA

Table II shows the distribution of the QoL scores of the patients according to the characteristics related to the disease. Table II shows that the clinical symptoms such as genital wound ($p = 0.003$), erythema nodosum ($p = 0.001$), joint involvement ($p < 0.0001$), tiredness ($p < 0.0001$), nausea or vomiting ($p = 0.03$), diarrhea ($p = 0.001$), rectal bleeding ($p < 0.0001$) , loss of sensation and weakness in arm ($p < 0.0001$) and leg ($p < 0.0001$), eye involvement ($p < 0.0001$), having an attack in the past year ($p < 0.0001$), number of attacks ($p = 0.001$) and disease activity ($p < 0.0001$) have the most statistically significant affect on QoL. The study found that the clinical symptoms such as presence of another chronic disease, duration of the disease, regular drug use, mouth sore, and headache do not make a statistically significant difference on QoL ($p > 0.05$).

Table II: Distribution of Quality of Life Scores According to Disease-Related Characteristics (n = 247).

Disease Characteristics	n (%)	BD-QoL (Avg ± SD)	p
Presence of another chronic disease	86 (34.8)	13.06 ± 5. 0 8	0. 26
Yes	161 (65.2)	11.43 ± 5.01	
No		t: 1.223	
Duration of disease	16 (6.5)	10.40 ± 4.76	0. 46
1 year and less	44 (17.9)	12.61 ± 3.96	
2-5 years	79 (32.1)	9.87 ± 4.45	
6-10 years	108 (43.5)	13.04 ± 4.10	
11 years and more		F: 1.88	
Regular drug use	170 (68.8)	12.47 ± 4.05	0. 22
Yes	77 (31.2)	10.8 9 ± 3.51	
No		t: 1.063	
Mouth sores	189 (76.5)	12:21 ± 4 21	0.41
Yes	58 (23.5)	11.14 ± 4. 68	
No		t: 0.814	
Genital wound	88 (35.6)	14.42 ± 6.06	**0.003 ᵀ
Yes	159 (64.4)	10.65 ± 6_ 89	
No		t: 3.057	
Erythema nodosum	77 (31.2)	14. 32 ± 5_ 70	**0.001 ᵀ
Yes	170 (68.8)	9 .85 ± 5.12	
No		t: 3.423	
Joint involvement	191 (77.3)	13. 61 ± 5.71	**0.000 1 ᵀ
Yes	56 (22.7)	6. 02 ± 2 .92	
No		t: 5.835	
Tiredness	223 (90.3)	12.57 ± 5 .21	**0.0001 ᵀ
Yes	24 (9.7)	6.33 ± 2.72	
No		t: 3.568	
Nausea or vomiting		14.35 ± 4.59	*0 .03 ᵀ
Yes	61 (24.7)	11.26 ± 4.15	
No	186 (75.3)	t: 2.721	
Diarrhea		14. 50 ± 6. 90	**0.001 ᵀ
Yes	86 (34.8)	10.64 ± 4.24	
No	161 (65.2)	t: 3.505	
Rectal bleeding		1 6.71 ± 5 .39	**0.000 1 ᵀ
Yes	37 (15.0)	11.35 ± 4.10	
No	210 (85.0)	t: 3.615	
Loss of sensation and weakness in the arm		15. 28 ± 6 .24	** 0.000 1 ᵀ
Yes	123 (49.8)	8. 78 ± 3.50	
No	124 (50.2)	t: 6.197	
Loss of sensation and weakness in the leg		14. 77 ± 7. 19	**0.000 1 ᵀ
Yes	122 (49.4)	9 .20 ± 3. 05	
No	1 25 (50.6)	t: 5.567	
Eye involvement		14. 55 ± 6 .50	**0.000 1 ᵀ
Yes	94 (38.1)	10. 11 ± 3.78	
No	153 (61.9)	t: 3.534	
Yes	145 (58.7)	12 .23 ± 4.84	
No	102 (41.3)	t: 1. 270	
Have you had an attack related to your disease in the last year?		13. 55 ± 4.03	** 0.000 1 ᵀ
Yes	137 (55.5)	10.06 ± 4.27	
No	110 (44.5)	t: 3.595	
How many attacks related to your disease have you had in the last year?		10 .89 ± 3.11	**0.001 ᵇ
0-2 attacks	146 (71.7)	12 .53 ± 4.18	
3-5 attacks	59 (23.9)	16 .30 5.63	
6 attacks and more	42 (17.0)	F: 5.426	
Is your disease active now?		13. 53 ± 5 .21	**0.000 1 ᵀ
Yes	177 (36.3)	8.09 ± 2 .89	
No	70 (14.3)	t: 3.975	
BD-QoL Total score	13 .96 ± 4.13		
Avg ± SD			

*p <0.05; **p <0.001; ᵀ t test ᵇ: ANOVA

The results of multiple regression analysis used to examine the variables affecting the QoL shows that joint involvement, rectal bleeding, eye involvement, number of attacks, and disease activity affect the QoL at a deterministic rate of 42.5% (R2 = 0.425, p <0.001) (Table III).

Table III: Examination of Quality of Life via Regression Analysis According to Disease Characteristics.

	BD-QoL			
	B	**Beta**	**t**	**p**
Constant	33.013		10.474	0.0001
Genital ulceration	-0.900	-0.083	-1.270	0.206
Erythema nodosum	-1.078	-0.097	-1.542	0.125
Joint involvement	-2.988	-0.245	-3.407	**0.001
Tiredness	-1.847	-0.113	-1.631	0.105
Nausea and vomiting	-0.256	-0.020	-0.307	0.759
Diarrhea	-1.224	-0.113	-1.681	0.095
Rectal bleeding	-2.622	-0.164	-2.388	*0.018
Weakness in the arm	-1.231	-0.118	-1.563	0.120
Weakness in the leg	-0.532	-0.051	-0.681	0.497
Eye involvement	-2.159	-0.200	-3.279	**0.001
Presence of attack	-0.320	-0.031	-0.408	0.684
Number of attacks	-0319	0.146	2.144	*0.034
Disease activity	-1.338	0.765	-1.748	*0.041
R= 0.652	R^2= 0.425	F=9.155	p<0.0001	

R = regression coefficient *p <0.05; **p <0.0

37.5% of the patients have been using CIHA for the last 1 year. Table IV shows CIHA usage and CIHA methods according to common clinical symptoms of BD. The study shows that BP with the symptoms of genital wounds (p = 0.01), rectal bleeding (p = 0.04), and loss of feeling in arm (p = 0.007) statistically used more CIHA (Table IV).

Table IV: CIHA's Used by Patients with BD According to Clinical Symptoms.

Yes	42 (47.7)	46(52.3)	*0.01 ¹	St. John's wort oil 8 (19.0)	Bioenergy 2 (4.7)
No	51 (32.0)	108(68.0)		Baticonol 6 (14.3)	Ozone 2 (4.8)
				Olive oil 8 (19.0)	Molasses-flour mix 1 (2.4)
				Acupuncture 3 (7.1)	
Erythema nodosum				Mulberry molasses 12 (39.0)	
Yes	31(40.3)	46(59.7)	0.56	Cupping 7 (23.0)	
No	62(36.5)	108(63.5)		St. John's wort oil 9 (28.0)	
				Leech 3 (10.0)	
Tiredness				Reiki 4 (5.0)	
Yes	83(32.7)	140(62.8)	0.69	Bioenergy 3 (4.0)	
No	10(41.7)	14(58.3)		Acupuncture 6 (7.0)	
				Honey 40 (48.0)	
				Ozone 4 (5.0)	
				Propolis 15 (18.0)	
				Cupping 11 (13.0)	
Nausea-vomiting					
Yes	19(31.1)	42(68.9)	0.22	Thyme 4 (21.0)	
No	74(39.8)	112(60.2)		Lemon 6 (32.0)	
				Reiki 2 (11.0)	
				Cupping 2 (11.0)	
				Kefir 2 (11.0)	
				Mint 3 (14.0)	
Yes	68(35.6)	123(64.4)	0.21	Cupping 11 (15.5)	Dandelion 3 (4.0)
No	25(44.6)	31(55.4)		Hot spring 6 (9.0)	Ozone 3 (4.0)
				Mulberry molasses 5 (8.0)	Sweetgum 2 (3.0)
				Turmeric capsule 4 (6.0)	Lemon-garlic cure 5 (8.0)
				Bioenergy 4 (7.0)	Soaking feet in rock salt 1 (1.5)
				Okra seeds 3 (5.0)	Cabbage and sycamore leaf mix 4 (7.0)
				Applying black seed oil 2 (3.0)	St. John's wort oil 4 (7.0)
				Apply a mixture of black seed oil and rosehip 2 (3.0)	Nettle 3 (4.0)
					Leech 3 (4.0)
					Acupuncture 3 (4.0)
Joint involvement					
Yes	68(35.6)	123(64.4)	0.21	Cupping 11 (15.5)	Dandelion 3 (4.0)
No	25(44.6)	31(55.4)		Hot spring 6 (9.0)	Ozone 3 (4.0)
				Mulberry molasses 5 (8.0)	Sweetgum 2 (3.0)
				Turmeric capsule 4 (6.0)	Lemon-garlic cure 5 (8.0)
				Bioenergy 4 (7.0)	Soaking feet in rock salt 1 (1.5)
				Okra seeds 3 (5.0)	Cabbage and sycamore leaf mix 4 (7.0)
				Applying black seed oil 2 (3.0)	St. John's wort oil 4 (7.0)
				Apply a mixture of black seed oil and rosehip 2 (3.0)	Nettle 3 (4.0)
					Leech 3 (4.0)
					Acupuncture 3 (4.0)
Headache			0.97	Cupping 9 (17.0)	
Yes	53(36.6)	92(63.4)		Peppermint oil 8 (15.0)	Bioenergy 4 (7.5)
No	40(39.2)	62(60.8)		Olive oil laurel mix 8 (15.0)	Sugar-free coffee 4 (7.5)
				Rosemary 8 (15.0)	
				Hot spring 6 (11.5)	
				Vicks 6 (11.5)	
Diarrhea	33(38.4)	53(61.6)	0.86	Quince seed 5 (15.0)	Ginger 8 (24.0)
Yes	60(37.3)	101(62.7)		Blackberry leaves, 5 (15.0)	Black pepper 7 (22.0)
No				Rosehip, 8 (24.0)	
Rectal bleeding				Honey 7 (25.0)	Kefir 6 (22.0)
Yes	84(40.0)	126(60.0)	*0.04 ¥	Cinnamon 4 (14.0)	Green tea 4 (14.0)
No	9(24.3)	28 (75.7)		Banana 7 (25.0)	
Loss of sensation and weakness in arms				Cupping 7 (20.0)	Hirudotherapy (Leech therapy) 4 (11.0)
				Exercise 3 (8.0)	Acupuncture 2 (5.5)
Yes	57(45.9)	67(64.1)	**0.007 ¥	Hot Spring 7 (20.0)	Bioenergy 2 (5.5)
No	36(29.2)	87(70.8)		Black seed oil 11 (30.0)	
Loss of sensation and weakness in legs				Cupping 7 (17.0)	Leech 4 (9.5)
Yes				Exercise 11 (26.0)	Acupuncture 3 (7.5)
No	42(34.4)	80(65.6)	0.31	Hot Spring 9 (21.0)	Reiki 4 (9.5)
	51(40.8)	74(59.2)		St. John's wort oil 4 (9.5)	
Eye involvement					
Yes	38(40.4)	56(59.4)	0.48	Acupuncture 7 (18.0)	Bioenergy 5 (13.0)
No	55(35.9)	98(64.1)		Reiki 4 (11.0)	Pollen-propolis 5 (14.0)
				Cupping 14 (37.0)	

The results of multiple regression analysis examined the clinical symptoms affecting the use of CIHA according to clinical symptoms show that the loss of sensation in the arm and the genital wound have a determinative affect on the use of CIHA at a rate of 0.07% (R2 = 0.070, p = 0.005) (Table V). The study shows that BP use CIHA such as black mulberry molasses (32.0%), carbonated water (14.6%), alum (9.3%), coriander (9.3%), pollen-propolis mixture (5.3%) and thyme juice mouthwash for oral aphthous (4%), wet cupping (24.0%), St. John's wort oil (19.0%), olive oil (19.0%), baticonol and water (14.3%) and leech therapy (4.7%) for genital wounds, mulberry molasses (39.0%), wet cupping (23.0%), St. John's wort oil (28.0%) and leech (10.0%) for erythema nodosum, honey (48.0%), propolis (18.0%), wet cupping (13.0%), acupuncture (7.0%), Reiki (5.0%) and bioenergy (4.0%) for fatigue, lemon (32.0%), thyme (21.0%) and mint (14.0%) for nausea and vomiting, wet cupping (15.5%), hot spring (9.0%), mulberry molasses (8.0%), lemon-garlic cure (8.0%), cabbage and sycamore leaf mixture (7.0%), St. John's wort (7.0%), okra seeds (5.0%) and dandelion (4.0%) for joint involvement, wet cupping (17.0%), peppermint oil (15.0%), olive oil-laurel mixture (15.0%) and rosemary (15.0%) for headache, quince seed (15.0%), rosehip (24.0%), black pepper (22.0%) and blackberry leaves (15.0%) for diarrhea, honey (25.0%), cinnamon (14.0%), banana (25.0%) and kefir (22.0%) for rectal bleeding, wet cupping (20.0%), hot spring (20.0%), black seed oil (30.0%) and leech therapy (11.0%) for loss of sensation and weakness in the arm, exercise (26.0%), hot spring (21.0%), wet cupping (17.0%) and acupuncture (7.5%) for loss of sensation and weakness in the leg, wet cupping (37.0%), acupuncture (18.0%) and bioenergy (13.0%) methods for eye involvement (Table IV).

Table V: Investigation of Use of CIHA According to Clinical Symptoms with Regression Analysis.

	Use of CIHA			
	B	**Beta**	**t**	**p**
Constant	1.840		9.424	< 0.0001
Genital ulcer	0.180	0.178	2.854	**0.005
Rectal bleeding	-0.137	-0.101	-1.612	0.108
Weakness and loss of sensation in the arm	-0.173	-0.178	-2.842	**0.005

R = 0.264 R^2 = 0.070 F = 6.078 p = 0.001

DISCUSSION

Evaluation of the QoL of patients with BD with disease-specific scales such as BD-QoL is valuable since it enables the comparison of the QoL in patients living in different cultures, determination of common factors affecting the QoL in these patients, and ultimately the possibility of creating a common strategy to reduce negative factors. This study is the first to examine the CIHA used by patients with BD to cope with symptoms and their relationship with QoL. Therefore, it will be instrumental in filling the gaps in this area and will shed light on new studies to be conducted on patients with BD.

BD, which is a chronic disease, adversely affects the physical and mental health, and the QoL of the patient due to both multisystem organ involvement, and high morbidity and mortality, and physical disabilities (8,10,11). Especially, clinical findings seen in patients with BD chronic and multi-systemic involvement affect QoL negatively. Recurrent and painful oral aphthous cause eating problems, and painful genital ulcers cause negative perception of body image difficulties/unhappiness/dissatisfaction in sexual intercourse, and negative perception of body image (8,10,11). Eye involvement and loss of vision cause significant morbidity and loss of workforce, and joint involvement causes pain, limitation of movement and loss of workforce, which negatively affects QoL.

When QoL was evaluated according to clinical symptoms in

this study, although oral aphthous and headache were common symptoms, it did not affect QoL. Other symptoms such as genital wound, erythema nodosum, joint involvement, tiredness, nausea or vomiting, diarrhea, rectal bleeding, loss of sensation and weakness in legs and arms, and ocular involvement affected QoL at a statistically significant level. According to the studies conducted, the clinical findings that seem to be the most important factors that negatively affect the QoL, include tiredness (8,24,25), genital ulcers (8,11), joint involvement (1,8,11,25) and ocular involvement (8,11,13,25) similar to our study. Results of the regression analysis showed that especially joint involvement, rectal bleeding, ocular involvement, number of attacks, and disease activity were determinants by 42.5%. Bernabe et al. (2010) reported that the most powerful symptoms that negatively affect QoL are joint, stomach and intestinal involvement, similar to our study (1).

Our study showed that having an attack in the past year, increased number of attacks, and having an active disease decreased QoL. Similar to our findings, different studies have shown that the QoL decreases when the disease is active (15,24,25).

Our study showed that 37.5% of patients with BD have been using CIHA for the last 1 year. Since this study is the first study on the use of CIHA in patients with BD, the findings will be discussed with the research results regarding the use of CIHA in similar symptoms arising from other etiologies.

Nowadays, the interest in using CIHA has increased due to patients' desire to take more control and responsibility in their own treatments, efforts to reach interventions to reduce symptoms, insufficient time of the healthcare team, high cost of current treatments, desire to feel better mentally, and inability to satisfy with modern medical methods (26,27).

Therefore, Behçet's patients may have preferred CIHA because they could not cope with recurrent symptoms that negatively affect QoL, were not satisfied with the treatment and were afraid of drug side effects. Our study found that those with genital ulcers, rectal bleeding, and those with loss of sensation in the arm used statistically significant more CIHA. Genital ulcers seen in BD are painful. In addition to pain, it causes difficulties in physical activity. One or more may exist. Genital ulcers are one of the symptoms that usually heal in 10-30 days and most affect QoL in BD. This is also true for patients with rectal bleeding. The reason that these patients have preferred CIHA may be the sociodemographic structure of our country; perhaps they avoided consulting a physician because they were embarrassed about genital and rectal examinations (28). In addition, they may have tried to use these methods rather than going to the clinic because they have access to these methods more easily, and they think they are more natural. We found that patients frequently used wet cupping (24.0%), St. John's wort oil (19.0%), olive oil (19.0%) and acupuncture (7.1%) to cope with this symptom.

Erras et al (2013) reported that wet cupping application in patients with oral and genital aphthouses significantly reduced the number of attacks per month, the number of ulcers per attack, and the duration of attacks, and 91.7% of the patients in the intervention group had a complete response to oral aphtosis (29).

We found that St. John's wort which is used in many areas such as smaller wounds, sunburns, blunt traumata, ulcers, varicose, hemorrhoids, myalgia, decubitus, keloid scars, and tooth extraction, is also used by patients with BD for genital ulcers. St. John's wort, a medicinal plant widely used in skin diseases such as atopic dermatitis, psoriasis and herpes infection with its anti-inflammatory, antimicrobial, and anticancer properties, is clinically effective against herpes labialis and herpes genitalis (30). St. John's wort produced significant reductions in genital ulcer symptom scores (such as pain and itching, blister number and size of the affected area) in two independent double-blind, randomized, placebo-controlled studies (30). Therefore, randomized controlled trials (RCTs) can be conducted to use St. John's wort oil in BD. We also found that 7.1% of the patients used acupuncture for genital ulcers.

We found that the weakness and loss of sensation in the arm in BD are determinative in the use of CIHA. Clinics observe neurological symptoms for five years after the diagnosis of BD. Different studies reported that the frequency of neurological involvement varies between 2.2-50% (31). The National Health Interview Survey (NHIS) (2007) reported that 44.1% of patients over the age of 18 with neurological disorders did not benefit from traditional drug treatments, and used at least 1 CIHA (32). The debilitating symptoms that cause loss of sensation in the arm can lead to significant impairments in the patient's working life and daily life activities (33). This may have led patients with BD to the use of CIHA. We found that the patients used cupping (20.0%), spa (20%), black cumin oil (30.0%) and Hirudotherapy-leech (11.0%) to cope with the symptom of loss of sensation and weakness in the arm. A systematic review published on the use of cupping therapy in many medical conditions reported that it is frequently used for facial paralysis, stroke rehabilitation, and cervical spondylosis, and has beneficial effects for painful conditions and facial paralysis (34). Patients with BD may also have used it to deal with loss of sensation in the arm and leg.

Also, when we examine CIHA that patients with BD use for other common clinical symptoms, we see that black mulberry molasses (32.0%), carbonated water (14.6%), alum (9.3%), coriander (9.3%), pollen-propolis mixture (%5.3) and thyme juice mouthwash (4%) are frequently used for oral aphthous. QoL of patients with BD with oral aphthous is worse than those without oral aphthous, and oral aphthous cause pain and negatively affect the patient's social life and daily activities. Oral health-related quality of life is low in patients with BD. Therefore, patients may have applied to CIHA methods (12). Demir Dogan et al. (2017) reported that black mulberry molasses prevented the development of radiation-induced oral mucositis and reduced its severity (35). Coriander is an effective plant against oral pathogens, it has antioxidant, anti-inflammatory, analgesic and antimicrobial properties (36). Studies reported that coriander oil applied in patients with oral infections like periodontal abscess, periapical abscess, chronic periodontitis, periapical granuloma, dental

caries has antibacterial activity against Streptococcus salivarius, Streptococcus sanguis and Lactobacilli acidophilus (37). Studies reported that mouthwash formulations consisting of thyme, laurel, rosemary and sage oils are effective against microorganisms affecting the oral cavity (38). Therefore, patients with BD may have tried and benefited from these products. So, experimental studies are needed related to the use of these methods by patients with BD.

We found that patients with BD frequently used honey (40.0%), propolis (18.0%), wet cupping (13.0%), Reiki (5.0%), bioenergy (4.0%) in order to cope with tiredness, which is a common symptom seen in the majority of BD (90.3%). Propolis is a bee product commonly used for tiredness. It activates macrophages, contains flavonoids, amino acids, and many vitamins, has antibacterial, antiviral, and anti-inflammatory effects (39). Other than this, we found that patients with BD use energy therapies such as Reiki and bioenergy to cope with tiredness. The studies on the therapeutic effect of Reiki reported that it has effects such as relieving pain (especially postoperative and cancer), reducing anxiety/-depression, improving QoL, and reducing tiredness (40,41). It is noteworthy that Reiki, which is most commonly used to relieve tiredness in cancer patients (40,41), is also used in BD. This situation can be taken into account in experimental studies where tiredness will be evaluated in BD.

We see that patients with BD suffering from joint involvement, which is the most important symptom affecting QoL in BD, use methods such as wet cupping (15.5%), hot spring (9.0%), bioenergy (7.0%), lemon-garlic cure (8.0%), black cumin oil. In another disease group, osteoarthritis, pulsatile dry cupping has been reported to reduce joint pain and improve QoL (42). Also, a RCT in which the effect of the hot spring was examined in patients with knee osteoarthritis reported that the application of the hot spring reduced pain and was effective in improving physical function in patients with arthritis (43). Therefore, it is inevitable for BD to apply methods such as cupping and hot springs for joint involvement, which is the symptom that most affects QoL by causing movement limitation and pain in BD.

We see that they use cupping (37.0%), acupuncture (18.0%) and Reiki (11.0%) for ocular involvement, which is another symptom that negatively affects the QoL in BD.

We see that acupuncture is also used by patients with BD for ocular involvement. Acupuncture is used for macular degeneration, glaucoma, watery eyes, dry eyes, cataracts and many eye ailments (44). A study evaluating the effect of acupuncture on visual function in patients with nystagmus, reported improvement in visual functions and increase in QoL (45).

Limitations of the study

Our findings are limited to the research sample and cannot be generalized to all Behçet's patients. Therefore, we recommend that researches on the subject be conducted in larger sample groups.

And, since this study is the first study on the use of CIHA in patients with BD, another study limitation is that the discussion part is conducted with different disease groups.

CONCLUSION

We determined that there are factors such as having an attack in the past year, the number of attacks, and the disease activity in addition to symptoms such as genital ulcers, erythema nodosum, joint involvement, fatigue, nausea or vomiting, diarrhea, rectal bleeding, loss of sensation and weakness in the arms and legs, eye involvement, that are affecting the QoL highly. In addition, we found that 37.5% of the patients have used the CIHA in the last 1 year to cope with the symptoms. Symptoms of the genital ulcer and loss of sensation in the arm were found to be determinant in the use of CIHA. Physicians and nurses working in rheumatology or related fields should routinely evaluate each symptom separately while taking the patient's medical history into consideration, and question the CIHA they use specific to each symptom. Thus, patients should be prevented from using CIHA hidden and unconsciously, and their treatment being adversely affected.

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Ethics Committee Approval:

This research complies with all the relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration, and has been approved by the University Human Research Ethics Committee, Zonguldak Bulent Ecevit University (approval number: 805).

Informed Consent:

All the participants' rights were protected and written informed consents were obtained before the procedures according to the Helsinki Declaration.

Author Contributions:

Concept| - Z.E.; Design - Z.E., M.A.K.; Supervision - Z.E; Resources - Z.E., M.A.K. U.D; Materials - Z.E., M.A.K.; Data Collection and/or Processing – M.A.K; Analysis and/or Interpretation - Z.E; Literature Search – Z.E., M.A.K. U.D; Writing Manuscript - Z.E., M.A.K. U.D; Critical Review - Z.E., M.A.K. U.D.

Conflict of Interest:

The authors have no conflict of interest to declare.

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