Investigation of the Effects of Physical Therapy and Spa Treatment on Pain and Sleep Quality in Patients with Osteoarthritis

Investigarea Efectelor Kinetoterapiei și ale Tratamentului Balnear asupra Durerii și Calității Somnului la Pacienții cu Osteoartrită

Aysel Gürcan ATÇI1

Abstract

Introduction: Osteoarthritis (OA) is a very common degenerative process that increases with age, is slowly progressive, and leads to articular cartilage destruction. It has been determined that especially falling asleep, frequent sleep interruption, and waking up early are the main sleep problems in patients with arthritis. In the international treatment guidelines of patients with osteoarthritis, follow-up is primarily done by combining pharmacological treatments with non-pharmacological treatments. Another important treatment method is spa therapy. In this study, we tried to understand the effectiveness of the treatment by following the sleep quality index and Visual Analogue Scale (VAS) score values of the patients with osteoarthritis who received physical therapy or spa treatment in an inpatient or outpatient setting. Materials and Methods: This prospective, randomized controlled study was conducted in Kütahya Yoncali Physical Therapy and Rehabilitation Hospital on 122 patients diagnosed with osteoarthritis between 2012 and 2014 and admitted to the inpatient or outpatient program. The cases were divided into 5 groups. Group 1 is the control group. Group 2 consisted of outpatient physical therapy. The third group consisted of 16 patients who received outpatient spa treatment. The fourth group was hospitalized for 15 days and 1-hour physical therapy. The fifth group consisted of 31 patients who received inpatient spa treatment. The patients were evaluated before the treatment (1st measurement), at the end of the treatment (2nd measurement). Pain assessments (VAS), physician's and patient's global assessment were made with the Pittsburgh Sleep Quality Index (PSQI). Results: According to the cut-off value of the PSQI total score, a decrease in sleep quality was detected in 86.5% of the patients (PSQI>5). A significant difference was found especially between the entry and exit PSQI values in group 4 cases. (p< 0.05). Discussion: As a result, OA is a degenerative process that is frequently encountered in daily practice and that impairs sleep quality, as sleep quality disorder increases, movement disorders and pain that limit daily life increase. One of the most

Accepted for publication on 25.03.2022; Published online on 29.03.2022;

For citation: Atci, A.G. (2022). Investigation of the Effects of Physical Therapy and Spa Treatment on Pain and Sleep Quality in Patients with Osteoarthritis. Revista Română de Kinetoterapie. 28(48),35-45

¹ Baltalimanı Metin Sabancı Bone Diseases Training and Research Hospital, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Istanbul, Turkey; drburakatci@hotmail.com

effective treatments in non-pharmacological treatment is spa and balneotherapy. As a result of our observations and study, we think that inpatient physical therapy and spa treatment made a significant improvement in the patient's pain scores and contributed positively to the treatment process by increasing the sleep quality.

Keywords: osteoarthritis, spa treatment, sleep quality

Rezumat

Introducere: Osteoartrita (OA) este un proces degenerativ foarte frecvent a cărui incidență crește odată cu vârsta; evoluează lent, progresiv și duce la distrugerea cartilajului articular. S-a stabilit că în special adormirea, întreruperea frecventă a somnului și trezirea devreme sunt principalele probleme de somn la pacienții cu artrită. În ghidurile internaționale de tratament ale pacienților cu osteoartrită, continuarea tratamentului se face în primul rând prin combinarea tratamentelor farmacologice cu tratamente non-farmacologice. O altă metodă importantă de tratament este terapia balneară. În acest studiu, am încercat să înțelegem eficacitatea tratamentului urmărind indicele de calitate a somnului și valorile scorului Visual Analog Scale (VAS) la pacienții cu osteoartrită care au urmat un program de kinetoterapie sau tratament balnear în regim de spitalizare sau în ambulatoriu. Materiale și Metode: Acest studiu prospectiv, randomizat controlat, a fost realizat la Kütahya Yoncali Physical Therapy and Rehabilitation Hospital pe 122 de pacienți diagnosticați cu osteoartrită între 2012 și 2014, care fie au fost internați în spital fie s-au prezentat la serviciul ambulatoriu. Cazurile au fost împărțite în 5 grupuri. Grupul 1, grupul de control. Grupul 2 a urmat programul de kinetoterapie în ambulatoriu. Al treilea grup a fost format din 16 pacienți care au primit tratament spa în ambulatoriu. În al patrulea grup au fost pacienți spitalizați timp de 15 zile și care au făcut câte 1 oră de kinetoterapie zilnic. Al cincilea grup a fost format din 31 de pacienti care au primit tratament balnear. Pacientii au fost evaluați înainte de tratament (prima evaluare), la sfârșitul tratamentului (a doua evaluare). Evaluarea durerii (VAS) și evaluarea globală au fost făcute cu Pittsburgh Sleep Quality İndex (PSQI). Rezultate: Conform valorii de limită a scorului total PSQI, a fost detectată o scădere a calității somnului la 86,5% dintre pacienți (PSQI>5). O diferență semnificativă a fost găsită în special între valorile PSQI de intrare și de ieșire în grupul 4 (p<0,05). Discutie: Ca urmare, OA este un proces degenerativ care este frecvent întâlnit în practica zilnică și care afectează calitatea somnului, pe măsură ce tulburarea calității somnului crește, tulburările de mișcare și durerile care limitează viața de zi cu zi cresc. Una dintre cele mai eficiente abordări în terapia non-farmacologică este spa-ul și balneoterapia. Ca rezultat al observațiilor și studiului nostru, credem că kinetoterapia și tratamentul balnear în regim de internare au adus o îmbunătățire semnificativă a scorurilor durerii pacientului și au contribuit pozitiv la procesul de tratament prin creșterea calității somnului.

Cuvinte cheie: osteoartrita, tratamentul balnear, calitatea somnului

Introduction

Osteoarthritis (OA) is a very common degenerative process that increases with age, is slowly progressive, and leads to articular cartilage destruction. It is frequently seen in the knee, hip, and waist joints in the joints that are significantly loaded. The frequency is higher in women [1]. It can completely affect individuals' quality of daily life and increase mortality and morbidity rates with age. The pain experienced by patients with osteoarthritis affects every aspect of their lives, and as a result of limited mobility, some patients cannot be very mobile and live dependent on home. As a result, this process leads to mental problems, sleep quality deteriorates in patients, and this process lowers the pain thresholds of patients [2].

It has been reported in publications that sleep disorder accompanies many rheumatic diseases. It has been determined that especially falling asleep, frequent sleep interruption, and waking up early are the main sleep problems in patients with arthritis [3]. It is also known that disturbed sleep can have negative effects on pain, fatigue and psychological state; therefore, there is a relationship between sleep quality and clinical and psychological symptoms of the disease, there is a multifaceted interaction [4].

In the international treatment guidelines of patients with osteoarthritis, follow-up is primarily done by combining pharmacological treatments with non-pharmacological treatments. Since OA is seen especially in elderly patients, the side effects of pharmacological treatments limit the use of drugs in these patients. Non-pharmacological treatments include: patient education, diet and weight loss, exercise, acupuncture, transcutaneous electrical nerve stimulation (TENS), laser, pulsed electromagnetic field (EMF), ultrasound (US), insoles, orthotic devices (knee brace/patellar tape/elastic bandage).

Another important treatment method is spa therapy. In the rheumatic diseases diagnosis and treatment guidelines published in our country in recent years, it has been reported that at least two weeks of balneotherapy and/or SPA treatment can be applied in combination with physical therapy agents and exercises, provided that the physical therapy physician approves [1]. It can be combined with physical therapy or it can be given independently.

The term balneotherapy comes from the Latin *balneum* (bath). Thermal waters generally refer to mineral-rich waters with an average temperature of 34 degrees. With Hydrostatic forces (Archimedes' principle) as its mechanism of action, water provides relative pain relief by reducing the load on the painful and arthritic joint. In addition, it is also used to reduce oedema and pain relief in painful joints. Taking a bath at certain intervals in mineral or thermal water has soothing, decongestant, muscle relaxant, analgesic, regenerative and vasodilator effects [2]. In addition, considering the sulphur-rich hot spring waters, the effect of sulphur compounds on joint tissues and reducing rheumatic symptoms may be effective.

In this study, we tried to understand the effectiveness of the treatment by following the sleep quality index and Visual Analogue Scale (VAS) score values of the patients with osteoarthritis who received physical therapy or spa treatment in an inpatient or outpatient setting.

Materials and Methods

Design

This prospective, randomized controlled study was conducted in Kütahya Yoncalı Physical Therapy and Rehabilitation Hospital on 122 patients diagnosed with osteoarthritis between 2012 and 2014 and admitted to the inpatient or outpatient program. Approval was obtained from the Clinical Research Ethics Committee of Kütahya Faculty of Medicine in 2014.

Participants

122 patients diagnosed with Osteoarthritis and admitted to the inpatient or outpatient program in Kütahya Yoncalı Physical Therapy and Rehabilitation Hospital between 2012 and 2014 were evaluated by the researcher for suitability for the study.

Inclusion Criteria:

- 1. Between the ages of 40-70;
- 2. Diagnosed with primary knee, hip, shoulder, waist osteoarthritis according to the diagnostic criteria of the American College of Rheumatology;
- 3. Those who have not received spa treatment or balneotherapy in the last 1 year.

Exclusion Criteria:

- 1. Those with secondary osteoarthritis due to various diseases
- 2. Having obvious pathology in the waist, hip and ankle joint that will affect the results,
- 3. With decompensated organ failure,
- 4. With active tumours,
- 5. Having a disease progressing with bleeding,
- 6. Having an infectious disease with fever,
- 7. Those who have undergone severe trauma or surgery for osteoarthritis in the last 6 months
- 8. Patients with advanced hypertension, coronary artery disease, chronic obstructive pulmonary disease.
- 9. Those who have a known psychiatric disease and receive medical treatment.

All patients with CAD, HT and COPD were treated if physical therapy and or spa treatment were allowed after the opinion of a cardiology and chest diseases specialist.

Randomization

122 patients who met the study criteria and approved the patient information form were divided into groups using a random numbers table on the computer using the simple randomization method. It was then evaluated by the physician and statistician who performed the study.

Attempt

The cases were divided into 5 groups.

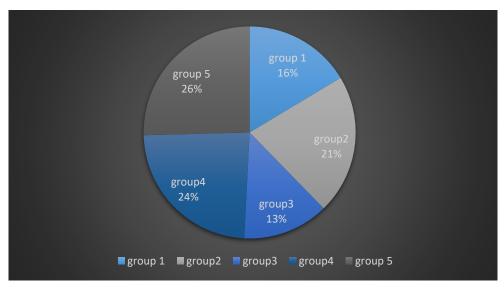
Group 1 is the control group and was not included in the spa or physical therapy protocol. Physical therapy protocol - a total of 10 sessions of physiotherapy were applied to the patients for 10 days, one session per day. Treatment applications were applied in order of hot pack, TENS, short wave diathermy. The physiotherapy program did not include exercise. First, a hot pack was applied to the diseased joint for 20 minutes. Then, TENS between 60-100 Hz was applied to the diseased joints for 20 minutes, with a pulse duration of 60 ms. The frequency was increased until it reached the frequency that the patient felt comfortable and did not cause contraction. It was applied as continuous short-wave diathermy at 27.12 MHz frequency for 20 minutes. Group 1 was followed up for 15 days and paracetamol 500 mg twice a day was started in cases with severe pain. It consisted of 20 patients.

Group 2 consisted of outpatient physical therapy. Total consisted of 26 patients. The patients received outpatient physical therapy for 1 hour, 5 days a week.

The third group consisted of 16 patients who received outpatient spa treatment.

The fourth group was hospitalized for 15 days and 1 hour of Physical therapy was applied in a single session 5 days a week. It consisted of 29 patients in total.

The fifth group consisted of 31 patients who received inpatient spa treatment. (Graphic 1)



Graphic 1: Patients in study groups.

The patients in the second group (Traditional application group = Group 2) received spa treatment for 2 weeks, 5 days a week (10 sessions in total), and the patients in the third group (Alternative application group: Group 3) received spa treatment 2 times a week for 5 weeks (10 sessions in total). In the treatment, a plain water bath at 38°C was applied in the pool for 20 minutes a day. The spring outlet temperature of Yoncalı Thermal Water is 40-44 degrees and the total mineral concentration is 782.565 mg/lt. In Table 1, thermal water properties and mineral concentrations are indicated. All patients were allowed to take a maximum of 2 g/day oral paracetamol in proportion to the severity of pain.

Table 1: Yoncalı Thermal Water mineral concentration

Parameter	Scale unit	Result	Result	
Sodium	Mg/L	107,4		
Chlorine	Mg/L	10,9		
Sulfate	Mg/L	162,2		
Magnesium	Mg/L	31,64		
Calcium	Mg/L	111,8		
Fluoride	Mg/L	1,92		
Bicarbonate	Mg/L	429,4		
Cilicate acid	Mg/L	50,3		

Evaluation of the Patients

The patients were evaluated before the treatment (1st measurement), at the end of the treatment (2nd measurement), and at the 12th week after the treatment (3rd measurement); pain assessment (VAS), physician's and patient's global assessment (VAS) were made with the Pittsburgh sleep quality index (PSQI).

The VAS consists of a 10 cm (or 100 mm) long line drawn on the horizontal or vertical axis. The distance from the lowest VAS value to the patient's mark is measured in mm (0-100) [5].

The Pittsburgh Sleep Quality Index evaluates sleep quality over the last month in 19 questions. It consists of seven components that assess subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep medication, and daytime dysfunction. The response of each is scored between 0-3 according to symptom frequency. The total score ranges from 0-21 (range = 0-21). Scores of six or higher indicate impaired sleep quality [6].

Statistical analysis

Statistical analyses were performed using IBM SPSS for Windows, version 22.0 (IBM Corporation, Armonk, NY, USA). The normality of continuous numerical variables was investigated using the Shapiro–Wilk test. The results of numerical variables were presented as mean ± standard deviation. Because the variables were not normally distributed, non-parametric tests were used for intergroup comparisons. To find the level of significance between the groups, the Kruskal–Wallis test was used for continuous variables and the Chi square test or Fisher's exact test was

used for categorical variables to compare the data. Correlations were evaluated using Spearman's rho correlation coefficient. A p value of <0.05 was considered to be statistically significant.

Results

Our study was conducted on a total of 122 patients. Group 1 was the control group and no treatment was given. Group 2 was the outpatient physical therapy group and the total number of patients was 26. Group 3 was the outpatient spa patients and the number of patients was 16.

Group 4 is the group in which inpatient physical therapy and rehabilitation is applied, and the total number of patients is 29. Group 5 is the group in which inpatient spa treatment is applied, and the total number of patients is 31. The mean age of patients with OA was 57.35DI. 79.5% of the patients were female, 85% of the female patients were in the postmenopausal period, 86% of the patients with OA were married. 65 of 122 patients had gonarthrosis, 38 had coxarthrosis and gonarthrosis, and 17 patients had coxarthrosis.

There was Hypertension accompanying OA in 35 patients, Hypertension and Diabetes in 11 patients, hyperthyroidism in 3 patients, coronary artery disease in 3 patients, asthma in 2 patients and Diabetes in 18 patients.

According to the cut-off value of the PSQI total score, a decrease in sleep quality was detected in 86.5% of the patients (PSQI>5). A significant difference was found especially between the entry and exit PSQI values in group 4 cases (p< 0.05). (Table 2)

Table 2: Clinical and demographic characteristics of patients diagnosed with OA and healthy controls (mean \pm SD, or n, %).

	Group 1	Group 2	Group 3	Group 4	Group 5
Age, years (mean±SD)	57 ±4.25	56.9 ±5.18	58.5 ±4.13	57.36 ±5.36	56.65 ±5.14
Gender	F:16	F:16	F:12	F:25	F:28
	M:4	M:10	M:4	M:4	M:3
Education					
Illiterate	8	12	7	9	14
Basic education	10	14	9	13	17
High school/ University	2			3	
Disease Duration		4.4 years	3.1 years	3.9 years	3.2 years
Smoking					
Yes	5	7	3	7	9
No	15	19	15	18	24
VAS Score		B:7,6±3.06	B:7,75±2.19	B:7,28±1.94	B:8,16±2.78
		A:5.48±2.02	A:5,08±1.82	A:4,8±1.49	A:4,80±1.44
		P:0.224	P:0.212	p:0.212	P: 0.212

Group 1: Control group. Group 2: Patients coming to outpatient daily physical therapy. Group 3: Patients coming to outpatient spa treatment. Group 4: Inpatient Physical therapy Group 5: Patients who were hospitalized and treated with spa treatment. B: Before treatment. A: After treatment. P<0.05 was considered statistically significant.

Table 2: Mean PSQI scores of patients with osteoarthritis and controls (mean \pm SD) Data are presented as mean \pm standard deviation (median). P<0.05 was considered statistically significant.

	Group 1	Group 2	Group 3	Group 4	Group 5
Sleep quality	0.40±0.11	B:1.32±0.75	B:1,77±0.71	B:2.35±0.50	B:2.20±0.70
		A:1.02±0,28	A:1.55±0.60	A:1.60±0.10	A:1.10±0.35
Sleep latency	0.13±0.09	B:1.62±0.66	B:2.10±0.32	B:1.92±0.70	B:1.85±0.54
		A:1,32±0.40	A:1,10±0.21	A:1,05±0.25	A:0.90±0.15
Sleep efficiency	0.40±0.21	B:0.82±0.66	B:1.51±0.66	B:1.96±0.66	B:1.17±0.66
		A:0,53±0.12	A:1,11±0.32	A:1,20±0.58	A:0,90±0.59
Sleep duration	0.20±0.04	B:1.44±0.66	B:2,21±0.70	B:1.56±0.70	B:2.27±0.62
		A:1,12±0.49	A:1,51±0.56	A:1,41±0.32	A:1,11±0.32
Sleep	0.0	B:0.20±0.11	B:0.15±0.14	B:0.52±0.05	B:0.12±0.09
medication		A:0.20±0.11	A:0,15±0.02	A:0,42±0.02	A:0,12±0.02
Daytime sleep	0.18±0,074	B:1.78±0.70	B:1.61±0.40	B:1.92±0.61	B:1.36±0.70
dysfunction		A:1,54±0.32	A:1,12±0.12	A:1,23±0.35	A:0,46±0.28
Sleep	0.51±0.25	B:1,94±0.70	B:1,84±0.32	B:2,25±0.72	B:2,14±0.49
disturbance		A:1,44±0.43	A:1,34±0.20	A:1,20±0.36	A:1.05±0.17
Total score	1.83±0.92	Before:9.12	Before:11.25	B:13.8	B:12.6
		After:7.17	After:7,83	A:8.04	A:6.01
P value	P>0.05	P>0.05	P>0.05	P>0,05	P<0.05

Discussion

OA and sleep disturbance are very common. Sleep problems occur in approximately two-thirds of patients with osteoarthritis. The prevalence of sleep disorders in people of the same age group is 2 times higher in individuals with OA. Pain has been identified as the main cause of sleep disturbance. They associated increased daytime pain with poor quality sleep, and it was found that the pain increased after one day.

In studies involving OA and sleep quality analysis, it was reported that OA was impaired in sleep quality in a study involving knee and hip OA patients over 60 years of age [7, 8]. Hawker et al. reported that knee OA patients over 60 years of age had problems falling asleep (31%), maintaining sleep (81%), waking up early in the daytime (51%) at least once a week [7]. Also, this study reported that sleep was disturbed in 66% of patients with knee and hip OA, and also determined the severity of arthritis, pain, depressive symptoms, and restless legs syndrome as independent risk factors for sleep disturbance.

In a study conducted on 2682 patients with a diagnosis of knee and hip OA, sleep disturbance was reported to be an important problem in the patient group, and it was shown that regardless of the symptoms, only radiographic knee osteoarthritis did not affect sleep quality [9]. In another study comparing patients with knee OA and patients without radiographic knee OA, it was stated that both groups had similar sleep problems, and it was also emphasized that knee pain was the main factor causing sleep disturbance [10].

In our study, the average sleep quality index scores of the patients before the treatment were determined as 12.3. In particular, the patients stated that they had difficulty falling asleep and sleeping problems, which supports the literature, and stated that they woke up more tired the

next day and more painful than the previous day. They reported that the patients in our study had difficulty in maintaining their normal routine life the next day, when the sleep disorder lasted more than 3 days a week. This situation increases the pain that will occur the next day and puts the patient in a vicious circle. Breaking this cycle should be the main treatment practice in OA patients, both to reduce the patient's pain and to provide mental relief. The sleep disorder in question cannot be treated with medical treatment alone. For this reason, it is obvious that spa and SPA treatment, which can both reduce the patient's pain and relieve the patient spiritually, is a very important modality in the current and most effective treatment. However, when the literature was reviewed, no comprehensive study was found on the sleep quality index for OA, including physical therapy and spa treatment.

In OA cases, the frequency of spa treatment can be determined by determining the method and dose, and it can be applied at regular and repeated intervals, in various forms such as bathing, drinking and inhalation, and in combination with other treatments (such as physical therapy agents, exercise [11, 12]. The mechanism of action of spa treatments has not been fully explained today. It is stated that the therapeutic and relaxing effect can be mechanical, chemical and thermal effects. Thermal therapy has beneficial effects on muscle tone, joint mobility. A series of chemical and physical reactions occur in a person immersed in 35-degree spa water. Diuresis, natriuresis and cardiac output increase. However, literature studies have reported a decrease in the circulating values of Prostaglandin E2 (PGE2) and leukotriene B4 (LTB4) a parameter that increase in inflammation after spa therapy. In addition, there is literature in which adipocytokines, which play an important role in the pathophysiology of OA, especially with their proinflammatory effects and cause joint and cartilage deterioration, regress after spa treatment [13, 14, 15]. As it can be understood from the literature review, spa treatment has efficacy in the non-pharmacological treatment of OA.

In studies where the effect of applying thermo-mineral waters of various heat and chemical properties as a bath for 3-6 weeks and for an average of 20 minutes in patients with knee, hip and vertebral OA who were followed up due to OA, pain severity, analgesic drug use, It has been reported that there is a significant improvement in functional status and quality of life [16].

In addition, in another study comparing spa treatment applied only as a bath with home exercise program and non-steroidal drug use, it was shown that spa treatment applied for 1-3 weeks was superior in terms of pain level and functionality. [17]

In our study, a significant decrease was found in the mean VAS scores after the spa treatment. The best results were obtained in the group that received physical therapy together with the spa treatment.

Conclusion

As a result, OA is a degenerative process that is frequently encountered in daily practice and that impairs sleep quality, as sleep quality disorder increases, movement disorders and pains that limit

daily life increase. One of the most effective treatments in non-pharmacological treatment is spa and balneotherapy. As a result of our observations and study, we think that inpatient physical therapy and spa treatment made a significant improvement in the patient's pain scores and contributed positively to the treatment process by increasing the sleep quality.

Ethics: Written informed consent was obtained from the participants in accordance with the Helsinki Declaration. Approval was obtained from the Clinical Research Ethics Committee of Kütahya Faculty of Medicine in 2014.

Funding: 'No Funding' in the manuscript research.

Author Contribution: The study was planned, executed, concluded and written by the author.

Conflict of Interest: The author has no conflicts of interest to declare.

References

- [1] Tuncer, T.; Cay, H.F.; Kacar, C.; Altan, L.; Atik, O.Ş.; Aydın, A.T. et al. (2012). Evidence-based recommendations for the treatment of knee osteoarthritis: Consensus report of the Turkish Rheumatism Research and Control Association. *Turk J Rheumatol.* 27:1-17.
- [2] Quintela, M.M. (2004). Thermal knowledge and therapies: a comparative view of Portugal and Brazil. *Hist Cienc Saude- Manguinhos*. 11:239-60.
- [3] Drewes, A.M.; Nielsen, K.D.; Hansen, B.; Svendsen, L. (2000). A longitudinal study of clinical symptoms and sleep parameters in rheumatoid arthritis. *Rheumatology (Oxford)*. 39:1287-1289.
- [4] Taylor-Gjevre, R.M.; Gjevre, J.A.; Nair, B. et al. (2001). Components of Sleep Quality and Sleep Fragmentation in Rheumatoid Arthritis and Osteoarthritis. *Musculoskeletal Care*. doi: 10.1002/msc.208.
- [5] Gallagher, E.J.; Liebman, M.; Bijur, P.E. (2001). Prospective validation of clinically important changes in pain severity measured on a visual analog scale. *Ann Emerg Med.* 38(6):633-638
- [6] Buysse D.J.; Reynolds, C.F.; Monk, T.H. et al. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res.* 28:193-213.
- [7] Hawker, G.A.; Mian, S.; Bednis, K.; Stanaitis, I. (2011). Osteoarthritis year 2010 in review: non-pharmacologic therapy. *Osteoarthritis Cartilage*. 19:366-374
- [8] Wilcox, S. (2000). Factors related to sleep disturbance in older adults experiencing knee pain or knee pain with radiographic evidence of knee osteoarthritis. *J Am Geriatr Soc.* 48:1241-1251
- [9] Allen, K.D.; Renner, J.B.; DeVellis B. et al. (2008). Osteoarthritis and sleep: the Johnston County Osteoarthritis Project. *J Rheumatol*. 35:1102e1107.
- [10] Hadler, N.M. (1992). Knee pain is the malady not osteoarthritis. *Ann Intern Med*. 116:598-599
- [11] Hizmetli, S. (2011). Hydroclimatology balneotherapy applications for elderly people Education. *Turkish Journal of Physics Medicine Rehab*. 55(Suppl 2):100-3

- [12] Hizmetli, S.; Hayta, E. (2011). Spa treatment. Turkey Clinics. JPM&R. 4:29-34.
- [13] Bellometti, S.; Galzigna, L. (1998). Serum levels of a prostaglandin and a leuko- triene after thermal mud-pack therapy. *J Invest Med.* 46:140-5. 39.
- [14] Ardic, F.; Ozgen, M.; Aybek, H.; Rota, S.; Cubukçu, G.; Gökgöz, A. (2007). Effect of balneotherapy on serum IL-1, PGE2 and LTB4 levels in fibromyalgia patients. *Rheumatol Int*. 27:441-6.
- [15] Fioravanti, A.; Cantarini, L.; Bacarelli, M.R.; de Lalla, A; Ceccatelli, L.; Blardi, P. (2011). Effects of spa therapy on serum leptin and adiponectin levels in patients with knee osteoarthritis. *Rheumatol Int.* 31:879-82.
- [16] Fioravanti, A.; Valenti, M.; Altobelli, E.; Di Orio, F.; Nappi, G.; Crisanti, A. et al. (2003). Clinical efficacy and cost-effectiveness evidence of SPA therapy in of "Naiade" Italian project. *Panminerva Med.* 45:211-7
- [17] Fioravanti, A.; Iacoponi, F.; Bellisai, B.; Cantarini, L.; Galeazzi, M. (2010). Short- and long-term effects of spa therapy in knee osteoarthritis. *Am J Phys Med Rehabil*. 89:125-32.