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Is Hyperbaric Oxygen Therapy Effective in Early-Stage Avascular Necrosis of The Femoral Head?

Erken Evre Femur Başı Avasküler Nekrozlu Olgularda Hiberbarik Oksijen Tedavisi Etkili midir?

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Özet

Amaç: Bu çalışmanın amacı, erken evre (Ficat Evre 1 ve 2a) femur başının avasküler nekrozu hastalarında atmosfer basıncının normalden üç kat daha yükseğe çıktığı basınçlı bir odada yüksek düzeyde oksijene maruz kalmanın (Hiperbarik Oksijen Tedavisi) klinik ve radyolojik sonuçlarını araştırmaktır.

Gereç ve Yöntem: Şubat 2016 ile Kasım 2019 arasında Ficat evre 1 ve 2a FBAN tanısı ile hiperbarik oksijen (HBO) uygulanan ve takip edilen hastalar geriye dönük olarak incelendi. Her hastanın demografik verileri, hastalık özgeçmişleri, tedavi öncesi ve sonrası dönemde uygulanan Harris Kalça değerlendirme formları, iki projeksiyonda (ön-arka ve lateral) konvansiyonel kalça röntgenogramı ve kalça eklem manyetik rözenans görüntüleri (MRG) incelendi. Ficat evrelendirmesine göre hasta patolojileri sınıflandırıldı ve işlem öncesi-sonrası değerler istatistiksel olarak karşılaştırıldı.

Bulgular: Mevcut çalışmada ortalama yaşı 45,4±11,4 (aralık: 22-67) olan 19 erkek ve 6 kadından oluşan 25 hasta değerlendirildi. Hastalara ortalama 40,6±5,32 (aralık: 36-65) gün içerisinde ortalama 30,4±3,55 (aralık: 27-47) seans HBO tedavisi uygulandığı görüldü. HBO tedavisi sonrasında ise 11 hastanın Ficat evresinin ilerlediği, iki hastanın evresi gerilerken yedi hastanınsa sabit kaldığı tespit edildi (p: 0,002). Harris Kalça değerlendirme skoru ortalama toplam değeri işlem öncesinde 43,82±18,55 iken işlem sonrasında 78,47±17,05 seviyesinde olduğu tespit edildi. İşlem sonrası Harris kalça değerlendirme skoru, VAS ve eklem hareket açıklığı ölçümlerinde işlem öncesine göre istatistiksel olarak anlamlı değişim izlendi (p<0,001).

Sonuç: Özellikle genç hastalarda HBO destekleyici bir tedavi yöntemi olarak klinisyenler tarafından değerlendirmeye alınması gereken bir seçenek olarak düşünülebilir.

Anahtar Kelimeler: Hiperbarik oksijen tedavisi, femur başı avasküler nekrozu, kalça ağrısı

Abstract

Objective: The aim of this study was to investigate the clinical and radiological results of exposure to a high level of oxygen in a pressurized chamber in which the atmospheric pressure is raised up to three times higher than normal (Hyperbaric Oxygen Therapy) in patients with early-stage (Ficat Stage 1 and 2a) avascular necrosis of the femoral head (AVNFH).

Material and Method: A retrospective examination was performed on the patients who were administered Hyperbaric Oxygen (HBO) therapy and followed up due to Ficat Stage 1 and 2a AVNFH between February 2016 and November 2019. The Harris Hip Score forms, conventional radiography of the hip, and MRI were analyzed. The Ficat classification was used for grading avascular necrosis.

Results: A total of 25 patients with a mean age of 45.4 ± 11.4 years were evaluated. It was observed that the patients were administered an average of 30.4 ± 3.55 (range: 27-47) sessions of HBO therapy within an average of 40.6 ± 5.32 (range: 36-65) days. After the HBO therapy, it was found that the Ficat stage of 11 patients progressed, while the stages of two patients regressed, and seven patients remained stable (p: 0.002). While the mean total Harris Hip Score was 43.82 ± 18.55 before the procedure, it was found to be 78.47 ± 17.05 after the procedure. After the procedure, a statistically significant difference was observed in Harris Hip Scores, VAS, and the range of motion measurements compared to the values obtained before the procedure (p<0.001).

Conclusion: HBO can be suggested as an option to be considered by the clinicians as a supportive treatment method, especially in young patients.

Key Words: Hyperbaric oxygen therapy, avascular necrosis of the femoral head, hip pain

Objective

Avascular necrosis of the femoral head (AVNFH) is an irreversible disease, which usually causes osteoarthritis of the hip joint, especially in young people. Despite the fact that the reason for the onset of the pathological process has not been fully understood, it has been demonstrated that it can develop as a result of both traumatic and non-traumatic events (1). AVNFH has been defined as a pathological process caused by decreased blood

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perfusion of the bone tissue and a high level of intraosseous pressure. Femoral head ischemia results in the death of marrow and osteocytes and usually results in the collapse of the necrotic segment (2). Since it is difficult to treat the disease and prevent the necrotic process, it is essential to determine the staging of AVNFH carefully and administer the accurate treatment (3). The treatment for the patient varies according to the stage of the avascular necrosis (4). Ficat and Arlet Staging, which is performed based on radiological findings, is of the most common systems used in the staging of AVNFH. It can help predict the collapse on the surface of the joint (5). Conservative treatment methods may be beneficial in patients diagnosed within the asymptomatic period; however, the place of conservative treatment is limited within the current treatment strategy. In the treatment, the primary aim is to eliminate or postpone the need for joint replacement using conservative interventions and interventions involving hip protectors (6). Conservative treatment can be considered as a treatment option in all patients, except for the patients with subchondral fractures within the early stages of the disease (Ficat Stages 1–2). There are many conservative treatment options in the literature, ranging from weight-bearing restrictions and pharmacological agents (bisphosphonates, anticoagulants, statins, and vasodilators) to biophysical therapy (extracorporeal shock wave therapy, pulsed electromagnetic fields, hyperbaric oxygen) (7). These treatments may be ineffective when administered alone; therefore, it is stated in the literature that combined procedures should be preferred (3, 8). Treatment methods, which can be preferred for early-stage AVNFH, aim to change the course of the pathophysiological process that causes the disorder. Hyperbaric Oxygen (HBO) Therapy, which is one of the conservative treatment methods that can be administered, increases tissue oxygenation and reduces edema. In addition, it increases the possibility of improvement of necrosis by inducing angiogenesis. Thanks to the increased vascular network, intraosseous pressure decreases, thereby improving venous drainage and microcirculation (9). The evidence on the clinical validity of this theoretical concept is not yet sufficient; however, HBO therapy in the treatment of AVNFH is thought to be a promising procedure and is recommended as a supportive treatment option, albeit not sufficient alone (10, 11). The aim of this study was to investigate the clinical and radiological results of exposure to a high level of oxygen in a pressurized chamber in which the atmospheric pressure is raised up to three times higher than normal (HBO Therapy) in patients with Ficat Stage 1 and 2a avascular necrosis of the femoral head.

Material and Method

A retrospective analysis was performed on the patients who were administered hyperbaric oxygen therapy due to Ficat Stage 1 and 2a AVNFH between February 2016 and November 2019 in the institution where the authors were employed. The present study included the patients, who were followed up in the Undersea Medicine, Hyperbaric Oxygen and Orthopedics Clinic due to AVNFH, had symptomatic hip pain, had normal results in the conventional radiography, were observed to have necrosis in the femoral head accompanied by bone marrow edema according to the results of the magnetic resonance imaging (MRI), and who had "Kerboul" angle of fewer than 150 degrees. In the retrospective analysis, patients, who had been administered irregular and insufficient HBO therapy, patients with incomplete patient files and imaging archives, and patients, who had no findings other than bone marrow edema in their MRI (Philips, Ingenia 1.5 T, Best - Netherlands), were excluded from the study. The study protocol was approved by the Antalya Training And Research Hospital Ethics Committe (Date: ,12.09.2019, Issue: 20/8) Detailed informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki. Each patient was examined in terms of their demographic data and medical history. In addition, the Harris Hip Score forms, conventional radiography of the hip in two projections (anteroposterior and lateral), and MRI of the hip joint performed before and after the therapy were examined. The diseases of the patients were classified according to Ficat staging.

Hyperbaric Oxygen Therapy: Patients were exposed to 100% inspired oxygen at an absolute 2.5 atmospheres for 90 minutes in a multi-zone pressure chamber using a high-level demand regulator and an oral-nasal mask (Information on minutes, including 45 minutes of oxygen, 10 minutes of air, and 45 minutes of oxygen. During the HBO sessions, 1000 units of vitamin E and 500 mg of vitamin C were administered to the patients per day, as free radical scavengers.

Table 1: Baseline demographic and clinical characteristics of the patients.

Age (years±SD)	Mean + SD	45.4±11.4
	Median (min-max)	44 (22 - 67)
Follow- up (month)	Mean + SD	30.4 ± 9.31
	Median (min-max)	30 (18 - 45)
Average Number of HBO Sessions	Mean + SD	30.4±3.6
	Median (min-max)	30 (27 - 47)
Sex (M/F)	n	19/6
	%	76/24
Etiology (Trauma / Idiopathic / Steroid usage)	n	5/9/11
	%	20/36/44
Affected Side (Right / Left)	n	12/13
	%	48/52
Pre-HBO Ficat Stage	n	13/12
(Stage 1 / Stage 2A)	%	52/48
Post-HBO Ficat Stage	n	5/10/6/4
(Stage 1 / Stage 2A / Stage 2B / Stage 3)	%	20/40/24/16
Progression in the Ficat Stage (Yes / No)	n	11/9

Table 2: Functional outcomescof patients undergone hyperbaric oxygen therapy

N=25		Mean + SD	Median	Mean Difference	p
HHS 1 (Pain)	pre	16.80±8.02	20	-20.00	0.001[1]
	post	31.84±10.80	30		
HHS 2 (Function)	pre	23.32±13.09	19	-18.50	0.001[1]
	post	39.32±7.95	41		
HHS 3 (Defotmity)	pre	1.00±0.76	1	-1.50	0.001[1]
	post	2.48±1.05	3		
HHS 4 (ROM)	pre	2.72±0.94	2.50	-1.65	0.001[1]
	post	4.20±0.97	4.67		
HHC Total	pre	43.82±18.55	40.15	-36.18	0.001[1]
	post	78.47±17.05	80.55		
VAS	pre	6.64±1.60	6	4.00	
	post	3.84±2.34	4		0.001[1]
Hip flexion	pre	41.20±20.27	40	-40.00	0.001[1]
	post	78.40±22.85	90		
Hip extension and external rotation	pre	9.0±4.56	10	-7.50	0.001[1]
	post	15.0±4.78	15		
Hip Abduction	pre	16.40±7.97	10	-17.50	0.001[1]
	post	27.80±8.90	30		
Hip Adduction	pre	6.80±2.84	5	-7.50	0.001[1]
	post	12.20±3.84	15		

[1]Wilcoxon signed-ranks test
HKS: Harris Hip Score
ROM: Range of Motion
VAS: Vizuel Analog Score
SD: Standart Deviasyon

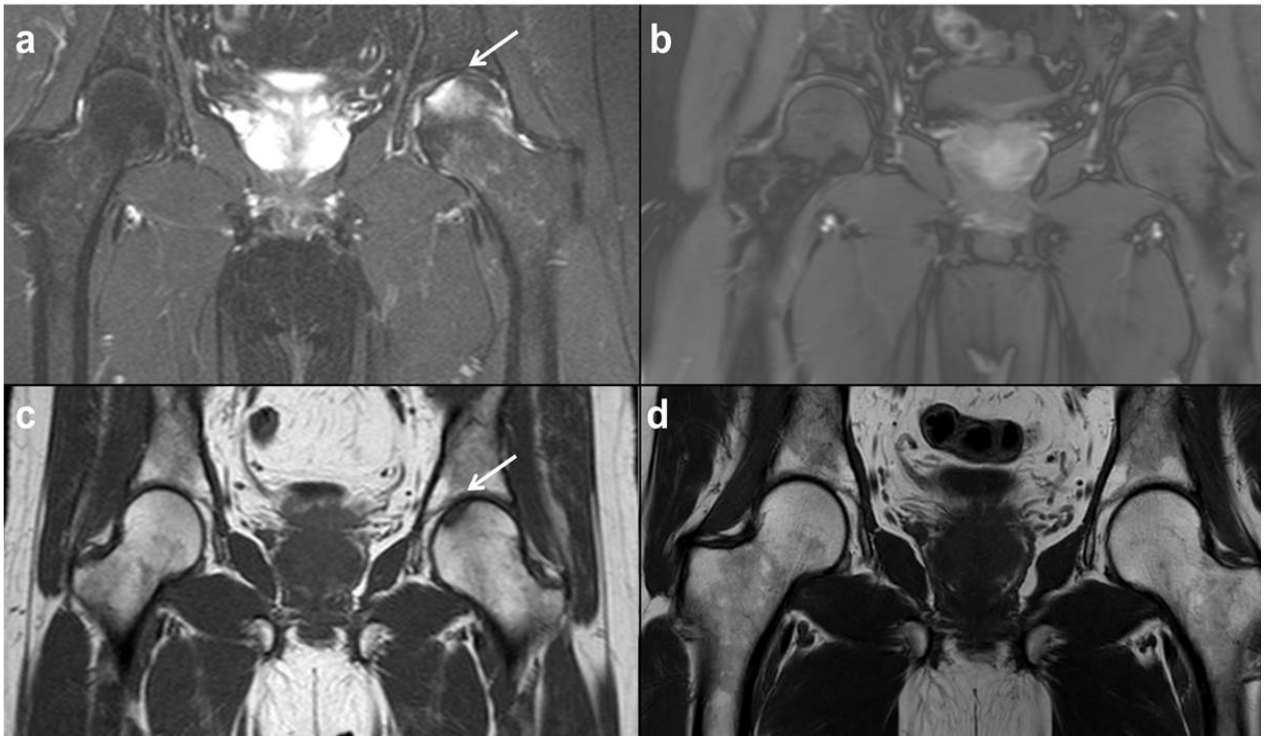

Figure 1. MR scans of a 57-year-old man with a three-week history of left hip pain.(a-c) Coronal T2- and T1-weighted image showing a subchondral low signal intensity line in the superior part of the left femoral head bordered by a very thin line of high signal intensity (white arrow), and by diffuse intramedullary oedema of high signal intensity. (b-d) Completed the 30 daily sessions full HBO treatment protocol. Follow-up MR scan obtained eighteen months after the first MRI showing complete resolution of the oedema and a normal image on both sides.

Statistical Analysis: Descriptive statistics for the continuous variables were presented as Mean and Standard deviation, while count and percentages for categorical variables. Normality test of the variables was performed with Kolmogorov-Smirnov test. Wilcoxon Signed Ranks Test was used for comparing pre and post values for non-normally distributed variables. Statistical significance level was considered as 5% and SPSS (ver: 23) statistical program was used for all statistical computations.

Results

In the present study, a total of 25 patients, consisting of 19 male and six female patients with a mean age of 45.4 ± 11.4 (range: 22-67) years, were evaluated. The mean follow-up period of the patients was 30.4 ± 9.31 months (range: 18 – 45 mo.). While five of the patients had a medical history of trauma and eleven had a history of steroid use, no etiological cause of AVNFH was found in the other nine patients. It was observed that the patients were administered an average of 30.4 ± 3.55 (range: 27-47) sessions of HBO therapy within an average of 40.6 ± 5.32 (range: 36-65) days. Of the patients included in the study, 13 were at Ficat Stage 1, and 12 were at Ficat Stage 2A before the HBO therapy. Following the HBO therapy, Ficat stages progressed in 11 patients, regressed in 2 patients, and seven patients remained stable (p: 0.002) (Table 1). While the mean total Harris Hip Score was 43.82 ± 18.55 before the procedure, it was found to be 78.47 ± 17.05 after the procedure. After the procedure, a statistically significant change was observed in the total Harris Hip Score and each sub-parameter, compared to the values obtained before the procedure ($p<0.001$). Regarding the changes in the pain observed in the patients, the visual pain assessment score decreased by an average of four points after the procedure ($p<0.001$). After the procedure, it was found that hip flexion changed positively by 40 degrees ($p<0.001$), extension and external rotation changed positively by 7.5 degrees ($p<0.001$), abduction changed positively by 17.5 degrees ($p<0.001$), and adduction changed positively by 7.5 degrees (p:0.001) (Table 2). There was no

disruption, atrophic change in the muscles, or decreased range of motion in any of the patients. After the HBO therapy, regression was detected in the MRI results of the two patients, who had significant edema of the femoral head before the therapy (Figure: 1).

Discussion

The most important finding of the present study was that although 55% of the patients were in the advanced radiologic stage, they had better clinical conditions in terms of pain scores and functional conditions after the HBO therapy. While the functional scores of all patients changed positively, their range of motion was observed to have increased in all directions. In a study conducted by Reis et al. on 12 patients, who were evaluated as Steinberg Stage 1, after an average of 100 sessions of HBO therapy, the MRI results of 81% of the patients were reported to have returned to normal (10). In another study, where 78 hips at Stage 1 (39 patients) and 2 (39 patients) were evaluated radiologically, radiological improvement was reported in 88% of patients after an average of 80 ± 24 sessions of HBO therapy (12). In the present study, the stages were found to have regressed in 8% of the patients while progressing in more than half of the patients. This difference may be due to the fact that 48% of the patients were at Ficat stage 2A, the number of HBO sessions was lower compared to the mentioned studies, and that the follow-up period was relatively shorter. Nonetheless, the patients, who were found to have regression in the stages in the present study, were at Ficat stage 2A. In a prospective study evaluating the effect of HBO, 20 patients at Ficat Stage 2 were evaluated. It was reported that the hip joint range of motion of the patients increased significantly, and the pain was felt minimally after 30 sessions of HBO therapy (13). In a meta-analysis of nine studies where 305 healthy controls and 318 cases of HBO were evaluated, the HBO therapy was demonstrated to have a 4.95-fold positive clinical effect compared to the control group (14). In the present study, in which 25 patients were evaluated retrospectively, it was found that the hip joint range of motion and pain scores of the patients had significantly improved. In a study analyzing the change in the quality of life of 73 patients with AVNFH at stage 1 and 2, it was reported that the HBO therapy did not affect the quality of life of the patients, and it changed the Harris Hip Scores positively compared to the values obtained before the procedure (15). The Harris Hip Score of 18 patients who used crutches and were followed up after HBO therapy increased from 55.6 ± 7.8 to 88.8 ± 5.8 in the 3rd month after three months of treatment (16). In the present study, it was found that the total value of the Harris Hip Score increased to 78.47 ± 17.05, while almost all sub-parameters doubled, compared to the values obtained before the treatment. Oxygen is a very important factor in maintaining bone vitality as well as bone healing and remodeling. Osteocytes, osteoblasts, and osteoclasts, which are the three main cells of bone tissue, are oxygen-dependent cells. Among these, osteoclasts are the cells with the highest oxygen requirement. Experimental studies have shown that fibroblast-derived pluripotent stem cells transform into bone tissue when exposed to compressive forces and high oxygen concentrations (17, 18). In another experimental study, it was reported that HBO therapy had a positive effect on angiogenic activity, despite the fact that no positive effect was demonstrated on bone formation (19). The major limitations of the present study were the limited number of patients, relatively short follow-up period, and the retrospective evaluation. Other limitations of the study included the heterogeneity of etiological reasons, the absence of a control group, and the limited number of HBO sessions compared to the literature. Nonetheless, the data obtained from this study will provide preliminary information for future prospective controlled studies. In conclusion, it can be argued that HBO therapy improves pain and functional conditions in patients with Ficat stage 1 and 2a AVNFH. The aim of HBO therapy in the treatment of AVNFH is to postpone the surgical procedures as much as possible. Accordingly, HBO therapy can be suggested as an option to be considered by the clinicians as a supportive treatment method, especially in young patients. This study demonstrates a positive clinical result obtained as a result of HBO therapy at the 30.4 months follow-up in a small group of patients. It can be argued that HBO therapy has a potential role in the management of AVNFH treatment.

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