Original articles

The effect of hyperbaric oxygen therapy on lesion size in early-stage femoral head avascular necrosis

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Abstract
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Introduction: Femoral head avascular necrosis (AVN) is a common orthopaedic condition that occurs when intraosseous microcirculation is compromised. Hyperbaric oxygen therapy (HBOT) increases tissue oxygen concentration, reduces oedema, stimulates angiogenesis, lowers intraosseous pressure, and enhances microcirculation. The aim of this study was to evaluate the effectiveness of HBOT in early femoral head AVN based on magnetic resonance imaging (MRI) findings.
Methods: A total of 37 hips from 25 patients with Ficat Stage 1–2 femoral head AVN, followed between 2018 and 2021 and receiving HBOT at Kayseri City Training and Research Hospital, were retrospectively included. Thirty HBOT sessions of 90 minutes each were administered at 243 kPa pressure (2.4 atmospheres absolute) with 100% oxygen breathing, along with a weight-bearing restriction protocol.
Results: There were 20 females and five males. The mean (standard deviation) age was 46.9 (9.5). In pre-treatment MRI imaging, the mean lesion size was 29.87 (22.64) cm^3 in 20 right hips and 28.84 (14.95) cm^3 in 17 left hips ($P = 0.183$). At the second month after treatment, the lesion size was 12.39 (11.26) cm^3 in 20 right hips and 21.81 (13.56) cm^3 in 17 left hips ($P < 0.001$). The mean pre-post differences for the right and left hips was 17.48 (21.15) cm^3 and 7.02 (5.95) cm^3 respectively (both $P < 0.001$).
Conclusions: Femoral head AVN is a progressive disease, with femoral head collapse exceeding 40% in a five-year follow-up. This study demonstrated a reduction in lesion size associated with HBOT in early stage femoral head AVN. In our opinion, HBOT is an integral part of the treatment for early-stage femoral avascular necrosis.

Introduction

Femoral head osteonecrosis is a commonly encountered orthopaedic condition in the general population, manifesting when intraosseous microcirculation is disrupted.[1,2] Although increased use of corticosteroids, alcoholism, haemoglobinopathies, pregnancy, autoimmune disease, and trauma are recognised as risk factors, the aetiology remains unknown in most cases.[3] Early diagnosis and preservation of the shape of the femoral head are fundamental principles in treatment. Conservative approaches such as non-steroidal anti-inflammatory (NSAID) use, restricted weight-bearing, and physical therapy protocols often prove unsuccessful.[4] Spontaneous healing occurs in only a small percentage of osteonecrotic femoral heads. Approximately 67% of asymptomatic patients and 85% of symptomatic patients progress to femoral head collapse.[5]

Surgical treatment is an option for symptomatic hips, but the type of surgery varies based on the severity of the disease. Procedures that preserve the femoral head, such as vascularised or non-vascularised bone grafts with core decompression, pedicled muscle grafts, and derotation osteotomies, may be preferred in the early stages of avascular necrosis. In advanced stages of femoral head osteonecrosis, total hip arthroplasty is an effective treatment. Young patients

undergoing hip arthroplasty have a higher likelihood of revision throughout their lives compared to elderly patients. Therefore, joint-preserving treatments play a crucial role in femoral head osteonecrosis.

Hyperbaric oxygen therapy (HBOT) increases tissue oxygenation, reduces oedema, stimulates angiogenesis, lowers intraosseous pressure, and enhances microcirculation.[6] There is evidence supporting the effectiveness of HBOT in the early stages of the femoral head ostonecrosis.[7] The aim of this study was to evaluate the effectiveness of HBOT in early femoral head avascular necrosis (AVN) based on magnetic resonance imaging (MRI) assessments.

Methods

The protocol used in this study was approved by the ethics committee of Kayseri City Hospital. (no: 343 01.04.2021).

A total of 37 hips from 25 patients who were retrospectively followed between 2018 and 2021 due to Ficat Stage 1-2 femoral head AVN and received HBOT at Kayseri City Training and Research Hospital were included in the study.

Inclusion criteria were, age > 18 years, Ficat stage 1–2 femoral head AVN, patients followed up in the orthopaedic outpatient clinic, and completed 30 sessions of HBOT. Exclusion criteria were rheumatoid arthritis, septic arthritis, previous surgery on the relevant femoral head, malignancy, pregnancy.

The included patients underwent HBOT at 243 kPa with 100% oxygen breathing for 90 minutes per session. A total of 30 sessions were administered, along with a protocol restricting weight-bearing. The 30-session HBOT protocol was completed in our center over a total of six weeks, with five sessions per week. Patients who were undergoing HBOT and were smokers were encouraged to quit or reduce smoking by our hyperbaric and underwater medicine team. No additional medical therapy was applied. All patients who met the criteria and completed 30 sessions of HBOT were included in the study. Two patients who met the inclusion criteria during the relevant period but did not complete 30 sessions were not included in the study.

MRI images of the affected femoral head(s) taken at the 2nd month before and after HBOT were examined. Additionally, visual analogue score (VAS) measurements were compared for the patients before and six months after treatment. In the VAS scaling, the absence of pain was rated as zero (0), while the most severe pain experienced is rated as ten (10).

Hip MRIs were obtained using a 3T magnetic resonance imaging device (Magnetom Skyra; Siemens Healthcare, Erlangen, Germany) with a 13-channel body coil. The images were acquired in axial and coronal planes using T2-weighted turbo spin echo fat saturated (time to repetition – 3750 ms, time to echo – 60 ms, slice thickness – 3.5 mm, field of view – 320 mm, matrix: 256 x 256) and T1-weighted turbo spin echo (time to repetition – 400 ms, time to echo – 15 ms, slice thickness – 3.5 mm, field of view – 320 mm, matrix: 256 x 256) sequences. The avascular necrotic areas in the obtained images were quantitatively measured in volumetric values using the syngo.via software (Siemens Healthineers, Forchheim, Germany).

The data were transferred to electronic media and analysed using SPSS 22.0 software. Normality was tested with the Shapiro-Wilk test. Data were normally distributed and are therefore reported as mean (standard deviation [SD]). The Chi-square test was used for the analysis of categorical data, and the Kruskal-Wallis test was used for the analysis of independent variables. Results with a P-value < 0.05 were considered statistically significant.

Results

The study included 20 female and five male patients, with a mean age of 46.9 (SD 9.5). The demographic data of the patients are summarised in Table 1. The study included 11 smokers. Two patients had a history of steroid use, while the remaining 12 patients had idiopathic AVN.

Lesion sizes before and after HBOT are given for right and left hips separately in Table 2.

When patients were grouped according to the Ficat classification, in Stage 1, the mean difference in lesion

Table 1
Demographic data; F – female; M – male; SD – standard deviation

Parameter	Value
Number of Patients	25
Age, mean (SD)	46.9 (9.5)
Gender (F/M)	20/5
Smoking	11
Steroid use	2
Side	
- Right	8
- Left	5
- Bilateral	12
Ficat stage	
- Stage 1	12
- Stage 2	13
Dominant lower extremity	
- Right	21
- Left	4

Table 2
Lesion sizes before and after treatment in patients

Treatment stage	Lesion size, cm^3 Mean (SD)	
	Right hip	Left hip
Before	29.87 (22.64)	28.84 (14.95)
After	12.39 (11.26)	21.81 (13.56)
Mean difference	17.48 (21.5)	7.02 (5.95)
P-value	< 0.001	< 0.001

size before and after treatment was 2.71 (SD 1.62) cm^3 in the right hip, while in Stage 2, this difference was 25.32 (11.23) cm^3 ($P < 0.001$). In Stage 1, the difference in the left hip before and after treatment was 3.11 (0.60) cm^3, while in Stage 2, this difference was 9.77 (3.01) cm^3 ($P < 0.001$). The difference between stage I and II was statistically significant. A representative MRI image of a bilateral Stage 2 patient is shown in Figure 1.

In the group of patients who smoked, the mean difference between lesions in pre- and post-treatment MRI images was 6.35 (1.33) cm^3, while in the non-smoking group, this difference was 19.64 (4.05) cm^3 ($P = 0.03$).

The mean pre-treatment VAS score was 7.8 (0.7), and after six months of treatment this had decreased to 2.9 (0.9) ($P < 0.001$).

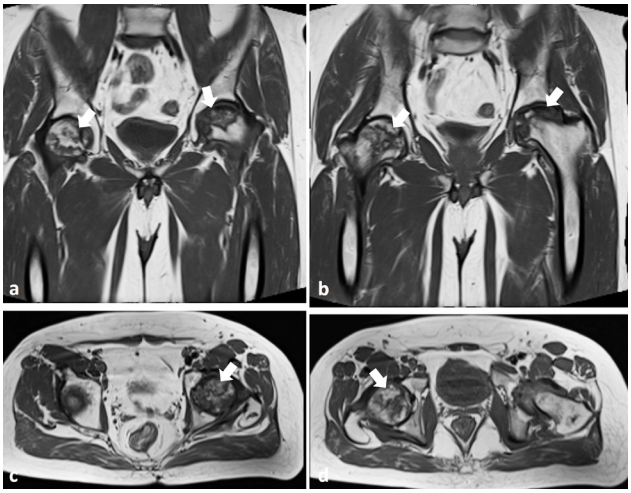
Discussion

Femoral AVN is an extremely progressive disease. Eighty percent of untreated cases progress to femoral head collapse and hip arthritis.[8] Historically, various treatment methods have been attempted, including both surgical methods such as core decompression, osteotomies, and bone grafting, as well as non-surgical methods.[9]

There are several classification systems for femoral AVN.[10–12] The classification system developed by Ficat and Arlet is highly useful in terms of clinical relevance.[13] Early intervention before the collapse of the cartilaginous roof is crucial for hip joint survival. In our study, Ficat-Arlet stages 1 and 2 patients were included.

Steinberg and colleagues emphasised the importance of joint-preserving treatments in early-stage (1–2) patients and demonstrated the potential benefits of HBOT in the early stages.[10] The exact mechanisms by which HBO facilitates

Figure 1
Coronal (a, b) and axial (c, d) T1-weighted magnetic resonance images of the same patient showing irregularly demarcated hypointense avascular necrosis areas in both femoral heads, indicated by white arrows



healing in AVN are unproven, though based on its known effects in other settings[14] it is possible to speculate. Elevated pressures of dissolved oxygen in the arterial blood create a standing osmotic gradient that might reduce bone marrow oedema. Higher dissolved oxygen pressures increase diffusion distance and improve oxygen supply to poorly perfused tissue where it is required to support oxygen-dependent healing processes. Intermittent hyperbaric oxygen has also been shown to stimulate angiogenesis in healing tissue. There is evidence that it modulates osteoclast and osteoblast functions.[15]

In a large series of patients with HBO treatment for femoral AVN, Steinberg et al. reported clinical results for 54 patients (58 hip joints) with idiopathic, traumatic, and secondary AVN in stages I and II. All patients received 90-minute HBO sessions six times a week, with an average of 80 sessions per patient. Over an average follow-up period of eleven years, four joints (7%), all of which had secondary AVN, underwent hip arthroplasty. This resulted in a 100% hip 'survival' rate for idiopathic and traumatic cases.[16] In a 30-year follow-up study by Currie et al., objective improvement was demonstrated in 71% of patients after HBOT according to MRI image results. It was also shown that subjective changes were good in 93% of patients.[17] These results are highly consistent with those reported here where the patients also reported subjective improvements that paralleled the observed reduction in lesion size.

Moghamis et al. reported one year follow-up data showing that femoral AVN patients receiving HBOT had equivalent Oxford Hip Score outcomes to patients receiving core decompression.[18] In another study, Oxford Hip Scores were found to be high in 73–86% of femoral AVN patients who received HBOT. In this patient group, a 92% improvement

in VAS scores was also reported.[19] In our study, consistent with the literature, pain scores decreased to satisfactory levels in 24/25 patients (96%).

In a recent review the hip survival in Ficat Stage 2 hips after HBOT was found to be 100%.[20] The amount of lesion regression was statistically higher in Stage 2 compared to Stage 1 in 13 patients. However, this may be related to the larger lesion size in advanced-stage patients.

Hirota et al. reported that smokers and individuals who have a smoking history of 10 pack-years have an increased risk of femoral head avascular necrosis.[21] This negatively affects healing due to microvascular circulation disorders. In our study, the reduction in lesion size in 11 patients who smoked was calculated to be significantly lower ($P = 0.03$). Based on this result, we think that more effective results can be obtained by encouraging patients with femoral AVN to quit smoking.

The difference in lesion sizes measured by MRI imaging before and after treatment in 25 patients included in the present study objectively demonstrated a beneficial change associated with HBOT. However, the limitation of this study is the small sample size and lack of a formal control group. The latter implies that conclusions must be drawn cautiously. One strength of the present study is the volumetric measurement method used which is superior to other studies. This allows for the most accurate measurement of progression, remission, and reactivation, guiding the course of treatment. It enables us to obtain more reliable data compared to two-dimensional measurements in other studies.

Conclusions

This study objectively demonstrated reduction in lesion size in early-stage femoral avascular necrosis patients associated with HBOT. The decrease in bone marrow oedema in the avascular necrosis area positively reflects on clinical outcomes. In our opinion, HBOT is an integral part of the treatment for early-stage femoral avascular necrosis. We hope that larger sample sizes and long-term prospective studies with controls will shed further light on this subject.

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Those interested in participating in this project can contact:
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