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Hyperbaric Oxygen for Stage I and II Femoral Head Osteonecrosis

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abstract

Hyperbaric oxygen therapy is a suggested joint-preserving treatment for symptomatic early-stage osteonecrosis of the femoral head. Limited studies of this treatment have been published. The goal of this study was to evaluate the effectiveness of this treatment in a relatively large patient cohort. The authors reviewed the files of 68 patients with 78 symptomatic joints with Steinberg stage I and II osteonecrosis of the femoral head. All patients were treated with hyperbaric oxygen at the authors' medical health center. Pretreatment and immediate posttreatment magnetic resonance imaging (MRI) findings were compared. On follow-up, a telephone interview was conducted to determine the survival of the joint. Modified Harris Hip Score and Short Form 12 health survey (SF-12) questionnaires of the start of treatment and at follow-up were obtained and evaluated for statistically significant differences. Half of the joints were stage 1 and half were stage II. Seventy-four joints underwent both pre- and posttreatment MRI. Eighty-eight percent of joints showed improvement posttreatment. On follow-up at a mean of 11.1±5.1 years, 54 patients (58 joints) were located and answered the questionnaires. At the time of follow-up, 93% of the joints survived. Mean Harris Hip Score improved from 21 to 81 ($P<.0001$), the mean physical component of the SF-12 improved from 24 to 46 ($P<.0001$), and the mean mental component of the SF-12 improved from 54 to 59 ($P<.0001$). The authors concluded that hyperbaric oxygen treatment is effective in preserving the hip joint in stage I and II osteonecrosis of the femoral head. [*Orthopedics*. 2015; 38(3):e200-e205.]

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Osteonecrosis of the femoral head is not a rare orthopedic disorder and affects mainly young and middle-aged patients.[1] The etiology of osteonecrosis of the femoral head can be divided into 3 categories: idiopathic; secondary, mainly caused by steroid use[2]; and trauma.[3] Patients in the idiopathic and secondary groups are relatively young, with a mean age of 47 years.[4] Young patients who undergo hip replacement are more likely to have a revision during their lifetime compared with older patients. For this reason, joint-preserving treatments in osteonecrosis of the femoral head play an important role. One treatment that has been proposed is hyperbaric oxygen treatment, which restores tissue oxygenation of the femoral head, reduces edema, and induces angiogenesis. By reducing intraosseous pressure, venous drainage is restored and the microcirculation is improved.[5] Therefore, hyperbaric oxygen treatment seems to be indicated in osteonecrosis of the femoral head because its actions address the specific needs of the endangered bone. The authors present their analysis of the results of hyperbaric oxygen treatment in patients with Steinberg stage I or II osteonecrosis of the femoral head.

Materials and Methods

Clinical and magnetic resonance imaging (MRI) data were reviewed for 68 patients (78 joints) with symptomatic stage I or II osteonecrosis of the femoral head treated with hyperbaric oxygen from July 1996 to August 2012. Staging was done according to the criteria of Steinberg et al.[6] All patients were diagnosed and staged by MRI scans reviewed by certified musculoskeletal radiologists. All patients followed a protected weight-bearing regimen for the duration of their symptoms and underwent a series of 6 daily sessions of hyperbaric oxygen treatment each week. The treatments were paid for by the patients' health insurance. Treatments were continued as long as they were covered by health insurance or until symptoms resolved. The hyperbaric oxygen treatment protocol involved breathing 100% oxygen at 2 to 2.4 atmospheres absolute in a multiplace pressure chamber for 90 minutes using an overboard demand regulator with an oral nasal mask breathing system. A subsequent MRI was performed within 2 months after the end of treatment. The endpoint was an improvement of immediate posttreatment MRI findings compared with the pretreatment MRI. On follow-up at a mean of 11.1±5.1 years, a telephone interview was conducted. Noted was the survival of the joint (hip replacement surgery or none). A modified Harris Hip Score questionnaire[7] was administered for the start of treatment and at follow-up. The same was done with the Short Form 12 health survey (SF-12), which has physical and mental components (PCS-12 and MCS-12, respectively).[8] The scoring was further analyzed for the subgroups of stage I and II and for the etiology groups of idiopathic, trauma, and secondary (mainly because of previous steroid treatment).

Data were analyzed by a qualified statistician using SPSS software for Windows, version 18.0 (SPSS Inc, Chicago, Illinois). The normality of the data was tested by Kolmogorov-Smirnov tests. When the quantitative parameters were not normally distributed, nonparametric tests were used. Paired *t* test and Wilcoxon tests were used for differences between pre- and posttreatment results whenever necessary according to the Kolmogorov-Smirnov results. A repeated measures analysis was conducted to determine whether there was a statistically significant difference in the etiology and stage subgroups for improvement in modified Harris Hip Score, PCS-12, and MCS-12. $P<.05$ was considered significant. The study was approved by the authors' institutional ethics committee (reference number 0337-12-RMB). No funding was needed for this research.

Table 1

Patient Characteristics

Characteristic	Value
Patients, No.	68
Age, mean±SD, y	43.3±11.7
Sex, male, No.	47 (69%)
Sessions, mean±SD, No.	78.3±24.2
Joints, No.	78
Side, No.	
Left	41 (53%)
Right	27 (35%)
Bilateral	10 (13%)
Stage, No.	
I	39 (50%)
II	39 (50%)
Etiology, No.	
Idiopathic	48 (62%)
Trauma	14 (18%)
Secondary	16 (20%)

Results

Table 1 details the demographic features of the study population. Mean age was 43.3±11.7 years. An equal number of patients had stage I and stage II osteonecrosis of the femoral head. Most of the patients had an idiopathic etiology (62%). Patients underwent 25 to 135 treatments (mean, 80±24 treatments). **Table 2** summarizes the improvement seen on MRI. Of 68 patients, 4 did not undergo posttreatment MRI. In the remaining 74 joints (64 patients) 88% or 65 joints showed improvement (reduced lesion size) on posttreatment MRI. Stage I showed 95% improvement and stage II showed 81% improvement. Ninety-three percent improved in the idiopathic group, 85% improved in the trauma group, and 75% improved in the secondary group.

Of 68 patients, 54 (58 joints) were located and completed the interview on follow-up. Mean follow-up was 11.1±5.1 years (range, 7 months to 16 years and 7 months). **Table 3** summarizes the results of joint survival. Only 4 joints (7%) had undergone hip joint replacement at the time of follow-up, for a 93% survival rate.

Table 2

Magnetic Resonance Imaging Results Immediately Posttreatment Compared With Pretreatment

		Stage		Etiology		
Endpoint	Total (N=74)	I (n=37)	II (n=37)	Idiopathic (n=45)	Trauma (n=13)	Secondary (n=16)
Improvement, No.	65 (88%)	35 (95%)	30 (81%)	42 (93%)	11 (85%)	12 (75%)

Table 3

Survival of Joints by Stage and Etiology

		Stage		Etiology		
Endpoint	Total (N=58)	I (n=29)	II (n=29)	Idiopathic (n=32)	Trauma (n=11)	Secondary (n=15)
Survival, No.	54 (93%)	28 (97%)	26 (90%)	32 (100%)	11 (100%)	11 (73%)

Table 4

Modified Harris Hip Score Before Treatment and at Follow-up, Excluding Replaced Joints

		Stage		Etiology		
Score	Total (N=54)	I (n=28)	II (n=26)	Idiopathic (n=32)	Trauma (n=11)	Secondary (n=11)
Modified Harris Hip Score before treatment, mean±SD	21±18	19±18	23±18	22±20	16±10	17±13
Modified Harris Hip Score at follow-up, mean±SD	81±28	87±23	75±31	79±28	81±28	87±23
P	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001

Stage I had a survival rate of 97% and stage II had a survival rate of 90%. Both the idiopathic and trauma groups had a survival rate of 100%. All cases of failure occurred in the secondary group (mainly steroid treatment); this group had a survival rate of 73%. Patients who underwent joint replacement were excluded from analysis of modified Harris Hip Score and SF-12 scoring, leaving 54 joints (**Tables 4-7**). Pretreatment mean modified Harris Hip Score was very low, 21 points, and it improved on follow-up to 81 points ($P<.0001$). In stage I, the improvement was from 17 points to 79 points ($P<.0001$) and in stage II, the improvement was from 21 points to 68 points ($P<.0001$). The pain component of the modified Harris Hip Score was also analyzed. It improved significantly from 7 points to 35 points ($P<.0001$). The mean PCS-12 score increased from 24 to 46 ($P<.0001$). The change was statistically significant also when comparison was made within stage I and II and when comparison was made by etiology. The mental component of the SF-12 also showed an overall significant change from 54 to 59 ($P<.0001$). The change was statistically significant when comparison was made within stage I and II. Concerning etiology, the difference was significant for the idiopathic group, but did not reach significance for the other groups.

Discussion

Survival rates of less than 60% have been reported for Steinberg stage I to stage III osteonecrosis of the femoral head at 5 years.[9,10] Many treatment modalities have been used in an effort to alter this natural history. Joint-preserving treatments focused on Steinberg stages I and II in which there is no subchondral fracture and joint surface collapse may still be avoided. These treatments included surgical procedures, such as core decompression, bone grafting, and osteotomies, and nonsurgical procedures, such as extracorporeal shock wave treatment, anticoagulative treatment, alendronate, and hyperbaric oxygen.[2] Hyperbaric oxygen treatment involves intermittent inhalation of 100% oxygen at greater than atmospheric pressure. This treatment is administered in a hyperbaric chamber, which is compressed with air, while the patient breathes oxygen at ambient pressure through a mask. Inspiration of oxygen at high pressure increases the amount of oxygen dissolved in the plasma in direct proportion to the rise in ambient pressure. Thus, when oxygen is inhaled at 2 to 2.4 atmospheres absolute, the plasma oxygen content increases from 0.32 volume percent to 4.8 to 5.76 volume percent. This high dissolved oxygen concentration improves oxygen delivery to bone tissue, reduces marrow edema, and thereby reduces intraosseous pressure, improving venous drainage and microcirculation. By flooding the extracellular fluid with diffused oxygen, the oxygen becomes available to the ischemic bone cells without the need for circulat-

ing hemoglobin. Hyperbaric oxygen treatment also stimulates angiogenesis that is needed for healing of osteonecrosis of the femoral head.[10] Furthermore, osteoclast and osteoblast function is stimulated by the high oxygen pressure levels.[11]

To the authors' knowledge, this article presents the largest series of hyperbaric oxygen treatment for osteonecrosis of the femoral head to date (74 joints for MRI results and 58 joints for joint survival, hip function, and quality of life) and has the longest follow-up (mean, 11.1 years for survival, hip function, and quality of life). Before MRI was available, Baixe et al[12] presented a report on 41 joints with osteonecrosis of the femoral head that were treated with 20 hyperbaric oxygen sessions. All joints survived after 24 months. Strauss et al[10] presented a meta-analysis in 2008 that included stages I, II, and III osteonecrosis of the femoral head. Of 86 joints treated with hyperbaric oxygen and followed for less than 24 months, 83 (97%) survived. Of 103 other joints followed for more than 24 months, 83 (81%) survived. According to the meta-analysis by Strauss et al,[10] the results with hyperbaric oxygen were superior to the results of natural history, core decompression, bone grafting, osteotomy, and electrical stimulation. Reis et al[13] treated 16 hips with stage I osteonecrosis of the femoral head with hyperbaric oxygen and compared them with the results of an observational study[14] that showed lesions of similar size on MRI. In this study, 81% of joints returned to normal on MRI compared with 17% in the untreated group. Camporesi et al[15] treated 10 joints with stage II osteonecrosis of the femoral head with hyperbaric oxygen and compared them with 9 patients who were treated with hyperbaric air. The hyperbaric oxygen treatment group showed improved pain scores, hip joint range of motion, and stabilometry scores.

In the current study, improvement on posttreatment MRI was substantial, 88% in the whole group and 95% for stage I and 81% for stage II. These radiologic findings are in keeping with the pain reduction shown on modified Harris Hip Score and the physical and mental improvement reflected by SF-12 scores.

Table 5

Pain Component of the Modified Harris Hip Score Before Treatment and at Follow-up, Excluding Replaced Joints

		Stage		Etiology		
Pain Component of the Modified Harris Hip Score	**Total (N=54)**	**I (n=28)**	**II (n=26)**	**Idiopathic (n=32)**	**Trauma (n=11)**	**Secondary (n=11)**
Pain pretreatment, mean±SD	7±8	6±8	7±9	8±9	4±7	7±7
Pain at follow-up, mean±SD	35±15	38±23	32±16	34±15	34±18	38±10
P	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001

Table 6

PCS-12 Before Treatment and at Follow-up, Excluding Replaced Joints

		Stage		Etiology		
Score	**Total (N=54)**	**I (n=28)**	**II (n=26)**	**Idiopathic (n=32)**	**Trauma (n=11)**	**Secondary (n=11)**
PCS-12 pretreatment, mean±SD	24±7	24±7	25±8	25±8	24±7	23±5
PCS-12 at follow-up, mean±SD	46±13	50±11	43±15	47±14	44±14	46±12
P	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001

Abbreviation: PCS-12, physical component summary of the Short Form 12 health survey.

Table 7

MCS-12 Before Treatment and at Follow-up, Excluding Replaced Joints

		Stage		Etiology		
Score	**Total (N=54)**	**I (n=28)**	**II (n=26)**	**Idiopathic (n=32)**	**Trauma (n=11)**	**Secondary (n=11)**
MCS-12 before treatment, mean±SD	54±9	53±10	56±8	56±8	54±9	51±8
MCS-12 at follow-up, mean±SD	59±5	57±7	60±3	59±2	58±8	57±8
P	<.0001	.009	.009	.012	.068	.056

Abbreviation: MCS-12, mental component summary of the Short Form 12 health survey.

The authors' observation at a mean of 11.1 years showed a combined survival rate for stage I and stage II of 93%. Stage I showed a survival rate of 97%, and stage II showed a survival rate of 90%. The nat-

ural history of survival of Steinberg stage I to III osteonecrosis of the femoral head is less than 60% at 5 years.[9]

Modified Harris Hip Score improved significantly between the start of treatment and follow-up. This finding shows that hip joint function improved and pain was reduced. The limitation of this modified score is that patients were not examined for range of motion of the joint.

The SF-12 had been shown to be reliable in evaluating the change in quality of life after hip joint treatment.[16] The survey has physical and mental components. Both showed a significant improvement at follow-up, reflecting physical and mental improvements achieved after treatment.

Etiology of osteonecrosis of the femoral head affected the outcome of treatment. The secondary group (mostly steroid treatment) did not show as much improvement on MRI as the other groups (75% vs 85% in the trauma group and 93% in the idiopathic group). Moreover, this group had a lower joint survival rate (73% vs 100% in the other groups). This may be related to the medical condition that necessitated steroid treatment. Further, some patients needed continued steroid treatment even after the diagnosis of osteonecrosis of the femoral head.

Other joint-preserving treatments of early-stage osteonecrosis of the femoral head also showed effectiveness. Alendronate treatment improved the survival rate of stage I osteonecrosis of the femoral head to 98% and the survival rate of stage II osteonecrosis of the femoral head to 92% at 8-year follow-up.[17] Core decompression led to survival of 96% of stage I joints and 74% of stage II joints after 10-year follow-up.[18] Implantation at the site of decompression with autologous bone marrow with or without hydroxyapatite-polyamide also proved effective.[19,20] Extracorporeal shockwave therapy and pulsed electromagnetic fields are other modalities of treatment that showed a beneficial effect on the outcome of early-stage osteonecrosis of the femoral head.[21,22] The combination of those treatments with hyperbaric oxygen might enhance the success rates of treatment and can be a focus of future research.

Limitations

The current study had some limitations. Analysis of MRI was used for comparison of pre- and posttreatment findings to determine reduction in the size of the lesion. The study did not include the exact measurement and location of the original lesion. However, pretreatment modified Harris Hip Score and SF-12 score showed that the patients were disabled, even at stage I.

The number of treatment sessions given at the authors' institution varied from 25 to 135 (mean, 80±24 treatments) because of variations in the coverage provided by the patients' health insurance. Future studies are needed to determine the optimal number of sessions.

The time of follow-up also varied from 7 months to 16 years and 7 months (mean, 11.1±5.1 years). Nevertheless, only 5 joints (8.6%) were followed for less than 2 years, and the improvement noted on the questionnaires showed that significant clinical improvement occurred.

Another limitation was that 25% of patients (20 joints) were lost to follow-up for the analysis of survival, hip function, and quality of life. Those patients could not be reached by telephone. The number of patients lost to follow-up was equal between stage I and stage II. Sixteen cases were of idiopathic etiology, 3 were related to trauma, and only 1 had secondary etiology that had a worse prognosis in the authors' analysis. Thus, the authors do not believe that the loss to follow-up affected the results.

Conclusion

The current study shows that hyperbaric oxygen treatment has a role in treating stage I and II osteonecrosis of the femoral head.

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