The use of hyperbaric oxygen for avascular necrosis of the femoral head and femoral condyle: a single centre's experience over 30 years

John RB Currie[1], Ian C Gawthrope[1], Neil D Banham[1]

[1] *Department of Hyperbaric Medicine, Fiona Stanley Hospital, Perth, Australia*

Corresponding author: *Dr John Currie, Department of Hyperbaric Medicine, Fiona Stanley Hospital, 102-118 Murdoch Drive, Murdoch WA 6150, Australia*
ORCiD: *0009-0009-0086-4953*
john.currie51@yahoo.co.uk

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Abstract
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Introduction: Avascular necrosis (AVN) is a rare progressive degenerative disease leading to bone and joint destruction. Patients often require surgical intervention. Femoral AVN is the most common anatomical location. Hyperbaric oxygen treatment (HBOT) has been shown to be effective in AVN. We present data collected from one centre over a 30-year period and compare the results with other published data.
Methods: A retrospective chart review of all patients receiving HBOT for AVN at Fremantle and Fiona Stanley Hospitals since 1989 was performed. The primary outcome was radiological appearance using the Steinberg score, with secondary outcomes being subjective improvement, the need for joint replacement surgery and rates of complications.
Results: Twenty-one joints in 14 patients (14 femoral heads and seven femoral condyles) were treated with HBOT since 1989. Two patients were excluded. Within the femoral head group, nine of the 14 joints (64%) had stable or improved magnetic resonance imaging (MRI) scans post treatment and at six months (minimum); 10 joints (71%) had good outcomes subjectively, three joints required surgical intervention, and three patients developed mild aural barotrauma. Within the femoral condyle group, all five joints had stable or improved post-treatment MRI scans (four had visible improvement in oedema and/or chondral stability), four joints reported good outcomes subjectively, none of the patients required surgical intervention (follow-up > six months).
Conclusions: This single centre retrospective study observed prevention of disease progression in femoral AVN with the use of HBOT, comparable to other published studies. This adds to the body of evidence that HBOT may have a significant role in the treatment of femoral AVN.

Introduction

Avascular necrosis (AVN) is a progressive degenerative disease affecting an estimated 300,000–600,000 people worldwide each year.[1,2] It is relatively rare yet its negative impact on joint function and quality of life is significant. The femoral head is by far the most common anatomical location and makes up 75% of all cases of AVN, while AVN of the femoral condyle, otherwise known as spontaneous osteonecrosis of the knee (SONK) makes up only 2.5%.[3] AVN develops secondary to compromised intraosseous blood supply causing necrosis and apoptosis of the bone, followed by structural instability and collapse.[4–6]

The causes of AVN generally fall into three categories: traumatic, idiopathic and secondary.[7] Risk factors for secondary AVN include prolonged steroid use (most common), diabetes mellitus, alcoholism, musculoskeletal decompression sickness and sickle cell disease.[8] The grading of AVN varies but one well established scale is the Steinberg classification which grades AVN from one to six (I–VI) based on radiological appearance and clinical symptoms (Table 1).[9,10]

The natural history of AVN has been well described in the literature and evidence suggests that without intervention it will progress in the majority of patients.[11] However, the rate of AVN progression can be hard to predict and can vary depending upon the aetiology of underlying risk factors and patient demographics. The progressive nature of the disease leads to radiological evidence of progression which can generally be observed within six to twelve months. One study followed-up patients with early (Stage I & II) AVN of the hip over a 12-month period and found statistically significant magnetic resonance imaging (MRI) progression with lesion width progressing from 22.4 mm to 26.4 mm.[12] Another found that 80–85% of symptomatic patients will go on to have subchondral collapse within two years.[13,14]

Table 1
Steinberg grading system; MRI – magnetic resonance imaging

Grade	Description
0	Normal radiographs, bone scan and MRI
1	Normal radiograph Abnormal bone scan and/or MRI
2	Abnormal radiograph with cystic and sclerotic changes
3	Subchondral collapse producing crescent sign
4	Flattening of the femoral head
5	Joint space narrowing
6	Advanced secondary degenerative changes

In view of this, specialists have traditionally managed AVN aggressively at early stages to slow or even prevent progression to subchondral collapse.

Treatment options for early AVN are all focused on reducing oedema and preventing further destruction of the joint, therefore delaying, or avoiding the need for joint replacement.[15]

The concept that hyperbaric oxygen treatment (HBOT) could be used as a treatment for AVN can be dated back to the 1990s when its potential beneficial effects were first hypothesised.[16] Hyperbaric oxygen can temporarily restore tissue normoxia and has been shown to reduce oedema at the level of the microcirculation which may lead to reduced venous stasis.[17–20]

In recent years HBOT has been used with increasing frequency in the treatment of early Stage I and II AVN of the femoral head and femoral condyle.[21,22] Despite this, there have only been a small number of human studies evaluating the effectiveness of HBOT in AVN of the femoral head and a single study assessing AVN of the femoral condyle.[23]

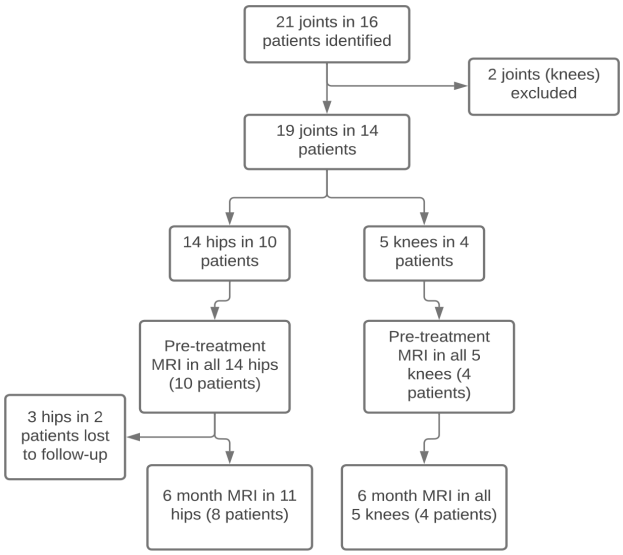
We present data collected from one centre (Fremantle Hospital Hyperbaric Medicine Unit (HMU) from November 1989 to November 2014, which transitioned to Fiona Stanley Hospital (FSH) HMU in November 2014) over the past 30 years and compare these results to those previously published and review the available literature.

Methods

Approval was obtained for data review and extraction by Governance, Evidence, Knowledge and Outcomes (GEKO) at FSH (Approval Number 42155).

A literature search of publications was performed using PubMed, with 25 relevant publications identified. Thirteen studies directly related to the use of HBOT for AVN of the femoral head and one study reported the use of HBOT for AVN of the femoral condyle.

Figure 1
Patient selection and follow-up flow diagram; MRI – magnetic resonance imaging



The FSH HMU database was searched for all cases of AVN receiving HBOT since 1989. Patients included in this study must have received at least 20 sessions of HBOT and have radiologically confirmed AVN with a pre-treatment Steinberg score of I–IV. A HBOT session was defined as treatment with 100% oxygen (O_2) at a pressure of at least 200 kPa (two atmospheres absolute [atm abs], 10 metres of seawater equivalent) for at least 60 minutes (Figure 1).

The primary outcome measure was interval change in MRI on follow-up imaging. Post-treatment MRIs were performed within six months of the last HBOT session. Secondary outcome measures included subjective improvement on follow-up (overall subjective satisfaction from one to five), the need for joint replacement surgery and complication rates.

STATISTICAL ANALYSIS

Observational results were collated on an encrypted Excel spreadsheet prior to statistical analysis. Results were analysed via IBM SPSS Statistics 28.0.1 software using ANOVA and paired *t*-tests. Significance was accepted when $P < 0.05$. The null hypothesis was that there would be no statistically significant difference in radiologic outcomes between the femoral head and femoral condyle AVN groups.

Results

We identified 21 joints in 14 patients (14 femoral heads and seven femoral condyles) treated with HBOT since

Table 2
Comparison of outcome measures between avascular necrosis (AVN) of the femoral head and femoral condyle groups; HBOT – Hyperbaric oxygen treatment; MRI – Magnetic resonance imaging; SONK – Spontaneous osteonecrosis of the knee

Outcome measure	AVN femoral head (*n* = 14)	SONK (*n* = 5)
Mean age (years)	38 (28–66)	58 (46–77)
Percentage females	36%	40%
Smoking history	8 (57%)	2 (40%)
Mean body mass index ($kg \cdot m^{-2}$)	2.3	2.2
Mean pre-HBOT Steinberg score	2.3	2.2
Mean number HBOT treatments	45 (30–76)	32 (30–38)
Stable/improved follow-up MRI	10 (71%)	5 (100%)
Satisfaction upon completion of HBOT	13 (93%)	5 (100%)
Satisfaction at six months	10 (71%)	4 (80%)

1989. Two patients were excluded (two joints); one patient had declined treatment and one failed to return after their fourth treatment. All patients were treated with a 243 kPa (2.4 atm abs) table either in a multiplace chamber (14:90:24 table – being compression to 14 metres of seawater equivalent [243 kPa] for a total of 90 minutes breathing 100% O_2 with a five-minute air-break then 24 minutes decompression on 100% O_2) or monoplace chamber (14:90:08 table).

The mean age of patients for AVN of the femoral head was 38 years (range 28–66). The age range in the femoral condyle group was greater (46–77) with a mean age of 58 years. In the AVN femoral head group 36% were female compared to 40% in the femoral condyle group. Within the AVN femoral head group, two patients (two joints) were identified as current smokers and a further five patients (six joints) were identified as ex-smokers while within the AVN femoral condyle group there were no current smokers, and two patients (two joints) were identified as ex-smokers. Amongst the smokers and ex-smokers there was a mean pack year history of 12 years within the AVN femoral head group vs 22 years amongst the AVN femoral condyle group. The mean body mass index (BMI) among the AVN femoral head cohort was 24.8 vs 27.6 $kg \cdot m^{-2}$ within the femoral condyle group. The number of HBOT administered varied between the two cohorts with the average in the AVN hip group being 45 (30–76) compared to 32 (30–38) in the femoral condyle group. Pre-treatment Steinberg score for both groups were similar (2.3 for femoral head vs 2.2 for femoral condyle). Patient demographics are shown in Table 2.

Within the femoral head group, nine of the 14 joints (64%) had stable or improved MRI scans post-treatment (within six months of completion) and on follow up after at least six months, 10 joints (71%) reported good outcomes subjectively (Table 2). Two of the 14 patients (three hips) had no follow-up MRI (one because of acute intercurrent illness and one because of the progression to joint replacement surgery). Of the AVN femoral head cohort 10 joints were followed up beyond six months (one to 10 years) with a mean follow-up of time of six years. Two joints had evidence of slight progression on MRI at 10 years. Five joints had stable or improved appearance on MRI at long term follow-up. A total of three joints (in three patients) required surgical intervention (two total hip replacements and one hip resurfacing). Of the patients requiring joint replacement surgery, all three had pre-intervention Steinberg scores of III or more. Of the 14 patients within the femoral head AVN group, three suffered from minor complications of HBOT (mild aural barotrauma). There were no serious complications documented.

Within the femoral condyle group, all five joints had stable or improved post-treatment MRI scans with four having visible improvement in oedema and/or chondral stability (Table 2). At six-month (minimum) follow-up, four of the five joints had a good subjective outcome. None of the five joints had required subsequent surgical intervention (follow-up time ranging from six months to two years). One patient sustained a Teed grade four aural barotrauma during HBOT necessitating otolaryngology consultation, but no long-term sequelae.

When the primary outcome measure between the two groups was compared, we found that 64% of the femoral head AVN group had no deterioration radiologically on follow-up MRI whereas none of the five patients in the femoral condyle group deteriorated. Subjective satisfaction at zero months and then six months were compared between the two groups. All patients (five joints) were satisfied on completion of HBOT in the femoral condyle group compared to 92%

(13 joints) in the femoral head group. At six months (four of five joints) in the femoral condyle group versus 71% (10 joints) in the femoral head group were satisfied with their outcomes. There was no statistically significant difference in primary outcome between the two groups ($P = 0.795$).

When data were combined for both groups, follow-up MRI showed that 15 joints (79%) had no deterioration radiologically with eight joints (42%) showing evidence of improvement. Subjectively, 10 patients (14 joints) (74%) were satisfied at six-month (minimum) follow-up. One patient (one joint) reported poor subjective outcome and another three patients (four joints) failed to complete the follow-up questionnaire.

Discussion

Avascular necrosis is a relatively rare condition, yet it is responsible for significant morbidity and its impact on quality of life can be profound. The secondary causes of AVN are most prevalent. Common risk factors for secondary AVN include prolonged steroid use, diabetes mellitus, alcoholism, musculoskeletal decompression sickness and sickle cell disease.[8] With diabetes rates increasing, the incidence of secondary AVN is increasing.[7]

The pathogenesis of AVN after disruption of bone microcirculation seems to be multifactorial but involves death of osteoclasts, bone marrow oedema and venous stasis.[10,24,25] It is also hypothesised that the imbalance of osteoclastic and osteoblastic cells is as a result of increased activity of receptor activator of nuclear factor-kappa B ligand (RANKL) and a comparative reduction in activity of osteoprotegerin (OPG) which leads to increased bone resorption and reduced production.[19] The consequence of these pathological processes is collapse of the necrotic bone leading to loss of normal anatomy. It is thought that HBOT acts to reduce oedema and venous stasis in compromised tissue by restoring normoxia at the tissue level and modulation of the RANKL:OPG system. It has also been shown that HBOT produces reactive oxygen and nitrogen species which initiate a multitude of anti-inflammatory pathways and induction of angiogenesis.[26] The initiation of new blood vessel formation along with suppression of inflammation may contribute to the therapeutic effect of HBOT in AVN.

Even though there appears to be a convincing biological basis for theorising that HBOT should be effective in AVN, there have been few studies. This study evaluated and compared the use of HBOT in AVN of the femoral head and femoral condyle. Despite the limitations of being a retrospective study with a small sample size, this study reported similar results for the use of HBOT in femoral AVN to other published studies. When we compare our results for AVN of the femoral head to the prospective study published by Reis et al in 2003 we found a 93% subjective improvement at six-month follow-up vs an 83% improvement in the Reis study.[16] Objective results using MRI found similar results with 79% of patients showing stable or improved MRI findings at follow-up vs 81% in Reis' study. When comparing the effectiveness of HBOT in AVN of the femoral condyle with AVN of the hip we found the results to be comparable with no significant difference though our study was too small to evaluate this reliably.

Conclusions

AVN of the femur is a debilitating disease that progresses towards subchondral articular collapse requiring surgical intervention if left untreated.[13] The results from this single centre retrospective study observed improved bone stability and prevention of disease progression on follow-up for femoral AVN treated with HBOT. This finding is comparable to other published data and suggests benefit when compared to the expected progression of disease both subjectively and radiologically.[11,12] We also observed several patients in both groups with both radiological and subjective improvement after HBOT. This study adds to the body of evidence that HBOT may have a significant role in the treatment of femoral AVN.

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