Hyperbaric Oxygen Therapy for Avascular Necrosis of the Femoral Head: A Comprehensive Review and Treatment Perspective

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Abstract

Avascular necrosis (AVN) of the femoral head is a progressive orthopedic condition marked by bone tissue death due to impaired blood supply. It predominantly affects young and middle-aged adults and can result in femoral head collapse, joint degeneration, and functional disability if left untreated. Conventional therapies, including pharmacological agents and surgical interventions, often fail to prevent disease progression or restore joint integrity, especially in advanced stages. This review aims to provide a comprehensive overview of AVN pathophysiology, clinical presentation, and classification systems, while critically evaluating the emerging role of hyperbaric oxygen therapy (HBO_2T) as an adjunct or alternative treatment. A structured literature review was conducted to synthesize clinical evidence from observational studies, randomized controlled trials (RCTs), case reports, and systematic reviews assessing the efficacy and mechanisms of HBO_2T in treating AVN of the femoral head.

The results showed that HBO_2T enhanced oxygen delivery to ischemic bone, stimulated angiogenesis, reduced inflammation and marrow edema, and promoted osteoblast activity–mechanisms directly addressing AVN pathogenesis. Clinical studies consistently report improvements in pain, function, radiographic outcomes, and a delayed need for surgical intervention, particularly when HBO_2T is initiated in early disease stages. Despite growing global support, HBO_2T research in Thailand remains limited due to funding constraints, despite an increasing pool of trained specialists.

In conclusion, HBO_2T represents a promising, biologically sound treatment for early-stage femoral head AVN. Its inclusion in clinical protocols may significantly improve patient outcomes and reduce the need for invasive procedures. Larger multicenter RCTs and investment in local research infrastructure are crucial to establish standardized treatment guidelines and expand access, particularly in resource-limited settings.

Keywords: avascular necrosis, femoral head, hyperbaric oxygen therapy, joint preservation, orthopedic treatment

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Introduction

Avascular necrosis (AVN), also known as osteonecrosis, is a severe orthopedic condition characterized by the progressive death of bone tissue resulting from disrupted blood supply. AVN can affect various skeletal sites, but involvement of the femoral head is particularly debilitating due to its pivotal role in hip joint function, weight-bearing, and overall mobility. The incidence of femoral head AVN is increasing globally, affecting predominantly young and middle-aged adults, typically between 30 and 50 years of age. The condition significantly impairs patients' quality of life by causing persistent pain, limiting mobility, and progressively leading to joint degeneration and functional disability[1-4].

Multiple etiologies contribute to the development of AVN, ranging from traumatic causes such as femoral neck fractures or hip dislocation to non-traumatic factors including chronic corticosteroid use, alcoholism, hematological disorders, autoimmune diseases, radiation therapy, and idiopathic cases where no clear cause can be identified. The multifactorial nature of AVN complicates early diagnosis, as the initial clinical presentation can be nonspecific and insidious, often delaying appropriate therapeutic intervention[5-8].

Current therapeutic strategies for managing femoral head AVN span conservative medical management, minimally invasive surgical interventions, and extensive surgical reconstruction or replacement procedures. Pharmacological treatments, such as bisphosphonates and anticoagulants, aim to delay progression by addressing underlying pathophysiological mechanisms like bone resorption and coagulation abnormalities. Surgical interventions, including core decompression, vascularized grafting, and total hip arthroplasty, offer varying degrees of success and come with associated procedural risks and complications[9-10].

Despite advancements in these conventional treatments, therapeutic outcomes remain inconsistent, with many patients eventually requiring total hip replacement at relatively young ages. This clinical gap underscores the ongoing need for alternative or adjunctive treatment modalities capable of halting or reversing early-stage AVN, minimizing symptoms, and preserving joint integrity without the significant risks associated with invasive procedures[11-13].

In recent years, hyperbaric oxygen therapy (HBO_2T) has emerged as a promising treatment modality, particularly for early-stage AVN. HBO_2T involves administering 100% oxygen under increased atmospheric pressure, enhancing tissue oxygenation and promoting reparative processes in hypoxic tissues. Its therapeutic potential is attributed to multiple beneficial biological effects, including stimulation of angiogenesis, reduction of inflammation, mitigation of bone marrow edema, and enhancement of bone regeneration. This multifaceted approach makes HBO_2T uniquely suitable for managing AVN by directly addressing the disease's complex pathophysiological underpinnings[14-16].

This comprehensive review aims to provide a detailed examination of AVN of the femoral head, including pathophysiology, clinical classification, presentation, and a thorough exploration of HBO_2T as a therapeutic intervention, supported by clinical evidence, procedural insights, and discussions on advantages, limitations, and future research directions.

Pathophysiology of Avascular Necrosis

The pathophysiology of avascular necrosis (AVN) of the femoral head involves a multifaceted interplay of vascular, cellular, metabolic, and biomechanical factors. The femoral head primarily relies on a precarious vascular supply from the medial and lateral femoral circumflex arteries, making it highly vulnerable to ischemic injury. Any disruption or compromise in these blood vessels, due to traumatic events such as fractures or hip dislocation, or non-traumatic conditions including corticosteroid use, alcohol abuse, hypercoagulable states, and autoimmune disorders, can lead to ischemia and subsequently bone necrosis[17-18].

Once blood supply is compromised, osteocytes rapidly undergo ischemic cell death due to oxygen deprivation, initiating a cascade of inflammatory and degenerative processes. Within hours to days, this cell death triggers a robust inflammatory response characterized by elevated pro-inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), which further exacerbate local tissue damage. Immune cell infiltration, particularly neutrophils and macrophages, amplifies inflammation, contributing to oxidative stress and the release of enzymes that degrade extracellular matrix and bone tissue[19].

Simultaneously, the ischemic bone environment attempts a reparative process through neovascularization and remodeling. However, persistent ischemia and ongoing inflammation typically limit these attempts at repair, leading to insufficient formation of new, functional vessels and incomplete or defective bone regeneration. Chronic ischemic conditions and inflammation eventually cause accumulation of microfractures and structural weakening of subchondral bone, ultimately precipitating collapse of the femoral head and secondary degenerative changes within the hip joint[20-25].

Moreover, increased intraosseous pressure due to marrow edema further compromises blood flow, exacerbating ischemia. The pathological increase in intraosseous pressure arises from adipocyte hypertrophy and intramedullary fat cell embolization, frequently associated with prolonged corticosteroid use or alcoholism. These changes further impair venous outflow and arterial inflow, creating a vicious cycle of progressive ischemia, necrosis, and bone deterioration[26].

Biochemically, alterations in bone metabolism and homeostasis also significantly contribute to AVN progression. Disrupted bone remodeling, characterized by an imbalance between osteoblast and osteoclast activities, leads to abnormal bone structure and impaired biomechanical properties. Increased osteoclastic resorption combined with insufficient osteoblastic bone

formation compromises structural integrity, making the femoral head susceptible to mechanical collapse under physiological loads[27-28].

Understanding the intricate pathophysiological mechanisms underlying AVN is crucial for identifying therapeutic targets and developing effective treatments capable of interrupting disease progression and promoting bone repair and regeneration[29].

Classification of Avascular Necrosis

Proper staging and classification are essential for accurate diagnosis, prognosis, and treatment decision-making. Several classification systems exist, with the Ficat and Arlet, Steinberg, and ARCO classifications being the most prominent[30].

Ficat and Arlet Classification: This system emphasizes radiographic findings and disease progression:

- Stage 0: Preclinical, identifiable only by biopsy.
- Stage I: Normal radiographs but abnormal MRI or bone scans indicating early ischemic changes.
- Stage II: Radiographic changes including sclerosis or cyst formation without collapse.
- Stage III: Radiographic evidence of subchondral collapse (crescent sign), femoral head shape maintained.
- Stage IV: Complete collapse with joint space narrowing and secondary osteoarthritis[31].

Steinberg Classification: This classification incorporates lesion size, providing prognostic value:

- Mild: Lesion involvement < 15% of femoral head.
- Moderate: 15 - 30% involvement.
- Severe: > 30% involvement. This granularity improves clinical decision-making regarding the urgency and type of interventions needed[32].

The ARCO classification: This classification integrates advanced imaging techniques and histopathology for improved diagnostic precision and staging accuracy[33].

Clinical Presentation of Avascular Necrosis

Patients with AVN typically present with progressive pain in the affected hip or groin region, which may radiate to the thigh, knee, or buttocks. The pain often worsens with activity and weight-bearing and improves partially or completely with rest. Initially, patients may report mild discomfort, but as the disease progresses, pain becomes more severe and constant,

significantly affecting mobility and daily activities. Some patients might present with limited range of motion, particularly during hip internal rotation and abduction, which can further contribute to gait disturbances and functional impairment[34].

Physical examination may reveal tenderness around the hip joint, muscle wasting of the affected limb, and pain on passive movement, particularly internal rotation. In the later stages, patients might exhibit a noticeable limp and limitations in hip movement, affecting overall patient quality of life. Due to its gradual onset and nonspecific early symptoms, AVN can frequently go unrecognized until advanced stages, highlighting the importance of early clinical suspicion, especially in high-risk groups[35].

Overview of Hyperbaric Oxygen Therapy

HBO_2T involves patients breathing 100% oxygen under elevated atmospheric pressure (typically between 2.0 and 2.5 ATA), significantly enhancing plasma oxygen levels independent of hemoglobin concentration. This allows efficient oxygen delivery to ischemic tissues even in compromised vascular environments, potentially reversing hypoxia-induced cellular damage[34].

Mechanisms of HBO_2T in AVN: HBO_2T provides several biological benefits that comprehensively address the pathophysiological mechanisms involved in AVN:

- Hyperoxygenation: HBO_2T significantly increases oxygen tension in ischemic bone tissue, enhancing cellular survival and metabolic function. By raising oxygen concentration, it effectively mitigates hypoxic injury, preserving the viability of osteocytes and other bone-forming cells. This oxygenation is vital in maintaining tissue integrity, especially during periods of compromised vascular supply[35].
- Promotion of Angiogenesis: HBO_2T stimulates angiogenesis by activating various growth factors such as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF). These growth factors promote the proliferation of endothelial cells and enhance the formation of new capillaries, improving local blood circulation and nutrient delivery, crucial for healing necrotic bone areas[36].
- Anti-inflammatory Effects: HBO_2T exerts significant anti-inflammatory properties by modulating inflammatory cytokines and reducing oxidative stress. It decreases pro-inflammatory mediators such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), thereby mitigating inflammation-induced damage. By controlling inflammation, HBO_2T may slow or halt the destructive processes associated with AVN[37].
- Reduction of Bone Marrow Edema and Intraosseous Pressure: HBO_2T effectively decreases bone marrow edema and intraosseous pressure, common findings in AVN that contribute to pain and progression of bone destruction. The reduction of

edema and pressure alleviates symptoms, enhances patient comfort, and can potentially slow disease progression by minimizing mechanical stress within the bone[38].

- Enhanced Osteoblast Proliferation and Differentiation: HBO_2T directly stimulates osteoblast activity, promoting cell proliferation, differentiation, and enhanced mineralization. This activity significantly aids in bone regeneration and remodeling, helping repair necrotic lesions and restore structural integrity of the femoral head. Furthermore, HBO_2T supports the balance between osteoblastic and osteoclastic activities, essential for effective bone remodeling and repair[39].

Collectively, these mechanisms demonstrate HBO_2T's comprehensive therapeutic impact on AVN, particularly when applied during early stages of the disease[40].

The Undersea and Hyperbaric Medical Society (UHMS) has recognized HBO_2T as an effective adjunctive therapy for selected AVN cases, particularly beneficial in early-stage disease. The UHMS endorses HBO_2T use based on emerging clinical evidence, highlighting its potential to reduce the need for invasive surgical procedures and improve patient outcomes[30].

HBO_2T Procedure and Protocols: Hyperbaric oxygen therapy is conducted in specially designed chambers that allow precise control of atmospheric pressure. During each HBO_2T session, patients breathe pure oxygen, typically delivered via face mask or hood systems, within a controlled hyperbaric environment. Standard pressure levels utilized for AVN management range between 2.0 and 2.5 atmospheres absolute (ATA). Each session usually lasts between 60 and 90 minutes, depending on clinical protocols and individual patient requirements[41].

The frequency and total number of HBO_2T sessions are critical for therapeutic success. Most clinical protocols recommend sessions to be performed five days per week, accumulating a total of approximately 30 to 60 sessions. The exact number may vary based on the stage and severity of AVN, as well as individual patient response and concurrent medical conditions[42]. Regular monitoring, typically involving clinical assessments, pain scoring, and radiographic evaluations such as MRI or X-ray, is essential to tailor treatment duration and intensity.

Prior to initiating HBO_2T, a thorough patient evaluation, including medical history, physical examination, and baseline imaging studies is conducted. Patients are screened carefully for contraindications to HBO_2T, including untreated pneumothorax, severe respiratory disease, or recent ear surgery. During HBO_2T sessions, careful monitoring of patients is performed to manage potential complications such as barotrauma, oxygen toxicity, or claustrophobia, although these events remain rare due to stringent safety protocols[43].

Following completion of an initial HBO_2T regimen, follow-up evaluations at regular intervals (usually every 3 - 6 months) are recommended to assess ongoing therapeutic benefits and to decide on the need for additional "booster" sessions or adjunctive treatments.

Patient adherence and compliance with therapy protocols significantly influence therapeutic outcomes, thus emphasizing the importance of comprehensive patient education and multi-disciplinary care[44].

Clinical Evidence Supporting HBO_2T in Avascular Necrosis

Hyperbaric oxygen therapy (HBO_2T) has increasingly been recognized as a promising intervention for the treatment of avascular necrosis (AVN) of the femoral head, especially in its early stages. Multiple clinical studies, including observational studies, case reports, randomized controlled trials (RCTs), and systematic reviews, provide substantial evidence supporting its efficacy.

Several observational studies and case reports have consistently demonstrated encouraging outcomes with HBO_2T in managing early-stage AVN. Reis et al.[22] reported significant pain reduction and radiographic improvements in 81% of their cohort following HBO_2T sessions. Similar positive outcomes were reported by Camporesi et al.[23], who observed significant functional improvement and decreased requirements for surgical interventions. Fioravanti et al. further confirmed these findings in idiopathic AVN cases, reporting symptomatic and imaging improvements following HBO_2T[24].

Controlled clinical trials further strengthen the evidence base. Koren et al.[25] conducted a randomized controlled study comparing HBO_2T to core decompression. They found that HBO_2T provided similar symptomatic relief and radiological stability, emphasizing its potential as a viable non-surgical alternative. Additionally, a systematic review by Zhang et al[26]. concluded that HBO_2T significantly improved clinical symptoms and radiographic outcomes compared to conservative treatments alone, suggesting a clear benefit in incorporating HBO_2T into standard AVN treatment protocols.

Moreover, studies have demonstrated that HBO_2T can significantly reduce the progression to femoral head collapse in early AVN cases, thereby reducing or delaying the need for total hip replacement. Clinical trials have also noted an improvement in patient-reported outcomes such as pain, mobility, and overall quality of life[45].

Specific patient groups, such as those with sickle cell disease, also appear to benefit notably from HBO_2T. Case reports and clinical observations in these populations have documented complete or substantial resolution of AVN lesions with prolonged HBO_2T treatment courses, highlighting the therapy's versatility and broad applicability[46].

Long-term follow-up studies have provided insights into the sustained efficacy of HBO_2T. Patients receiving HBO_2T have demonstrated stable clinical and radiological outcomes years after therapy completion, underscoring its lasting therapeutic impact and potential to alter the natural progression of AVN significantly[47].

Collectively, these diverse lines of clinical evidence robustly support HBO_2T's role as an effective treatment for AVN, particularly when administered during the disease's early stages. Continued research and larger randomized controlled trials will further clarify optimal patient selection criteria and treatment protocols, solidifying its place within standard clinical practice[45].

Conclusion

Avascular necrosis (AVN) of the femoral head presents a substantial challenge in orthopedic practice, often progressing towards debilitating joint destruction and significantly impacting patients' quality of life. Traditional therapeutic modalities, although beneficial, frequently fail to achieve consistent long-term outcomes, particularly in advanced stages of AVN. Hyperbaric oxygen therapy (HBO_2T), emerging as a powerful adjunctive and potentially primary therapeutic approach, holds promise in addressing this clinical gap effectively, especially in early-stage disease.

HBO_2T's efficacy is rooted in its comprehensive biological impact, addressing the core pathological mechanisms of AVN through enhanced tissue oxygenation, stimulation of angiogenesis, modulation of inflammatory processes, and promotion of bone regeneration. The robust clinical evidence from various studies, including observational data, randomized controlled trials, and long-term follow-up studies, underscores HBO_2T's ability to reduce symptoms, delay disease progression, and potentially prevent the need for invasive surgical interventions such as total hip arthroplasty.

However, despite its demonstrated benefits, HBO_2T faces challenges regarding widespread adoption, including high treatment costs, limited availability of hyperbaric facilities, variability in insurance coverage, and the necessity for extended treatment durations. Overcoming these barriers will require concerted efforts to increase awareness among healthcare providers, optimize cost-effectiveness, and advocate for policy changes to improve patient access to HBO_2T.

Future research should aim to further validate hyperbaric oxygen therapy (HBO_2T) through larger, multicenter randomized controlled trials to establish standardized protocols and clarify optimal patient selection criteria. Additionally, exploring the synergistic potential of HBO_2T with emerging regenerative therapies such as stem cell and growth factor treatments could enhance its therapeutic efficacy and broaden its clinical applications. While international studies increasingly support the effectiveness of HBO_2T, research in Thailand remains limited. Despite the growing number of medical experts trained in HBO_2T, the lack of adequate research funding continues to hinder domestic advancements in this field.

In conclusion, HBO_2T presents a compelling therapeutic option for managing AVN of the femoral head, particularly when initiated early in disease progression. Its integration into

comprehensive patient management strategies offers significant potential to improve clinical outcomes, reduce healthcare burdens, and enhance patient quality of life, thus warranting its continued exploration and expanded implementation within clinical practice.

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