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QUESTION 7: Is there a role for hyperbaric oxygen therapy (HBOT) and other non-antibiotic methods for the treatment of chronic osteomyelitis/implant infections?

RECOMMENDATION: There is limited evidence for the efficacy of hyperbaric oxygen (HBO) in the treatment of post-traumatic bone infections.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 86%, Disagree: 5%, Abstain: 9% (Super Majority, Strong Consensus)

RATIONALE

HBOT has been proposed as an adjunctive therapy in the management of refractory osteomyelitis, which was defined as chronic osteomyelitis that persists or recurs after appropriate interventions have been performed or where acute osteomyelitis has not responded to accepted management techniques [1]. The procedure involves the intermittent inhalation of 100% oxygen in chambers pressurized above one atmosphere absolute (typically to about 2 to 2.5 atmosphere absolute (ATA)). It is based on the premise that increased tissue oxygen levels will enhance healing. Although adverse events are typically self-limiting, more serious potential complications include baro-traumatic otitis, pneumothorax, myopia and seizures [2].

While initially there was some enthusiasm about the use of HBOT in refractory osteomyelitis, this appears to have waned with only one case series published since 2004 [3]. Prior to this, a small number of descriptive studies were published that reported encouraging results [4,5]. A systematic review by Goldman in 2009 examined the evidence for HBOT in wound healing and limb salvage. Five studies were classified as “moderate” strength evidence (the remaining 10 being either “low” or “very low”) [6]. In the first of these Morrey et al., reported on the outcomes of HBOT in 40 patients who had recurrent infection for more than 6 months after at least 1 surgical procedure [7]. Following surgery, antibiotics and HBOT, 85% of patients were reported to be disease-free at one year.

Davis et al. performed a retrospective study on 38 patients with actively draining wounds and at least 1 failed previous surgical procedure [8]. Complete healing was achieved, again in combination with

surgery and antibiotics, in 89% of cases. From 1998 to 2004 Chen et al., published three overlapping case series involving patients who presented with recurrence of infection following prior surgical treatment [9–11]. The success rate of standard treatment, involving aggressive debridement, antibiotics and HBOT, was reported as 79% to 92% (note that the 2003 study was not included in the Goldstein systematic review). The findings from all of these non-comparative studies are however difficult to interpret and confounded by the fact that HBO was used as part of a multi-modal treatment strategy. Furthermore, it is not clear if the initial failed surgical procedures were performed by experienced musculoskeletal infection surgeons. There was only one comparative study included in the Goldman systematic review. Esterhai et al. performed a prospective non-randomized controlled trial and found that HBOT had no effect on length of hospitalization, initial clinical outcome or the late recurrence of infection [12]. The only clinical study published since the systematic review in 2009, described the experience of a single center with HBOT in general and did not provide a detailed description specific to the chronic refractory osteomyelitis patients [3].

Recently, the effect of HBOT on implant-associated infection was further drawn into question. Büren et al. illustrated in a standardized murine model that HBOT did not have a beneficial effect on the local infection or the immune response to the infection compared to standard therapy alone [13]. Interestingly, they also noted delayed bone healing and a higher rate of non-unions at 28 days in the HBOT group. Ultimately, there is currently only limited evidence

supporting the use of HBOT in post-traumatic infections and the single study with a control arm reported no benefit.

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3.2. TREATMENT: SURGEON AND CARE TEAM

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QUESTION 1: Should all infected non-unions be treated in specialized septic centers?

RECOMMENDATION: The current literature, although rich in case series and observational studies, does not lend support to the recommendation that “specialized septic surgery centers” should care for infected non-unions. However, because of the complexities of infected non-unions, care in specialized centers may yield the best possible outcome.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 70%, Disagree: 21%, Abstain: 9% (Super Majority, Weak Consensus)

RATIONALE

Infected nonunion is the persistence of an infection at the fracture site and the surrounding tissue and failure of bone healing for eight months, (U.S. Food and Drug Administration). It could be considered as an osteomyelitis at an unstable fracture before the debridement and which remains unstable thereafter. It is commonly accompanied by soft tissue problems, adjacent joint stiffness, motor and sensory dysfunction of the limb, chronic pain, depression and unrelated medical problems leading to considerable physical, social, financial and mental impact on the life of the patient and the healthcare systems and may even become a limb-threatening complication.

Bone healing and eradication of the infection is the main but not the only objective because a non-functional and deformed limb with pain and stiffness of the adjacent joints will be an unsatisfactory outcome even if at some point the bone heals sufficiently. Treatment is aimed at returning the extremity and the patient to the fullest function possible during and after the treatment process. This process is usually long-lasting and must be planned accordingly so that in case of failure, further treatment alternatives remain available. Because of the various nonunion types and the multitude of possible problems related to the patient’s health and comorbidity, such as prior treatments and the bone and soft tissue defects, no simple treatment algorithms are possible. The recommended strategy, with an array of management alternatives, is: (a) the “infection-elimination first” by local radical debridement of all pathological tissue, followed by (b)

tissue and bone reconstruction and (c) targeted chemotherapy with local and systemic antibiotics.

A specialized team of orthopaedic surgeons with expertise in a broad spectrum of techniques must thoroughly evaluate the patient and carefully consider all available information about the general health status and the local tissue conditions. The prior failed treatments must be taken into account, as well as the optimization of all treatment modifiers. Where extensive surgical exposures have failed consideration is given to less invasive techniques that respect the surrounding soft tissues. Stable fixation, adequate vascularity, bone-to-bone contact, and bone grafting or strong bone regenerate are crucial factors for success. The potential need for future treatment should be considered when pursuing any particular intervention.

The care of the patients with infected nonunions may be best performed at specialized septic surgery centers with an expert team approach to achieve the ultimate goals of bony union and restoration of alignment and function, while limiting the extent of residual disability. A medical center that treats infected non-unions should provide all of the appropriate resources and a supportive team of consulting specialists to contribute to all aspects of care, both at the initial evaluation and throughout the course of treatment. The role of anesthesiologists is obvious as well as of the internists for patients with serious medical conditions. Plastic surgeons are often necessary to reconstruct the soft tissues