# Hyperbaric oxygen in the treatment of postoperative infections in paediatric patients with neuromuscular spine deformity

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ORIGINAL ARTICLE

# Hyperbaric oxygen in the treatment of postoperative infections in paediatric patients with neuromuscular spine deformity

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**Abstract** The aim of this study is to evaluate possible benefits of hyperbaric oxygen (HBO) therapy in the treatment of deep postoperative infections in six high risk paediatric patients with neuromuscular spine deformity. The study involved review of medical records including radiology, office visits, and telephone contacts for six patients, referred for postoperative HBO therapy in 2003–2005. Infection control and healing without removal of implants or major revision surgery with a minimum of 2-year follow-up after index surgery were considered to represent success. All infections were resolved. Median time for wound healing, normalisation of blood tests and antibiotic weaning were 3 months. Radiological bony fusion, intact implants without any signs of radiolucent zones were seen in all cases at a mean follow-up of 54 months (37–72). Side effects of HBO treatment were minor. HBO is a safe and potentially useful adjuvance in the treatment of early deep postoperative infections in complex situations with spinal implants in high risk paediatric patients.

**Keywords** Hyperbaric oxygenation · Spine deformity · Postoperative infection · Tethered cord · Spinal implants

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## Introduction

Early onset, non-idiopathic spine deformities are progressive and associated with increased respiratory and cardiovascular morbidity and mortality as well as functional deterioration in daily activities due to body balance disturbances. If untreated, the progress can continue throughout the adult life [1, 2]. The overall complication rate for surgery in neuromuscular spine deformities is reported to be very high, 30–65%, including implant-related problems, neurological sequele, pseudarthrosis, loss of correction and infections as well as mortality. Myelomeningocele-related deformities in specific are associated with high complication rate [3]. Additionally, this patient population has cardiovascular, endocrine and other multidisciplinary risk factors as well as frequent earlier surgeries and poor soft tissue quality, which make the treatment of postoperative complications even more delicate.

A deep wound infection can jeopardise the fusion and deformity correction. Standard management includes repeated surgical revisions, placement of drains, use of irrigation systems, long-term intravenous antibiotic therapy and use of suction devises such as vacuum-assisted closure (VAC). This is time and resource consuming and can constitute a physiological load in this patient category. Long-term immobilization can contribute to an additional deterioration of function and mobility. Since the literature shows a high complication rate including severe functional deterioration at repeated surgery and long rehabilitation if infections appear, we introduced HBO at the time of diagnosis of postoperative deep infection.

Hyperbaric oxygen has been reported [4] to heal postoperative spinal infections in adults with intact osteosynthesis material. The therapeutic effect of HBO treatment with regard to infections is mainly attributable to reduction of hypoxia in tissues with significant improvement in leucocyte phagocytic killing capacity [5].

Healing is impaired at low oxygen tensions which are often observed in wounds [6]. Cells such as neutrophils, fibroblasts, macrophages, osteoclasts and osteoblasts are all dependent upon an environment in which oxygen is not deficient in order to carry out their specific anti-infectious, inflammatory or repair functions [5]. HBO therapy increases oxygen tension in tissues, including bone, with increased bone-turnover and increased bone-metal contact [7].

This article reports the clinical potential usefulness of HBO therapy in the treatment of postoperative deep infections after major spine deformity surgery in a group of high risk paediatric patients.

## Patients and methods

During 2003–2005, 68 paediatric patients with a non-idiopathic spine deformity and multidisciplinary risk factors for surgery were treated by the same surgeon at Karolinska University Hospital. All patients had followed the existing treatment protocol including preoperative optimisation of cardiopulmonary status, nutrition, and infection control. A free period of 2 years from an earlier skeletal infection, no clinical signs of urinary tract infection and normal blood tests were required. Prophylactic antibiotics were given during surgery: cloxacillin or cefuroxim at the start of surgery and every 4th hour during surgery. Still, six high risk patients developed postoperative deep infections. The diagnosis was based on local signs, sepsis, laboratory tests and radiologically detectable pathological features.

An 18-month old child (patient #4, Tables 1, 2) with neurological unilateral deficiencies, lumbosacral instability, skeletal and intradural anomalies also presented a major hemangioma in the gluteal soft tissues and retroperitoneal space. During her first year, the hemangioma was infected, clean though before the present spine surgery.

The six patients with postoperative deep infections were expected to have a complicated course of their infection treatment, it was therefore decided to introduce HBO as an adjuvant without delay based on the earlier good results from the neurosurgical department of the same hospital [4]. They were not suitable candidates for plastic surgical flaps due to poor soft tissues, and unsuccessful earlier trials. High pressure lavage was avoided due to the large intradural neurosurgical interventions with exposed dura grafts etc.

The patients' age at surgery, body weight, diagnosis, number of previous spine surgeries, type and length of the present surgical procedure, relative bleeding and follow-up time are given in Table 1. The relative bleeding was calculated as 100× blood loss (ml)/75× weight (kg) to represent the percentage of the total blood volume. In 5/6 patients, the dura was opened in the neurosurgical procedure as part in the release of a tethered cord. It was performed at the same session as the one-stage combined anterior and posterior or posterior only deformity correction. Only titanium implants were used for the spinal correction. The caudal level of the fusion and instrumentation included the lumbosacral junction in all cases. The bone transplantation included autologous bone with complementary homologous or synthetic bone substitute. There had been earlier multiple spine procedures elsewhere in 4/6 cases. 4/6 patients had a chronic urinary tract infection and 5/6 had a subnormal bladder function prior to surgery.

Data from patient reports, including radiological examinations, from all concerned disciplines were collected.

### HBO treatment

All patients in the study were spontaneously breathing and treated in either of two acrylic monoplace chambers (model 2500B or 3200; Sechrist Industries, Inc., Anaheim, CA, USA) pressurised with 100% oxygen, which allows the patients to breathe without mask or hood. Chambers allowed continued intravenous therapy and monitoring when necessary. If needed, children were accompanied in the chamber by parent or one of the hyperbaric staff.

Hyperbaric oxygen was administered at a pressure of 2.5–2.8 bar (250–280 kPa), 3 × 25 min with 10 min airbrakes, i.e. 75 min of oxygen in each session. Treatment was administered once daily 5 days a week except in cases of severe infections/threatened tissues when initial treatments were given twice daily and on weekends. Treatment protocol was chosen according to clinical severity of the infection, as judged in cooperation by orthopaedic surgeon and HBO specialist. The youngest children were accompanied in the chamber by a parent throughout the HBO series; others were accompanied only initially until they grew accustomed to the therapy.

## Results

A satisfactory correction with a balanced spine and radiologically healed fusion was achieved in all cases. There

**Table 1** Patient age, body weight at the time of index surgery, number of earlier surgical procedures, type and length of surgery, relative bleeding as % of the total calculated blood volume, and follow-up time

| Pat. no | Age (years) | Body weight (kg) | Diagnosis | No of previous surgery | Type of surgery | Surgery time (min) | Relative bleeding (%) | Follow-up (months) |
|---|---|---|---|---|---|---|---|---|
| 1 | 13.5 | 45 | MMC,A | 3 | APN, UT | 860 | 59 | 72 |
| 2 | 4 | 14 | MMC,A | 2 | APN, UT | 480 | 62 | 67 |
| 3 | 14.7 | 77 | DMD | 0 | P | 360 | 10 | 58 |
| 4 | 1.5 | 15 | LA,T | 2 | APN, UT | 120 | 15 | 48 |
| 5 | 12.6 | 52 | MMC,A | 1 | APN, UT | 875 | 30 | 42 |
| 6 | 16.5 | 85 | MMC,A | 5 | APN, UT | 720 | 19 | 37 |
| Mean | 10.5 | 48 | | 2.1 | | 569 | 32.5 | 54 |
| Median | 13 | 50 | | 2 | | 600 | 25 | 53 |

Diagnosis in addition to spine deformity: *MMC* myelomeningocele, *DMD* Duchenne muscular dystrophy, *A* intraspinal anomaly, *LA* lumbosacral agenesis, *T* tumour

Type of surgery: *APN* combined anterior and posterior spine surgery and neurosurgery in one session, *UT* untethering procedure, *P* posterior only spine surgery

**Table 2** Bacterial cultures from the postoperative deep infection, no of surgical revisions, time from index surgery to clinical healing of infection, antibiotic treatment length, no of HBO treatments, cost (Euro) of HBO treatment

| Pat. no | Cultures | No revisions | VAC | No HBO | Time from index surgery to 1:st HBO months | Antibiotic treatment months | Clinically healed months | HBO cost Euro |
|---|---|---|---|---|---|---|---|---|
| 1 | *Pseudomonas*, *Enterococcus*, *coagulase-neg. Staphylococcus* | 2 | No | 51 | 0.5 | 2 | 4 | 19 618 |
| 2 | *Morganella Morgani*, *coagulase-neg Staphylococcus*, *Enterococcus*, *Streptococcus* | 1 | No | 64 | 1 | 3 | 3 | 28 002 |
| 3 | *Staphylococcus*, *Enterococci* | 0 | No | 64 | 1.5 | 6 | 3 | 27 562 |
| 4 | *Staphylococcus* | 0 | Yes | 28 | 0.5 | 3 | 3 | 23 730 |
| 5 | *Staphylococcus*, *Bacteroides Fragilis* | 2 | Yes | 11 + 76 | 0 | 3 | 4 | 43 690 |
| 6 | *Staphylococcus*, *Klebsiella*, *Enterococcus* | 4 | Yes | 6 + 100 | 0 | 3 | 3 | 44 762 |
| Mean | | 1.5 | | 67 | 0.6 | 3.3 | 3.3 | 31 227 |
| Median | | 1.5 | | 64 | 0.5 | 3 | 3 | 27 772 |

*VAC* Vacuum-assisted closure

were no neurological complications, neither any cardiovascular events during surgery nor during follow-up. The implants were neither removed nor changed in any of the patients due to infection during the study period. In one case, a prominent iliac screw was prophylactically extracted due to risk of skin break down. Radiologically, intact implants without any signs of radiolucent zone were seen in all cases. Despite extensive neurosurgical intervention, no case of meningitis was developed.

Wound healing and normal blood tests were achieved within 4 months, Table 2. No recurrence of infection or wound problems occurred during the follow-up, mean follow-up time was 54 months (37–72 months).

In addition to the local wound cleaning on the ward or at out patient clinic without anaesthesia, a surgical wound revision under general anaesthesia was performed in four patients, in one case skin transplantation (patient no 5) and in another case a plastic surgical flap (patient no 6) were included, Table 2.

All patients received antibiotics according to their bacterial cultures as advised by specialists in infectious diseases. The most common cultures from the location of the deep postoperative wound infection were *Enterococcus, Pseudomonas* and *Staphylococcus*. The length of antibiotic treatment varied from 2 to 6 months (mean and median 3 months). Three of the patients were also treated with VAC of the wound.

Total number of HBO sessions, cost of HBO, surgical procedures after the index surgery, cultures, time to healing are presented in Table 2; Figs. 1, 2.

The side effects of HBO were minor and consisted of a few problems with middle ear equilibrations. They were

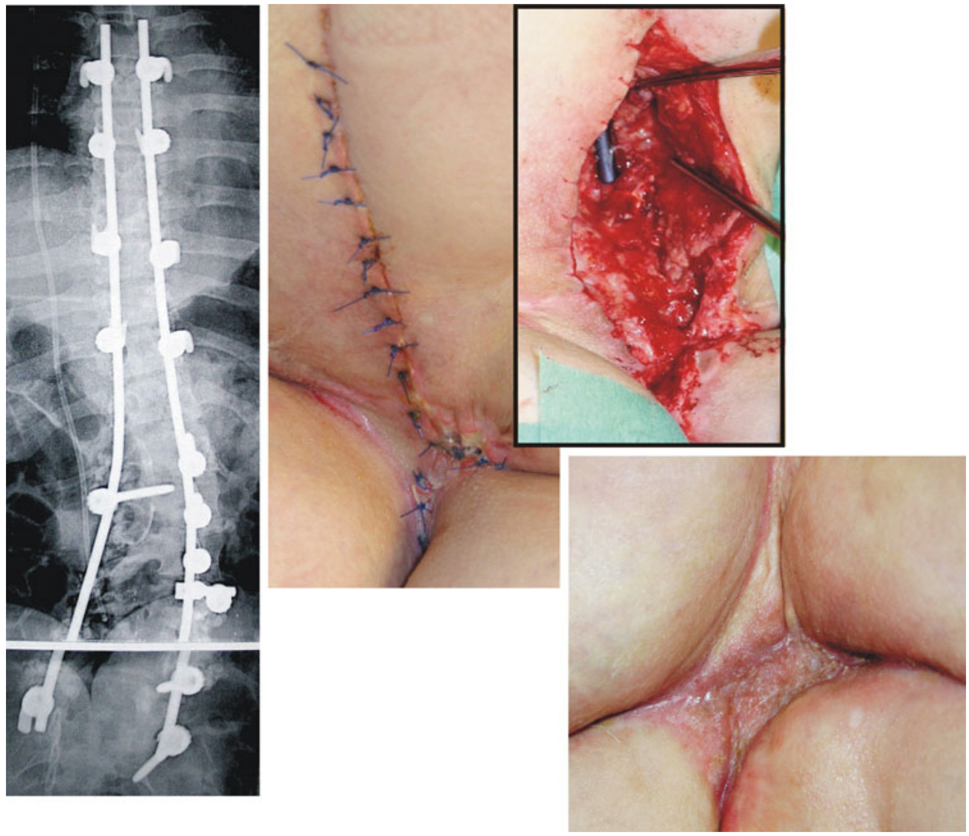

**Fig. 1** Patient nr 5. X-ray and signs of wound infection, which led to a deep infection and 15 cm rupture of the wound in the fibrotic scar tissue after earlier surgical interventions. After soft tissue revision and HBO treatment, increasing granulation tissue is seen in the bottom of wound. The wound heals without any plastic surgery intervention

**Fig. 2** Patient nr 4 during HBO-treatment together with her father

treated successfully with anticongestants. There were no seizures or episodes of central nervous system toxicity.

## Discussion

We report a consecutive series of six children with neuromuscular spine deformity who received HBO as an adjunct in the management of postoperative deep infection after complex correction surgery. Standard treatment is very time and resource consuming and can be hazardous for the patient. Removal of instrumentation or high pressure irrigation was not an alternative due to extensive intradural neurosurgical procedures. Literature still reports severe functional deterioration from repeated surgery with long convalescence periods.

Infection control and healing was achieved after surprisingly short time considering the poor soft tissue quality. All infections resolved and healing was on average reached in 3 months with a relatively short period of antibiotic treatment. No recurrence of infection was seen during the 3–6 year follow-up. The spinal implants remained intact without any bone healing problems or radiological signs of loosening. Two of the patients (no 5 and 6) started a planned HBO-treatment preoperatively because of the calculated high risk for infection. They had suffered postoperative infections at several previous surgical interventions, and did so despite HBO prophylaxis. They were treated with a prolonged HBO protocol including the use of vacuum-assisted wound closure (VAC), both these patients also healed without removal of implants [8].

Our results indicate that HBO therapy may reduce the number of revision surgeries and shorten antibiotic treatment and in-hospital time, which has a positive impact on the outcome and may reduce overall costs. It can be considered for use in more complex infections involving risk factors, such as multiple earlier infections, scarring after earlier surgery, occurrence of uncovered dura, bone tissue and implants.

A prospective randomized and controlled study was not possible due to the rare occurrence as well as complexity and variability of concurrent risk factors.

## Mechanism of action and rationale for HBO treatment

Most non-healing infected wounds are hypoxic [9] because of ischaemia. Ischaemia not only impairs oxygen delivery to tissues but also compromises antibiotic delivery and bacterial killing. These marginally viable ischaemic tissues are vulnerable to infection, exhibit poor infection control and poor wound healing despite meticulous wound care and antibiotic treatment. Infections, and the concurrent inflammation, increase oxygen consumption dramatically. In parallel with this, oxygen delivery is reduced because of tissue oedema and ischaemia. Wound tissue oxygenation and resistance to infection are thus further compromised.

Animal experiments using microelectrodes to measure oxygen partial pressures in normal, healing, and infected tissues and in tissues containing foreign material have demonstrated marked hypoxia, especially when infected foreign material was present [10]. Osteomyelitic bone exhibits decreased blood flow and a markedly reduced partial oxygen pressure [11].

A number of mechanisms can be postulated for the therapeutic benefits of HBO on infection and wound healing [5], [6]. HBO therapy restores intramedullary bone oxygen tension and phagocytic killing to normal or above-normal levels [11]. Leucocyte bacteria-killing capacity improves with normoxia, and is further enhanced with hyperoxia [12], [13]. The greatly increased tissue oxygen levels in ischaemic tissues during HBO therapy stimulate neovascularization [14, 6, 15], fibroplasia [16], and bone remodelling [7], making the tissues less ischaemic and improving long-term wound healing. Prolonged ischaemia and local inflammatory reactions may lead to paradoxal vasoconstriction and hyper-metabolic oedematous tissues. HBO induces vasodilatation in damaged tissues, increases perfusion, and has anti-inflammatory effects [17].

We found the typical slime-producing (biofilm) pathogens associated with implanted devices such as staphylococcus in the bacterial cultures from the postoperative deep infections. Biofilm formation is a major concern in nosocomial infections, especially with foreign bodies, because it creates a hypoxic milieu which protects the microorganisms from phagocytic killing as well as antibiotic agents. Hypoxia has been shown in both *Klebsiella* and *Pseudomonas* biofilm which restricts bacterial metabolic activity [18], [19] and leaves the neutrophils immobilized with diminished oxidative potential. During HBO this biofilm diffusion barrier, developed to protect the bacteria from phagocytosis, is subjugated.

Hyperbaric oxygen therapy has been added to treatment protocols in a variety of neurosurgical and orthopaedic infections and postoperative complications in bone and soft tissues [4], [20] with successful outcomes.

Treatment with normobaric 100% oxygen has no such effects.

These mechanisms, might explain the unusually fast healing of the infections in this study as compared to standard methods in clinical praxis. It might also explain the absence of recurrence of infection in spite of the short antibiotic treatment time and ability to save implants with few surgical revisions.

## Side effects

No adverse events were seen in the patients with a combined anterior and posterior surgery in the present study.

The side effects of HBO treatment were minimal and consisted of temporary pressure equalisation problems. According to earlier experience seizures may occur, especially when therapy is administered to patients with fever or when hypercapnia is present. An incidence of 1/10,000 treatments is often cited. Seizures are self-limiting, and sequelae are uncommon.

## Dose and duration

Dose and duration of HBO therapy was based on protocols of earlier clinical experience. To achieve infection control, treatment pressures of (2.8 bar) were initially used, twice daily 7 days a week. When a positive clinical response had been obtained, pressure was decreased (2.5 bar) and treatments were administered once daily, 5 days each week. The general principle was to treat patients until orthopaedic surgeon and hyperbaric specialist judged that host responses could sustain infection control and healing.

The present HBO treatment dose and duration indicates that infection control and establishment of the healing process can be rapid (1–2 weeks) and that many patients continue to exhibit improvement after cessation of HBO therapy. Optimal treatment protocol for bone-remodelling and long-term infection control need further studies. Our initial treatment schedule has been successful, but future refinements include a more customised approach tailored to individual responses.

## Conclusion

Hyperbaric oxygen therapy is a safe and potentially useful adjuvant treatment to the standard therapy of early post-operative deep infections in complex paediatric spine deformity patients with multidisciplinary risk factors.

**Acknowledgments** The study has been conducted in conformity with Ethical Principles for Medical Research Involving Human Subjects (World Medical Association Declaration of Helsinki, Geneva, 2000 and has been reviewed by the Ethics Committee of Karolinska Institutet (2007/1491-31/3). Stockholm City Council has supported this study with funds for ethical review.

**Conflict of interest** None.

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