Hyperbaric oxygen treatment of neonates: a case series

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Abstract

(Kavram G, Yasa B, Bor M, Bilgin L, Ince EZ, Mirasoglu B, Coban EA. Hyperbaric oxygen treatment of neonates: a case series. Diving and Hyperbaric Medicine. 2025 30 September;55(3):284–288. doi: 10.28920/dhm55.3.284-288. PMID:40986926.) Hyperbaric oxygen therapy (HBOT) administers oxygen under high pressure, mainly for decompression illness, carbon monoxide intoxication, wound healing, infections, and acute peripheral arterial ischaemia. There has been limited use in newborn infants. This case series aims to highlight the potential role of HBOT in management of rare and challenging conditions encountered in the neonatal period. Although HBOT is widely available, its application in newborns remains limited and not well established. We present three neonatal cases: acute peripheral ischaemia; vascular compromise due to thrombosis and compartment syndrome; and a non-healing surgical wound following omphalocele repair. We aim to emphasise the potential clinical benefit and discuss the safety profile of HBOT in select life or limb threatening neonatal pathologies. These cases demonstrate that HBOT, when use as an adjunctive therapy, may contribute to tissue salvage and overall improved outcomes in critically ill neonates. Our intention is to raise awareness and contribute to the limited literature regarding neonatal HBOT, particularly in contexts where usual treatment options are insufficient.

Introduction

Hyperbaric oxygen therapy (HBOT) is a medical treatment administered in a high-pressure environment by breathing 100% oxygen intermittently or continuously.[1] A minimum pressure of 203 kPa (2.0 atmospheres absolute [atm abs]) is recommended, which can be increased to a maximum of 284–304 kPa (2.8–3 atm abs).[2] Patients can be treated independently or as a group with other patients. The duration of treatment for most indications is 1.5–2 hours per session, usually to a maximum of four sessions per 24 hours. Courses of 20–60 treatment sessions are usually administered, depending on the indication.[3]

Both inspired oxygen and pressure potentially have therapeutic effects by enhancing gas distribution and oxygen transportation to ischaemic tissues. It induces hyperoxia independent of haemoglobin, stimulating anti-inflammatory cytokines, growth factors, and antioxidants. This way, HBOT promotes angiogenesis, disrupts bacterial respiration, and reduces inflammation by enhancing antioxidant formation and regulatory T-cell turnover.[4–6]

HBOT is predominantly used in adults for conditions like decompression illness, carbon monoxide poisoning, acute peripheral ischaemia, chronic wounds, and soft tissue infections.[7] Although its use in newborns is limited, there are previous case reports of treating non-healing wounds, necrotising enterocolitis, thrombosis, carbon monoxide poisoning, and hypoxic-ischaemic encephalopathy in which improvement seemed associated with application of HBOT.[8–13] Animal studies suggest neuroprotective effects in hypoxic encephalopathy, and reducing apoptosis and the impact of oxygen radicals within 72 hours post-damage.[14]

Use of HBOT in neonates and infants is an area where there is extremely limited experience and expertise worldwide. This small case series aims to present our experience using HBOT during the neonatal period. In all three cases, parents provided written informed consent for inclusion of their child's case history and images in this manuscript.

All three patients were treated in a multiplace chamber (Hipertech ZYRON 12, 2008) and a specially designed baby incubator was used for all (Figure 1). A continuous oxygen flow was provided in the incubator through a gas inlet and outlet. All treatments were accompanied by an inside attendant and a paediatric physician. Attendants intervened through the lid of the incubator when needed. Thermoregulation was provided by covering the baby with multilayer cotton sheets in the incubator, and if needed heated Mediflex® bags were placed under the sheets,

Figure 1
Adapted incubator for treating neonates (left) and in use in the hyperbaric chamber (right)

avoiding direct contact between the baby and the bags. Pacifiers were used during compression and decompression for enabling middle ear equalisation and patients were regularly examined by a paediatric specialist after each session for middle ear barotrauma. Tympanostomy tubes were not needed.

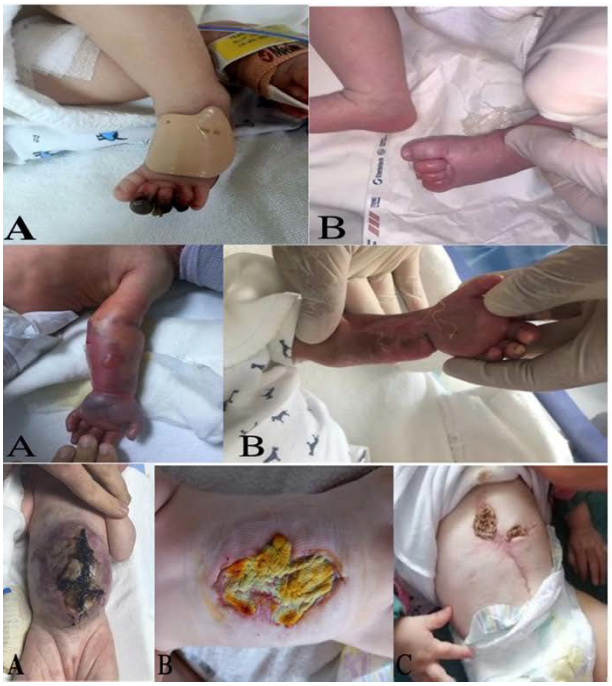
Case one

A 3,160 g girl, delivered by caesarean section at 36 weeks due to placenta previa, presented at day 21 of life with suspected peripheral arterial thrombosis involving toes on the left foot. She had three previous hospitalisations for jaundice and sepsis. Her mother and grandmother tested positive for COVID-19 infection one week before admission. Examination revealed bruising and necrosis on the left foot's second, third, and fourth toes (Figure 2). Arterial and venous Doppler ultrasound showed patent vessels and normal blood flow, ruling out current thrombosis. Metabolic and haematological investigations revealed normal homocysteine (7 $\mu mol \cdot L^{-1}$), vitamin B12 (579 $pg \cdot mL^{-1}$), and folate (12 $ng \cdot mL^{-1}$) levels. Lipid profile showed elevated triglycerides (200 $mg \cdot dL^{-1}$), low HDL (20 $mg \cdot L^{-1}$), normal LDL (47 $mg \cdot dL^{-1}$), and total cholesterol (107 $mg \cdot dL^{-1}$). Coagulation factors included factor 7 (65% of normal activity), factor 8 (224% of normal activity), factor 9 (78% of normal activity), factor 11 (40% of normal activity), and factor 12 (64% of normal activity). Protein C and S levels were normal. Factor V Leiden, methylenetetrahydrofolate reductase, prothrombin 20210 mutations, antiphospholipid and anticardiolipin antibodies were negative. Enoxaparin (two x 550 U subcutaneously) and pentoxifylline (intravenous, 30 $mg \cdot kg^{-1} \cdot day^{-1}$ as a six hour infusion per day, for five days) treatments were initiated. Plastic and reconstructive surgery recommended amputation, whereas underwater and hyperbaric medicine suggested HBOT. Despite a negative COVID-19 PCR test, IgG and IgM antibodies were positive. HBOT was administered twice daily for the first five days and then once daily for 21 sessions (243 kPa [2.4 atm abs], two hours each). The patient was discharged on the 37th day of life with complete healing without loss of extremity or function. Eye and hearing examinations yielded the expected results, and neurological evaluations detected no abnormalities (Table 1).

Case two

A 2,690 g girl born by elective caesarean section at 39 weeks gestation presented with a circulatory disorder in the left forearm on the first postnatal day. Physical examination revealed ecchymosis, bullous, exfoliative lesions, and a demarcation line on the left forearm (Figure 2). No radial pulse was detected in the left arm, and Moro and grasp reflexes were absent. Doppler ultrasound and CT angiography confirmed significant vascularisation loss in subclavian, axillary, and distal arteries and veins, with no blood flow observed in brachial, radial, and ulnar arteries and their branches. Sepsis could not be ruled out and antibiotic treatment with teicoplanin and cefotaxime was started. It was recommended to administer fresh frozen plasma in addition to heparin infusion, pentoxifylline infusion (30 $mg \cdot kg^{-1} \cdot day^{-1}$ infused for six hours per day, five days) and iliomedin treatments. The patient underwent HBOT three times a day for first week and twice a day for the following week. During the ongoing treatment, fasciotomy was decided upon due to a suspicion of compartment syndrome (10th day of life). Laboratory examinations to determine the cause of thrombosis were all within the normal range except for elevated protein S and factor 8 levels [homocysteine (7 $\mu mol \cdot L^{-1}$), vitamin B12 (579 $pg \cdot mL^{-1}$), folate (12.92

Figure 2
Photo montage of the three cases reported here



(Case 1).
A: Necrosis of the toes before treatment. **B:** Appearance of the toes one week after the treatment.

(Case 2).
A: Ecchymosis and bullae on the left forearm after birth.
B: Left arm healed with contracture of the wrist.

(Case 3).
A: Necrosis and circulation disorder around the 'mesh' on the 4th day of omphalocele surgery. **B:** Disappearance of necrotic tissue and regeneration at discharge.
C: Wound healing without flap surgery one year after discharge.

Table 1
Summary of neonatal cases treated with hyperbaric oxygen therapy in our clinic

Case	Indication	Birth week Age HBOT started	Dose/duration	Side effects	Result
One	Thrombosis	Week 36/40 21st day of life	243 kPa, two hours 21 sessions	Nil	Normal neurological exam at follow-up
Two	Thrombosis	Week 39/40 First day of life	243 kPa, two hours 28 sessions	Nil	Not followed up
Three	Wound	Week 36/40 34th day of life	243 kPa, two hours 15 sessions	Nil	Primary wound healing maintained at two years age

ng·mL^{-1}), protein C levels (47.7%), protein S levels (39.9%), Factor 8 (224.4%)]. Elevated factor 8 levels are associated with an increased risk of venous thromboembolism, such as deep vein thrombosis or pulmonary embolism. This is one of the most clinically significant implications of high factor 8 levels. Despite the development of mild contracture, the extremity was successfully preserved, and the patient was discharged on the 46th day with recommendations for physical therapy. Eye and hearing examinations yielded the expected results, and neurological evaluations detected no abnormalities (Table 1).

Case three

A 2,540 g girl, diagnosed with omphalocele antenatally was born by emergency caesarean section at 34 weeks gestation. The omphalocele sac, measuring 6 x 8 cm, was treated with wet sterile gauze upon delivery, and the baby was transferred to the neonatal intensive care unit. Surgery was performed to return the intestines to the abdomen and reposition the liver on the 5th and 21st day of life respectively, after which the abdomen was closed with a 'mesh'. Ampicillin and gentamicin antibiotic therapy which was started in the preoperative period was applied for six days and switched to vancomycin and meropenem due to an increase in acute phase reactants. Vancomycin-meropenem was completed at the fourteenth day of treatment. Micafungin was added on the sixth postoperative day (36th day of life) after the growth of *Candida* species was observed in the tracheal aspirate culture. The antifungal treatment was completed in 15 days. On the 32nd day of life (after the second operation), the patient was referred to underwater medicine due to skin loss around the incision line and compromised tissue circulation. Beginning at the 34th day of life, HBOT treatment was given eight hourly on the first day. It was planned to receive treatment twice a day for the next three days and once a day thereafter. HBOT was administered at (243 kPa [2.4 atm abs], two hours each). Fifteen sessions were administered

until the postnatal forty-fourth day. This was associated with regeneration of the area of skin loss around the incision line (Figure 2). Eye and hearing examinations yielded the expected results, and neurological evaluations detected no abnormalities. The patient was discharged on the 66th day of life (Table 1).

Discussion

Prior to these cases, in Turkey, a seven-day-old infant with carbon monoxide poisoning received HBOT, consisting of three 30-minute sessions daily at 243 kPa; however, one of the newborns included in our study was younger. Average neurological outcome was noted at discharge and six months of age.[12]

Thrombosis, while rare in neonates, poses a heightened risk in critically ill newborns, often leading to ischaemia-related limb loss.[14,15] HBOT has emerged as a promising intervention for neonatal extremity ischaemia due to thrombosis.[10,11] Wiebers et al. successfully administered HBOT together with thrombolysis and anticoagulation to a term male newborn with bilateral lower extremity thrombosis of undetermined aetiology, averting amputation in one extremity.[10] Similarly, HBOT in conjunction with heparin and fresh frozen plasma effectively treated a preterm newborn with purpura fulminans, yielding no adverse effects.[11] HBOT was administered for extremity ischaemia due to thrombosis in our cases one and two, both of which were discharged without any loss of extremity or motor function. While long-term outcomes were unreported, these infants remained fully recovered at the six-month follow-up.

Although peripheral arterial ischaemia is a common indication for HBOT in adults, there is limited literature on neonatal cases. The youngest known HBOT recipient for arterial gas embolism was a three-month-old baby who received HBOT for cerebral air embolism following a Glenn shunt operation for congenital heart disease, effectively resolving embolism. Despite bilateral tympanic membrane haemorrhage during treatment, the patient exhibited regular hearing examination at discharge.[16]

In another case report, a 17-month-old male patient with Noonan syndrome, idiopathic thrombocytopenic purpura, and bilateral undescended testicles developed haematoma and oedema in the scrotum and penis the day after bilateral orchiopexy and circumcision. Ischaemic appearances were observed on the penile and scrotal skin on the second postoperative day. Enoxaparin sodium and fresh frozen plasma were started on the recommendation of haematology. HBOT was initiated considering the possibility of tissue necrosis. A rapid healing was observed within five days. It was concluded that HBOT may be considered as an additional treatment option in patients with similar conditions.[17]

A retrospective study by Kangal et al. reported the outcomes and described difficulties encountered in infants 12 months old or younger undergoing HBOT; a rare patient population in this therapeutic intervention. Demographic data, clinical presentation, HBOT indication, chamber type, oxygen delivery method, total number of treatments, outcome and complications were extracted from clinical records. A total of 54 infants were included in the study. The patients' median age was 3.5 (range 0–12) months. The major HBOT indication was acute carbon monoxide intoxication ($n = 32$). A total of 275 HBOT treatments were administered, mostly performed in multiplace chambers ($n = 196$, 71%). Only one patient (2%) required mechanical ventilation. Acute signs were fully resolved in the most patients ($n = 40$, 74%). No complications related to HBOT were reported. In conclusion, it was suggested that HBOT may be a safe and effective treatment for infants.[18]

In another report, eight patients, six with hypoxic ischaemic encephalopathy and two with necrotising enterocolitis underwent HBOT at 203 kPa (2 atm abs). Neonatologists provided respiratory support during treatment. No adverse effects were observed in ophthalmological and central nervous systems. Neurodevelopmental examinations at three and six months post-treatment were standard for all patients. Long-term follow-up was conducted for two patients, both exhibiting normal neurological examinations at age five, with one case reporting mild attention deficit.[9]

HBOT is widely used for wound healing in adults but its use is limited in newborns.[7] HBOT has been successfully used in treating newborns after cardiac surgery and wound treatment due to necrosis of the glans penis.[13] In our case three, HBOT was administered to a patient with extensive necrosis post-omphalocele surgery. Following HBOT, reperfusion occurred in necrotic areas, demarcation lines formed, and wound healing was achieved without flap surgery.

In our experience, the limited use of HBOT in neonates is mainly due to concerns about the potential side effects associated with hyperoxia and challenges related to safe transportation, thermoregulation, and sedation during treatment. While term newborns possess relatively robust antioxidant systems, HBOT may pose risks, including respiratory morbidities and retinopathy, particularly for infants with a gestational age of less than 34 weeks and a birth weight under 1,200 g due to their immature antioxidant systems.[9]

HBOT side effects encompass barotrauma, visual auditory impairments, and potential oxygen toxicity to the central nervous system and lungs. While research on the neuroprotective effects of HBOT in adults has expanded, data on its long-term impacts on the developing nervous system in newborns are scarce.[19] None of our three patients experienced any side effects related to HBOT. Eye and hearing examinations yielded the expected (normal) results, and neurological evaluations detected no abnormalities.

Conclusions

HBOT shows promise for ischaemic and thrombotic events, but data on its use and risks in newborns are limited. Reporting long-term outcomes could improve its safety for challenging cases. In conclusion, HBOT can be a beneficial treatment option for difficult complications seen in neonates, including acute peripheral ischaemia, non-healing wounds and compromised flaps as in our case of omphalocele.

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