Hyperbaric oxygen in the treatment of asphyxia in two newborn infants

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Hyperbaric oxygen, hyperbaric oxygen therapy, neuroprotection, brain injury, children, case reports

Abstract

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Hypoxic-ischaemic encephalopathy (HIE) is a common cause of brain damage in the neonatal period. Approximately 10% of births involve some degree of asphyxia, and 1% of these are severe. Current treatment has been limited to supportive measures and the recent use of hypothermia. Beneficial effects of hyperbaric oxygen treatment (HBOT) in neonatal asphyxia have been reported in the Chinese literature. We report the use of HBOT to treat two term neonates with moderate HIE according to Sarnat's classification. Clinical improvement occurred following HBOT. A 50% decrease in the total creatine phosphokinase (CPK) level and a 40% decrease in the CPK myocardial fraction were observed within 24 hours of the first treatment. The decline in CPK levels may be related to a reduction in the overall systemic inflammatory process and cannot be attributed solely to a reduction in brain damage. HBOT may have a role in HIE.

Introduction

Perinatal asphyxia occurs at disruption or cessation of gas exchange at the placenta or lung, causing progressive hypoxaemia and hypercapnia. Approximately 10% of births involve some degree of asphyxia, and 1% of these are severe.[1] Hypoxic-ischaemic encephalopathy (HIE) is a common cause of brain damage in the neonatal period and remains an important cause of neonatal morbidity and mortality.[1,2] Current therapeutic strategies involve mainly supportive measures, e.g., adequate oxygenation and ventilation, blood pressure support, maintenance of a normoglycaemic state, and fluid management. Recently, hypothermia has been used to decrease the neurological sequelae of HIE.[2]

Theoretical and anecdotal evidence exists for the beneficial effects of hyperbaric oxygen therapy (HBOT) in neonatal asphyxia.[3–5] Meta-analysis of 20 Chinese trials demonstrated a significant reduction in mortality in neonates with HIE treated with HBOT compared to those not receiving HBOT (odds ratio (OR) 0.26, 95% confidence interval (CI) 0.14, 0.46). Neurological damage was also reduced in infants treated with HBOT (OR 0.41, 95% CI 0.27, 0.61).[6] However, these studies were not performed in a blinded fashion, and the results should be interpreted with caution.

Based on these data, HBOT was used for two newborns with HIE. Permission to report these cases was obtained from the parents. Clinical evaluation, using the Sarnat Scale,[7] and measurements of creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) levels were used to assess patient progress. Breathing 100% oxygen, each patient was compressed to 203 kPa for 30 minutes, followed by decompression over five minutes, followed by a further 30 minutes of oxygen breathing at room pressure. Both patients received standard care, including body temperature control, early nutritional support and glucose monitoring. Anticonvulsants and diuretics were not used.

Case 1

Following a traumatic vaginal delivery with a prolonged second stage of labour, Kristeller manoeuvres were performed for a cord round the neck. The child, weighing 4.2 kg, was diagnosed with perinatal asphyxia, ultrasound-documented subarachnoid hemorrhage and diffuse left renal injury. At 36 hours of age, the patient became lethargic, and the sucking reflex slowed. Examination revealed an incomplete Moro reflex, caput succedaneum, and a right parietal cephalohaematoma (Sarnat scale II); the head circumference was 37.5 cm. Total creatine phosphokinase (CPK), creatine kinase-myocardial fraction (CK-MB) and lactate dehydrogenase (LDH) values are shown in Table 1.

After obtaining informed consent from the family, three HBOT sessions were initiated, commencing at 42 hours of age. At 48 hours, after the first HBOT, clinical improvement had occurred and head circumference had decreased by 0.5 cm. A second HBOT was given at 68 hours of age and a third at 96 hours. Neurologic examination had normalised, and a significant decrease in the size of the cephalohaematoma was noted. CPK, CPK-MB, and LDH levels improved (Table 1). The patient was discharged without further complications. Auditory evoked potentials, cerebral ultrasound, and an electroencephalogram were normal.

Case 2

A newborn, weighing 2.9 kg, experienced moderate asphyxia secondary to uterine rupture and Caesarean delivery. Apgar

scores were 3, 4, 5, and 8 at 1, 5, 10, and 15 minutes, respectively. On admission to the neonatal intensive care unit, the newborn demonstrated a slow sucking reflex, increased muscle tone, decreased reflexes, and an incomplete Moro reflex (Sarnat scale II). Initial CPK, CPK MB and LDH are shown in Table 1.

After parental permission, two HBOT sessions were given, commencing at 12 hours of age. After the first, decreased irritability and improved reflexes were observed. After the second, completed by 36 hours of age, the newborn continued to demonstrate clinical improvement. Changes in CPK, CPK-MB, and CPK-BB levels are shown in Table 1. The patient was discharged without complications.

In both cases, ophthalmologic studies were performed subsequently to detect retrolental fibroplasia, and no evidence of retinal damage was found. Clinical and radiological studies also showed no lung damage as a consequence of HBOT. At six months of age, psychometric development in both babies was assessed by external evaluators and declared normal. Neither patient experienced seizure activity nor evidence of residual neurological damage.

Discussion

HBOT involves the administration of 100% oxygen at greater than atmospheric pressure to increase dissolved oxygen and improve overall oxygenation within tissues. HBOT can reverse local hypoxia by inhibiting post-ischaemic vasoconstriction, thereby decreasing reperfusion injury.[8] Neutrophils have been implicated as the primary culprit in reperfusion injury. Adhering to ischaemic vessel walls, they release proteases and produce free radicals, leading to pathologic vasoconstriction and extensive tissue destruction.[3,4] HBOT not only inhibits neutrophil adherence and post-ischaemic vasoconstriction, but also promotes collagen matrix formation, which is essential for angiogenesis and restoration of blood flow to injured tissue. HBOT will also reduce cerebral oedema.[3,8]

Typically, patients with HIE exhibit a progressive clinical deterioration. However in these two neonates, we identified an unexpected clinical course, with clinical improvement immediately after the first HBOT session, as measured by the Sarnat scale, and their enzyme levels decreased markedly. Normal serum CPK levels in the healthy newborn range from 10–200 U L^{-1}. Levels usually rise within the first six hours after ischaemic injury. If hypoxia is not sustained, CPK levels peak 18 hours after injury and return to normal within two to three days. A serum CK-MB level >92.6 U L^{-1} at eight hours, or >60 U L^{-1} at 24 hours is considered abnormal. Newborns with elevated serum CPK levels within the first six hours of birth should be closely monitored for the development of HIE.[9] The increased levels of enzymes in these two cases decreased more rapidly than expected. This drop in enzyme levels may actually reflect a decrease in a systemic inflammatory process rather than being a specific indication of neurological improvement.

Retinopathy of prematurity is similar to an ischaemic/reperfusion injury. HBOT has been used to manage and prevent ischaemic/reperfusion injury, and short exposures to oxygen pressures of 203 kPa for 45 minutes once or twice a day are unlikely to cause harm. Acute central nervous system oxygen toxicity is rare at 203 kPa or lower, and pulmonary oxygen toxicity is generally not seen with HBOT. The HBOT management scheme used in these two cases, combining both hyperbaric and normobaric oxygen was intended to minimise any risk of toxic side effects. This strategy has been used successfully in newborns with a history of hyaline membrane disease and/or bronchopulmonary dysplasia.[9] No evidence of lung damage or eye damage was identified in these two newborns following HBOT.

Promising clinical evidence of benefit exists for treatment of HIE using mild to moderate hypothermia (33–34ºC) using total body or selective head cooling applied within six hours of birth.[2,10] There are no studies reported comparing controlled hypothermia with HBOT or reports of their combined use.

Conclusion

Two neonates with HIE improved with HBOT consistent with previous reports of its potential benefit. HBOT may represent a viable alternative to, or be combined with controlled hypothermia.

Table 1
Enzyme levels in two neonates suffering from neonatal asphyxia before, during and after a short course of hyperbaric oxygen therapy (HBOT)

		Pre-HBOT	Post-HBOT 1	Post-HBOT 2	Post-HBOT 3
Case 1	CPK total (units)	3069	795	342	493
	CK-MB (units)	58	35	29	41
	LDH (units)	1036	730	645	657
Case 2	CPK total (units)	2156	1230	539	
	CK-MB (units)	77	43	30	

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