

Hyperbaric Oxygen Therapy In The Prevention Of Delayed Deterioration And Cerebral Palsy Following Periventricular Damage In The Newborn

Phillip B James, Wolfson Hyperbaric Medicine Unit, Ninewells Medical School, The University of Dundee, Scotland.

Keywords: Hyperbaric oxygen therapy, periventricular leucomalacia, cerebral palsy.

Introduction

The introduction of routine ultrasound screening in premature neonates can reveal evidence of cerebral damage prior to the development of clinical signs. Although far from being a sensitive tool, ultrasound can demonstrate the gross forms of periventricular hemorrhage and edema that characterize this form of brain damage. The mechanisms suggested for periventricular damage in premature neonates include hypertension and cerebral trauma,¹ but it is thought that these factors are only responsible for some of the cases.

Circumstantial evidence suggests that placental embolism and the passage of emboli through the patent foramen ovale may be a factor, but this is controversial². All of the mechanisms suggested are likely to be associated with tissue hypoxia.

It has been established clinically that many brain damaged infants may develop normally for some months, before the spasticity characteristic of cerebral palsy becomes apparent. In the first period, there is a clear evidence from the responses of the child that the upper motor neuron and the long tracts are operating and able to activate the lower motor neurons.

Why then should the spasticity develop after a delay? From pathological studies it would appear that in most premature infants the motor cortex is not affected and the deterioration is in the fibres of the pyramidal tract.¹

At the level of the internal capsule, the tracts pass close to the cerebral ventricles, the area affected in periventricular leucomalacia. The vasculature of the area is immature in infants of about 30 weeks gestation as demonstrated by microangiography.³ The development of hemorrhage at birth is unequivocal evidence of gross blood-brain barrier damage. It would seem likely that continued blood-brain barrier dysfunction and the resultant edema leads eventually to degeneration of the motor fibres in this area.

Evidence from the anatomical disposition of the fibres in the internal capsule accords with this view, as the legs are more commonly affected than the arms.

A further factor is likely to be related to failure of the myelination.

Normal myelination begins about two weeks before term and spreads from the brain stem. It is usually complete, including the cerebral hemispheres, by the end of the first year of life. If there is significant edema from the blood-brain barrier dysfunction in the internal capsule area, myelination is unlikely to take place, leaving the axis cylinders exposed and vulnerable. Secondary degeneration may then take place and spasticity of the appropriate limb develops. (NB What about sensory function) This accords with the developmental sequence from the correlation of the ultrasound, clinical and nuclear magnetic resonance findings described by Dubowitz et al.⁴ In a study of two survivors of triplets, M.R.I. has demonstrated failure of myelination in the child with periventricular leucomalacia. An important difference between preterm and term infants has been pointed out by Larroche in 1977.⁵ In pre-term infants, periventricular leucomalacia is often the only brain lesion present, but, in full term infants, cerebral damage is usually associated with evidence of neuronal necrosis.

Case Report

On the 23rd December 1987, identical twins (1435 and 1358 gms respectively) at 29 weeks gestation were born by emergency Caesarian section, after the mother went into premature labor. Ultrasound scanning on the third day post-delivery revealed a periventricular hemorrhage in the left cerebral medulla of the larger twin. A repeat scan on day 15 showed extension of this lesion and damage also on the right side. The parents were informed that the child would almost certainly develop spastic quadriplegia, visual defects and mental retardation. It was also felt unlikely that she would ever be able to sit up. Two and a half months post-delivery, just before discharge from the hospital, there was a mild hydrocephaly, but all four limbs were moving normally. The baby was feeding and gaining weight.

The child left hospital at the beginning of March 1988. In view of the very bad prognosis and the undoubted presence of cerebral edema, it was decided to see if hyperbaric oxygen therapy would assist in the maturation of the medulla and hopefully, by preserving the long tracts, avoid the development of spasticity. As the child was at term and normal retinal development had taken place retrolental fibroplasia would not be likely to occur. Therapy consisted of 1 hour sessions at 2 ATA in a monoplace chamber for six days a week for three months, five days a week for three months and finally three sessions a week to nine months. A plastic bowl was used for the head of the baby and a polythene sleeve enclosed in the body. A continuous flow of oxygen was provided from a Scott regulator on free flow and the chamber flushed regularly.

A Spitz valve was inserted at six months to relieve intracranial pressure.

Audiometry indicated deafness in the right ear at his time. At eighteen months there was no sign of spasticity, but recently therapy was restarted because of evidence of mild spasticity in the right leg. The child is alert and has some co-ordination, although well behind her twin in development.

The therapy was conducted on a single blind basis as none of the medical, nursing or paramedical staff were aware of the hyperbaric oxygen therapy being used. Although, even at this state, it is by no means certain that the child has escaped the gross consequences of cerebral damage, from the progress made to-date it would appear unlikely that dramatic deterioration will occur at this stage. The child is very alert and responsive. Head control is developing slowly. She is beginning to crawl and is able to place objects in her mouth.

Discussion

Unfortunately, it has not been possible to use magnetic resonance imaging to follow the extent of myelination in this child. Young children who sustain damage to the cerebral medulla from micro-embolism in cardiac surgery also develop enlargement of the cerebral ventricles demonstrable on computed tomography.⁶ However it is of paramount importance to recognize that this has been found to be reversed with regrowth of medullary tissue over a period of 6-11 months. The most likely explanation of this phenomenon is that it is due to remyelination, as most of the volume of the cerebral medulla is due to the bulk of the myelin sheaths. In adults, blood-brain barrier damage in the periventricular area, where the veins draining the area of the medulla run parallel to the wall of the lateral ventricle, leads to the characteristic demyelination of multiple sclerosis.⁷

The condition often progresses to a leucomalacia with ventricular dilatation identical to that seen in periventricular leucomalacia in the infant. From pathological studies and from M.R.I. there is unequivocal evidence of edema, which inevitably limits oxygen transport. Although mild degrees of hypoxia appear to act as a stimulus to capillary neogenesis, severe hypoxia in the words of J.S. Haldane⁸ not only stops the machine, but also wrecks what we took to be the machinery. In the developing infant this will impede the vascularisation of this critical area. Intermittent elevation of the partial pressure of oxygen under hyperbaric conditions not only improves the immediate oxygen availability, but also reduces tissue hydrostatic pressure and allows the resolution of edema. On scientific grounds there would appear to be an excellent rationale for the use of hyperbaric oxygen in the prevention of delayed deterioration in damage to the cerebral medulla in the preterm infant. Clearly prevention is better than cure and monitoring with magnetic resonance may allow the effect to be demonstrated in real time. Normobaric oxygen supplementation has already proven of value in the prevention of morbidity in babies with intra-uterine growth retardation, where there has been proven evidence of hypoxia.

Finally, hyperbaric oxygen has been shown to be of value in a case of foetal distress, probably associated with premature placental separation and amniotic fluid embolism.⁹ A mother close to term who had been admitted for observation after an antepartum hemorrhage collapsed with a left hemiplegia. She rapidly lost consciousness and developed stertorous respiration. Oxygen at normal atmospheric pressure produced only marginal improvement in her condition and, because of severe fetal distress, a Caesarian section was performed at 2 ATA in a multiplace

chamber. It is notable that, despite the use of hyperbaric oxygen, the uterus was noted to be slightly cyanosed and the maximum arterial oxygen tension achieved was 490 mm Hg. However the fetal heart rate which was 220 and irregular before compression, fell to 165 and became regular. A normal live female infant was born with an Apgar score of 9. There would appear to be reasonable grounds to suggest that all deliveries in premature labor should be undertaken under hyperbaric conditions to protect the fetus from hypoxia during this critical period. Apparently this is undertaken by colleagues in Russia and may be important in the prevention of the blood-brain barrier damage that leads to periventricular haemorrhage and leucomalacia.

It is clear that hypoxia complicated many facets of obstetric and neonatal practice. The rapid reversal of hypoxia by hyperbaric oxygen in limited the extent of tissue damage may prove to be critical to the reduction of many distressing forms of infant morbidity.

References

1. Pape KE, Wigglesworth JS. Haemorrhage, ischaemia and the perinatal brain. Clinics in developmental medicine. Nos 69/70 William Heinemann Medical Books, London, 1979.
2. James PB. Placental embolism : a possible cause of respiratory distress and cerebral damage in the newborn. Submitted to : Med Hypoth 1989.
3. Takashima S, Tanaka K. Development of cerebrovascular architecture and its relationship to periventricular leukomalacia. Arch Neurol 1978;35:11-16.
4. Dubowitz LMS, Bydder GM, Mushkin J. Developmental sequence of periventricular leukomalacia. Arch Dis Child 1985;60:349-55.
5. Larroche JC. Developmental pathology of the neonate. Amsterdam: Excerpta Medica 1977.
6. Muraoka R, Yokota M, Aoshima M, et al. Subclinical changes in brain morphology following cardiac operations as reflected by computed tomographic scans of the brain. J Thorac Cardiovasc Surg 1981;81:364-69.
7. Allen IV. The pathology of multiple sclerosis: fact, fiction, and hypothesis. Neuropath Appl Neurobiol 1981;7:169-82.
8. Haldane JS. Respiration. Yale University Press, 1923.
9. Ledingham I McA, McBride TI, Jennett WB, et al. Fatal brain damage associated with cardiomyopathy of pregnancy with note on Caesarian section in a hyperbaric chamber. Br Med J 1968;4:285-87.

Presented at the 2nd International Hyperbaric Oxygen Society Conference Kos 1988