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Research

Clinical effectiveness of treatment with hyperbaric oxygen for neonatal hypoxic-ischaemic encephalopathy: systematic review of Chinese literature

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Abstract

Objectives To investigate the clinical effectiveness of treatment with hyperbaric oxygen for neonates with hypoxic-ischaemic encephalopathy. This treatment is frequently used in China but much less often in the West.

Data sources Western (Cochrane controlled trials register and database of systematic reviews, Medline, Embase, CINAHL, and HealthSTAR) and Chinese (China Hospital Digital Library, Chinese Medical Journal Network) databases and hand search of Chinese journals. No language restrictions.

Review methods Randomised or quasi-randomised controlled trials of treatment with hyperbaric oxygen compared with "usual care" in term neonates with hypoxic-ischaemic encephalopathy. Outcomes included mortality and long term neurological sequelae. Standardised forms were used to extract and compare data. Criteria of York Centre for Reviews and Dissemination were used to assess quality. Analysis was mainly qualitative but included meta-analysis.

Results 20 trials were found, mainly from Chinese sources. The reporting quality of trials was poor by Western (CONSORT) standards. Treatment with hyperbaric oxygen had better outcomes than the comparator in almost all trials. The odds ratios of the meta-analyses were 0.26 (95% confidence interval 0.14 to 0.46) for mortality and 0.41 (0.27 to 0.61) for neurological sequelae.

Conclusion Treatment with hyperbaric oxygen possibly reduces mortality and neurological sequelae in term neonates with hypoxic-ischaemic encephalopathy. Because of the poor quality of reporting in all trials and the possibility of publication bias, an adequately powered, high quality randomised controlled trial is needed to investigate these findings. The Chinese medical literature may be a rich source of evidence to inform clinical practice and other systematic reviews.

Introduction

Hypoxic-ischaemic encephalopathy is a severe complication of asphyxia that occurs before, during, or after birth. It can result in death or neurological damage, which can manifest in the short term (within 12-24 hours) as seizures, altered reflexes, or altered level of consciousness (or a combination), and in the longer term by developmental delay, epilepsy, mental retardation, or cerebral palsy (or a combination). Diagnosis is by a history of asphyxia that has caused acidaemia, a low Apgar score, neurological damage, and the involvement of many organs. The condition is commonly graded as mild, moderate, or severe. Sarnat stages can be used to classify the neurological damage—stage I is least severe and stage III most severe.[1] The condition occurs in 3.5-6/1000 live births, and the outcome is worse for more severely affected neonates.[2] One case series of 38 births reported 14 deaths and 13 patients with a poor outcome.[3] In another series of 42 survivors with moderate hypoxic-ischaemic encephalopathy followed up at one year, two were dead, 13 had cerebral palsy, one had another severe disability, four had mild developmental delay, and 22 had developed normally.[1] Treatments evaluated for this condition include hypothermia, magnesium sulphate, anticonvulsants, mannitol, dexamethasone, nicardipine, and caffeic acid phenethyl ester, but none has been effective.[4–7] Management usually consists of supportive care and keeping oxygen saturation at 95%.[2]

Patients treated with hyperbaric oxygen inhale 100% oxygen inside a hyperbaric chamber that is pressurised to >0.1 MPa (megapascals). This treatment has been evaluated in the West for a wide range of conditions, including cerebral oedema, brain injuries, and cerebral palsy, but not for hypoxic-ischaemic encephalopathy.[8–10] In Russia, hyperbaric oxygen has been used to treat neonatal injuries (fetal asphyxia), and this treatment is used for hypoxic-ischaemic encephalopathy in China, but apparently not in Hong Kong.[11–13] Hyperbaric oxygen is usually given one to three times per day at 0.15-0.17 MPa for 60-120 minutes, with the aim of increasing oxygen in the tissues.[14] The rationale for this treatment is that it may reverse local hypoxia, inhibit post-ischaemic vasoconstriction, and promote the formation of collagen matrix, which is essential for angiogenesis and restoration of blood flow to injured tissue.[14] This systematic review investigates whether hyperbaric oxygen is clinically effective for the treatment of neonates born at term with hypoxic-ischaemic encephalopathy.

Methods

The protocol for this systematic review was developed as part of a masters degree in health technology assessment.

The search strategy comprised a search of Western electronic databases and a search of Chinese databases and other sources. We searched the Cochrane controlled trials register and database of systematic reviews, Medline, Embase, CINAHL, and HealthSTAR up to November 2004 using search terms "hyperbaric oxygen", "hyperbaric oxygenation", "neonate(s)", "newborn(s)", "infant newborn(s)", "hypoxic-ischemic", "encephalopathy", "encephalopathies", "brain injury", "brain injuries", "brain damage", "brain ischemia", "hypoxia brain", and "birth asphyxia". We also searched a variety of Chinese electronic

Table 1 Characteristics of 20 trials investigating treatment with hyperbaric oxygen in hypoxic-ischaemic encephalopathy

Study	No of patients*		Diagnostic criteria (severity*)	Baseline comparisons	Age at start of treatment		Treatment‡	Usual care
	Intervention	Control			Treatment	Usual care†		
Chen 2000[17]	37	36	Ji Nan conference (I, II, and III)	No statistically significant difference in status of consciousness, convulsion, muscle tone, reflexes, or computed tomography results	2-5 days	NA	0.14-0.16 MPa (concentration=80%); 20 min/30 min/20 min; once a day ×10 days; 1-5 courses; not clear	General
Ding 2003[18]	92	86	Han Zhou conference (NA)	No statistically significant difference in sex, age, status of asphyxia, or clinical symptoms	<48 hours	<24 hours	0.15-0.17 MPa; 15 min/30 min/20 min; once a day ×10 days; not clear; not clear	General and drug that promotes cerebral metabolism
He 2000[19]	I: 4; II: 18; III: 10	I: 4; II: 17; III: 9	Han Zhou conference (I, II, and III)	No statistically significant difference in birth weight, degree of asphyxia, or main clinical symptoms	<72 hours	<24 hours	0.15 MPa; 15 min/30 min/15 to 30 min; once a day ×10 days; not clear; not clear	General and drug that promotes cerebral metabolism
Li 2004[20]	20	20	Hu and Jiang (I, II, and III)	No statistically significant difference in birth weight, sex, age, or Apgar score	I and II: 15 hours to 7 days; III: >7 days	NA	Not clear; not clear; 10 times; I and II=1-2 courses, III=3-5 courses; 10-15 days	General
Lin 2000[21]	30	30	NA (I, II, and III)	No statistically significant difference in ways of delivery, sex, gestational age, birth weight, age, or clinical grade	NA	≤1 day	Not clear; not clear; once a day ×10 days; not clear; not clear	General
Liu 2003[22]§	II: 61; III: 39	II: 60; III: 38	Han Zhou conference (II and III)	No statistically significant difference in sex, birth weight, illness status, maternity age, parents' social status, or family status	Within 24 days	Within 24 days	0.15-0.17 MPa; 15 min/30 min/20 min; once a day ×10 days; not clear; not clear	General
Lu 2001[23]	II: 19; III: 10	II: 16; III: 8	Han Zhou conference (II and III; excluded cerebral haemorrhage)	No statistically significant difference in birth weight, gestational age, time starting treatment, or clinical grade	2-8 days	NA	0.12 MPa. 20 min/30 min/20 min; once; not clear; not clear	General
Lu 2003[24]	37	34	Han Zhou conference (II and III; included cerebral haemorrhage)	No statistically significant difference in sex, birth weight, or degree of asphyxia and anoxia	<48 hours after admission; stable if with cerebral haemorrhage	NA	0.16 MPa; 20 min/30 min/20 min; once a day ×10 days; II=2 courses, III=3 courses; not clear	General and drugs that promote cerebral metabolism
Lu 1999[25]§	I: 15; II: 11; II: 6	I: 12; II: 13; III: 5	Han Zhou conference (I, II, and III)	No statistically significant difference in sex, birth weight, status of asphyxia and anoxia, or clinical symptoms	<48 hours	<24 hours	0.15-0.17 MPa; 15 min/30 min/20 min; once a day ×10 days; not clear; not clear	General and drugs that promote cerebral metabolism and eliminate free radicals
Si 1999[26]	I: 11; II: 27; III: 19	I: 10; II: 22: III: 17	Han Zhou conference (I, II, and III; excluded those with brain malformation and severe decompensation)	No statistically significant difference in sex, birth weight and status of asphyxia.	<48 hours after admission	NA	0.2 MPa; 20 min/60 min/20 min; once a day ×7 days; not clear; not clear	General
Song 2000[27]§	51	50	Han Zhou conference (II and III)	No statistically significant difference in sex, birth weight, clinical grade, **maternity** age, and family status	<48 hours	<24 hours	0.15-0.17 MPa; 15 min/30 min/20 min; once a day ×10 days; not clear; not clear	General
Sun 2000[28]	I: 21; III: 21	I: 19; III: 21	Ji Nan conference (I and III)	NA	NA	<3 days	NA	General (3rd arm not included)
Sun 1998[29]	I: 10; II: 18; III: 4	I: 7; II: 13; III: 2	Ji Nan conference (I, II, and III; included complications of cerebral haemorrhage)	No statistically significant difference in various aspects including symptoms	NA	NA	0.14 MPa (1.4 atm); 15 min/40 min/20 min; once a day ×7-10 days; not clear; not clear	General
Wang 2002[30]	I: 15; II: 22; III: 11	I: 16; II: 20; III: 10	Ji Nan conference (all)	No statistically significant difference in sex, birth weight, or degree of asphyxia and anoxia	NA	<2-3 days	0.14 MPa; 20 min/50 min/25 min; 7 days; I=1 course, II=2-3 courses, III=3-4 courses; 3-5 days	General, antioxidants, and cerebrolysin
Wang 1999[31]	II: 14; III: 9	II: 15; III: 7	Han Zhou conference (II and III; excluded cerebral haemorrhage from birth injury and malformation)	No statistically significant difference in sex, birth weight, gestational age, or Apgar score	72 hours	NA	0.15-0.16 MPa; (concentration=80%); 20 min/30 min/20-30 min; once ×5–8 days; not clear; not clear	General and nicholin

Wang 2001[32]	80¶	I: 24; II: 36; III: 20	Defined in text (I, II, and III)	No statistically significant difference in illness status	As early as possible	NA	Not clear; 20 min/60 min/20 min; once a day ×10 days; not clear; not clear	General
Wang 2001[33]	I: 26; II: 46; III: 12	I: 24; II: 45; III: 11	Jin and Huang (I, II, and III; except congenital disease)	No significant difference in age, gestational age, illness status, or family status	NA	30 min to 3 days	0.15 MPa; total time=60-70 min each time; once a day ×5-7 days; not clear; not clear	General
Wen 2001[34]	38	38	Han Zhou conference (II and III)	No significant difference in sex or age	<3 days	NA	0.13 MPa; 15 min/30 min/15 min; once a day ×10 days; not clear; not clear	General
Yuan 1999[35]	I: 16; II: 9; III: 5	I: 17; II: 8; III: 5	Ji Nan conference (I, II, and III)	Listed symptoms but did not compare	Within 2 days of admission	24-48 hours	0.14-0.16 MPa; 20 min/30 min/20-30 min; not clear; I=2-3 times, II=5 times, III=10 times; not clear	General
Zhang 2000[36]	60	56	Jinan conference (II and III)	No statistically significant difference in sex, gestational age, birth weight, or Apgar score	NA	NA	0.16 MPa, 10-15 min/30 min,/15-20 min; once a day ×10 days; II=2 courses, III=3 courses; 1 week	General

MPa, megapascals; NA=not available.
*Severity grade: I=mild, II=moderate, III=severe.
†The age starting usual care was assumed as the time of admission.
‡Pressure; time of increasing/stable/decreasing pressure; 1 course; length; interval. Time is the duration increasing/stable/decreasing pressure of a single treatment, length is the number of courses of treatment, and interval is the time between two courses of treatment.
§Alternate patient allocation.
¶The numbers given for severity grades I (26) II (37) and III (21) add up to 84 but the total number in the intervention group was given as 80.

databases and hand searched selected Chinese journals (see box) to July 2004.

We identified relevant studies by searching electronic databases, scanning reference lists, and consulting experts in the specialty. Publications in any language were eligible. Reference lists were hand searched for further references. We examined titles, abstracts, and keywords of citations as given on the databases for the terms for "hyperbaric oxygen therapy for neonatal hypoxic-ischaemic encephalopathy". Where possible, we obtained the full text of all potentially relevant citations.

The predetermined inclusion criteria were fully published randomised or quasi-randomised controlled trials of treatment with hyperbaric oxygen compared with "usual care" in full term neonates (more than 36 weeks' gestation) with hypoxic-ischaemic encephalopathy and a history of perinatal asphyxia. We accepted alternate allocation as quasi-randomised. Outcomes were mortality and incidence of long term neurological sequelae (developmental delay, epilepsy, mental retardation, or cerebral palsy, or a combination). One reviewer (ZL) assessed studies for inclusion and this was checked independently by a second reviewer (TX). Both reviewers independently extracted data from the papers using a standardised, predesigned data extraction form, and no disagreements were encountered. We assessed the quality of the included trials by using criteria of the York Centre for Reviews and Dissemination; we focused on randomisation, allocation concealment, presence of blinding, explanation of withdrawals, and presence or absence of intention to treat analysis.[15]

We tabulated the characteristics and results of all the included studies; analysis was mainly qualitative. We carried out meta-analysis using Metaview 4.1 (Cochrane Collaboration Review Manager 4.1 software). We used fixed effects models when statistical heterogeneity was absent and random effects models when heterogeneity was present. Statistical heterogeneity was present if χ^2 values were greater than the degrees of freedom.[16]

Chinese data sources

Electronic databases

China Hospital Digital Library, administered by the Department of Education of China and sponsored by Tsinghua University and the Chinese Medical Association. This database provides full text data from published periodicals and newspapers in China on medical specialties, bioscience, government of hospitals, library science, and information science. The main component is the China hospital knowledge database, which contains more than 1300 professional periodicals and 3000 related periodicals; it covers 96% of articles on medicine published in China. Relevant keywords were used for searching

An online bibliographical database from the China Hyperbaric Oxygen Medicine Information Centre, which contains data on relevant literature published in Chinese medical journals

Chinese Medical Journal Network for full text medical literature

Hand searches

Selected journals in Chinese: *Journal of Clinical Pediatrics* and *Chinese Journal of Practical Pediatrics*

Results

We found six citations in Western databases, but none met the inclusion criteria. We identified 126 citations from the Chinese searches. Twenty trials met the inclusion criteria and 106 were excluded (59 had the wrong study design, 37 did not specify the term neonate, two had different interventions, and eight had different outcomes).[17–36] All of the included trials were conducted in China and published in Chinese language medical journals. The

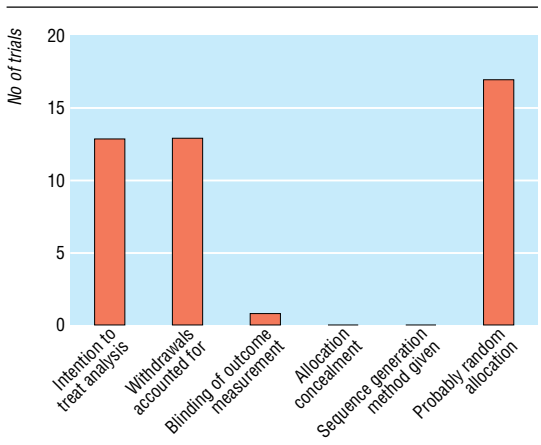

Fig 1 Quality assessment of trials of hyperbaric oxygen to treat hypoxic-ischaemic encephalopathy

Table 2 Results of 20 trials investigating treatment with hyperbaric oxygen in hypoxic-ischaemic encephalopathy

Study	Total effectiveness rate (measurement index)	Mean (SD) days to recovery	Length of follow-up; losses to follow-up	Long term neurological sequelae	Mortality	Adverse events
Chen 2000[17]	NA	Seizures controlled, consciousness, and muscle tone. 2-5 fewer days in I than C	12-24 months; none	I: 8.1% (3/37), C: 19.4% (7/36) (numbers in text do not add up)	I: 5.4% (2/37), C: 5.5% (2/36)	NA
Ding 2003[18]	I did significantly better than C; P<0.005 (clinical symptoms disappeared in 10 days)	NA	>10 days; NA	NA	NA	None
He 2000[19]	I: 94% (30/32), C: 67% (20/30); P<0.01 (clinical symptoms disappeared in 10 days)	Days in hospital. I: 12.5 (2.8), C: 15.5 (3.1)	NA; none	NA	I: 0% (0/32), C: 6.7% (2/30)	None
Li 2004[20]	I: 90% (18/20), C: 60% (12/20); P<0.05 (clinical symptoms—cerebral oedema by ultrasound disappeared in 5 days)	NA	3 years; probably none	I: 10.0% (2/20), C: 20.0% (4/20)	NA	None
Lin 2000[21]	I: 97% (29/30), C: 73% (22/30); P<0.05 (clinical conditions improved in 1 week)	NA	5 months to 2 years; none for total effectiveness rate, 7 for neurological sequelae	I: 3.3% (1/30), C: 23.3% (7/30)	NA	NA
Liu 2003[22]*	I: 90% (90/100), C: 67% (66/98); P<0.01 (clinical symptoms disappeared in 10 days)	NA	6-14 months; 34	I: 20.4% (18/100), C: 44.7% (34/98)	I: 4.0% (4/100), C: 20.4% (20/98); P<0.05	NA
Lu 2001[23]	NA	Symptoms. I: 4.3 (2.3), C: 5.8 (2.0); P<0.001	NA; none	NA	I: 0% (0/29), C: 4.2% (1/24)	None
Lu 2003[24]	I: 92% (34/37), C: 74% (25/34); P<0.01 (clinical symptoms—cerebral oedema—disappeared in 10 days; how cerebral oedema was detected not given)	Muscle tone. Grade II†: I: 6.94 (2.06), C: 7.48 (2.20); P<0.05; grade III: I: 11.17 (2.57), C: 12.44 (3.32); P<0.01. Reflexes. Grade II: I: 4.54 (1.53), C: 5.47 (1.96); P<0.01; grade III: I: 9.29 (2.57), C: 10.33 (2.74); P<0.01. Consciousness. Grade II: I: 3.19 (1.04), C: 3.88 (1.49); P<0.05; grade III: I: 5.14 (1.81), C 6.44 (1.87); P<0.01	NA; none	I: 16.2% (6/37), C: 26.5% (9/34); P<0.01	NA	None
Lu 1999[25]*	I: 97% (31/32), C: 70% (21/30); P<0.05 (clinical symptoms disappeared in 10 days)	NA	>10 days; none	NA	NA	None
Si 1999[26]	I: 93% (53/57), C: 76% (37/49); P<0.01 (clinical symptoms and convulsions disappeared in 10 days)	Days in hospital. I: 12.8, C: 17.6	3 months to 4 years; none for total effectiveness, not clear for long term sequelae	I: 7.0% (4/57), C: 12.2% (6/49)	I: 5.3% (3/57), C: 16.3% (8/49)	NA
Song 2000[27]*	I: 90% (46/51), C: 66% (33/50); P<0.01 (clinical symptoms disappeared in 14 days)	NA	6-14 months; I: 3, C: 11	I: 18.8% (9/50), C: 43.6% (17/50); P<0.05	I: 5.9% (3/51), C: 22.0% (11/50)	NA
Sun 2000[32]	I: 93% (39/42), C: 58% (33/40); (cured, improved, alive; time to outcomes not given)	NA	Not clear; none	NA	I: 7.1% (3/42), C: 17.5% (7/40)	NA
Sun 1998[33]	I: 100%, C: 76% (numbers not given); P<0.01 (measurement index not mentioned)	NA	NA; NA	NA	NA	None
Wang 2002[34]	NA	Seizure controlled; recovery of muscle tone, reflexes, and consciousness. 4-6 days fewer in I than C	NA; none	NA	NA	NA
Wang 1999[35]	I: 97% (22/23), C: 68% (15/22); P<0.05 (clinical symptoms disappeared in 10 days)	NA	>10 days; none	NA	NA	NA
Wang 2001[36]	I: 100% (80/80), C: 80% (64/80); P<0.05 (cerebral oedema—by computed tomography—disappeared in 10 days)	Symptoms. At least 3 days fewer in I than C	10 days; none	NA	NA	NA
Wang 2001[37]	I: 90% (76/84), C: 76% (61/80); P<0.05 (clinical symptoms disappeared in 1 week)	NA	Not clear; none	NA	NA	NA
Wen 2001[38]	NA	Muscle tone. I: 9.13, C: 11.80; consciousness: I: 4.37, C: 5.60	Not clear; NA	NA	NA	NA
Yuan 1999[39]	I: 93% (28/30), C: 70% (21/30); P<0.05 (clinical symptoms and cerebral oedema disappeared in 10 days. How cerebral oedema was detected not given)	NA	>10 days; none	NA	NA	NA
Zhang 2000[40]	NA	Symptoms. I: 5 (2.9), C: 7.8 (1.2); P<0.001	Not clear; none	NA	NA	Rentrolental fibroplasia I: 1.6% (1/60), C: 1.8% (1/56)

C=control group; I=intervention group, NA=not available.
*Alternate patient allocation.
†Severity grade: I=mild, II=moderate, III=severe.

trials studied between 40 and 198 patients. Four different sets of criteria were used to diagnose hypoxic-ischaemic encephalopathy (see table 1).[37–40] These sets are similar and the criteria used are an abnormal obstetric history of fetal anoxia and distress; asphyxia after birth resulting in a low Apgar score and disturbance of consciousness; change in muscle tone; and abnormal reflexes within 12 hours of birth. The severity of hypoxic-ischaemic encephalopathy varied and grading of severity was probably not applied uniformly across the trials. Trials used various doses of hyperbaric oxygen and some had additional treatments, such as antioxidants and neurotrophic agents in each arm. Populations and the delivery of hyperbaric

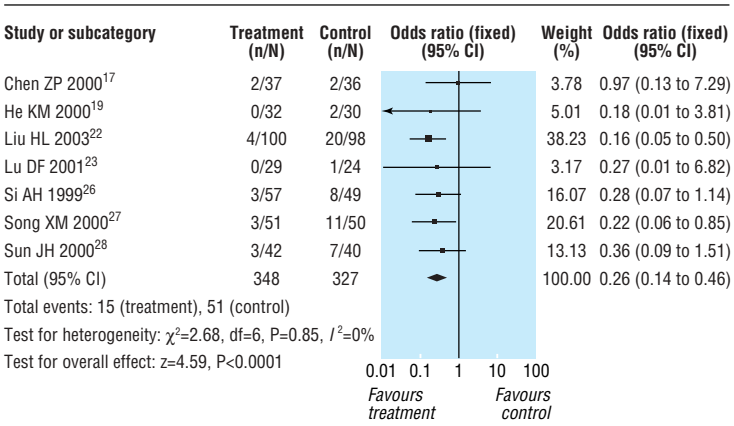

Fig 2 Effect of treatment with hyperbaric oxygen on mortality in hypoxic-ischaemic encephalopathy

oxygen varied greatly. Table 1 shows the characteristics of the studies.

Seventeen of the 20 studies mentioned "random" in the methods section, but few other trial details were given. None of the randomised trials mentioned the method of sequence allocation or whether allocation was concealed. In the other three studies treatment was allocated on an alternate basis. They were included because order of birth was considered to be a random event.[22 25 27] Selection bias may have been more prominent in these studies, but because of the uniformly poor methodological quality of reporting this could not be determined. Only one trial mentioned blinding (of outcome assessment).[22] No trials with losses to follow-up described reasons for the losses. The only trials with intention to treat analysis were those without losses to follow-up. Figure 1 shows quality factors.

Table 2 shows the results of the studies. Not all outcomes were reported in each trial, but overall, treatment with hyperbaric oxygen had a better outcome than the comparator. Only seven trials reported mortality (fig 2). Hyperbaric oxygen significantly reduced mortality in hypoxic-ischaemic encephalopathy (odds ratio 0.26, 95% confidence interval 0.14 to 0.46). Seven trials measured neurological sequelae (fig 3). Neurological sequelae were significantly reduced in neonates treated with hyperbaric oxygen compared with controls (0.41, 0.27 to 0.61). Little heterogeneity was seen between the trials for both comparisons.

Adverse events were reported in only one trial—rentrolental fibroplasia occurred in one case each in the intervention group and the control group at follow-up.[36] Seven trials reported no adverse events, and the remainder did not mention adverse events (table 2).

Discussion

The results of this systematic review suggest that treatment with hyperbaric oxygen may reduce mortality and neurological sequelae in term neonates with hypoxic-ischaemic encephalopathy. Hyperbaric oxygen has been used to treat various conditions for several decades and has been used in neonates. Although this form of treatment is controversial, it has developed rapidly in China over the past decade and is widely used there.

Limitations

Trial reports were of poor quality according to the criteria of the York Centre for Reviews and Dissemination, were not written to CONSORT standards, and lacked many details. Publication bias is a possibility as studies with negative results may not have been published. The 20 trials differed greatly in terms of the severity and status of the condition, exposure to hyperbaric oxygen, time to treatment and other baseline characteristics, and the measurement of outcomes. In addition, little information was given on side effects such as retrolental fibroplasia.

Implications

An adequately powered, high quality, randomised controlled trial is needed to investigate the effectiveness of hyperbaric oxygen in term neonates with hypoxic-ischaemic encephalopathy. If the effectiveness of this treatment is confirmed, this will have two

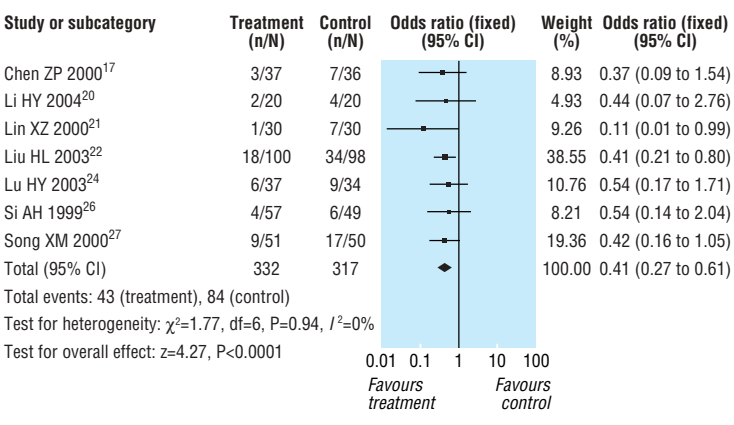

Fig 3 Effect of treatment with hyperbaric oxygen on neurological sequelae in hypoxic-ischaemic encephalopathy

main implications. Firstly, the treatment of hypoxic-ischaemic encephalopathy will change radically in the West and hyperbaric oxygen chambers will be required in all special care baby units. The costs of providing this treatment could be high, but they might be outweighed by fewer neonatal deaths and reduced requirements for specialist paediatric medical and nursing care. Secondly, evidence of the effectiveness of this treatment came from Chinese sources that are not routinely searched when systematic reviews are carried out in the West. It is not known at present how much useful evidence will be found once researchers start to look. This may also be true for evidence collected in Russia. To determine whether the inclusion of Chinese and Russian trials would reinforce or change the conclusions of systematic reviews, Chinese and Russian trials of interventions should be reviewed and the results compared with currently available systematic reviews. In future, it may become general policy to check these databases, so systematic review groups would need reviewers skilled in these languages who also have access to the relevant databases and journals.

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Contributors: ZL conducted the original systematic review submitted for the masters degree in full. TX checked the inclusions and duplicate data extraction. CM supervised the original systematic review, wrote the journal article from it, and is guarantor.

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Ethical approval: Not required.

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What is already known on this topic

Hypoxic-ischaemic encephalopathy is a severe complication of asphyxia before, during, or after birth and occurs in 3.5-6/1000 live births

Current treatment in the West consists mainly of best supportive care

Hyperbaric oxygen is commonly used in China to treat this condition

What this study adds

This systematic review of 20 Chinese trials found that treatment with hyperbaric oxygen reduced mortality and neurological sequelae such as epilepsy, mental retardation, and cerebral palsy, but in all trials reporting of methods was poor and publication bias is a possibility

A high quality randomised controlled trial is needed to investigate and confirm the effectiveness of this treatment

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