Adjunctive HBO Treatment of Children with Cerebral Anoxic Injury

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Hyperbaric oxygen (HBO) therapy has been successfully used to treat a variety of medical disorders, including brain injury. This study evaluated the effects of adjunctive HBO therapy on functional outcomes in nine military dependent children with anoxic brain injury and attempted to identify the optimum number of treatments. Baseline and serial evaluations using multiple functional measures showed improvement in gross motor function and reduced total time of custodial care in the children with cerebral palsy (CP). Early intervention with HBO therapy seemed to effect overall improvement. An optimum number of treatments remains undetermined since improvements were noted to the end of the study.

Cerebral anoxia can result in severe mental and physical disabilities. This condition has many causes including near-drowning, carbon monoxide poisoning, and cardiac arrest. Medical conditions associated with anoxia include stroke and CP. Anoxic brain injuries in children impress their devastation not only on the afflicted child but also their family. Currently, the only treatment options for children with such injuries are supportive and palliative. Most children who suffer an anoxic brain injury are left with lifelong disabilities to include mental retardation, spasticity, seizures, and a myriad of physical deficits. As most of these disabilities are chronic, they are met with multiple co-morbid conditions such as orthopedic deformities, skin breakdown, and recurrent pulmonary infections.

Cerebral palsy is a collation of diverse symptoms of varying etiologic and anatomic types affecting the motor system. The motor disorder is categorized by muscle tone (spasticity vs hypotonia) and anatomic involvement (diplegia, quadriplegia, etc). In addition, there may be mental retardation, epilepsy, and abnormalities of speech and vision. This usually nonprogressive brain injury can occur during the prenatal, perinatal, or postnatal period. Major causes include hemorrhage of fragile brain vasculature and hypoxic-ischemic encephalopathy.[1]

The underlying mechanisms in the development of brain injury due to ischemia are complex.[2] Following a global insult, cerebral perfusion and oxygen availability are reduced. However, not all areas of the brain are equally affected. When critical flow threshold is reached, there is cessation of neuronal electrical activity and failure of ion homeostasis, causing irreversible cellular damage.[3] In the surrounding areas of tissue less affected by hypoxia, there is sufficient oxygen for cells to maintain ion pumping mechanisms and cellular integrity, but not enough for them to generate action potentials and function as neurons.[4,5] The critical parameter in all cases is tissue oxygen availability.

The effects of HBO on hypoxic brain tissue include: relief of hypoxia, improvement in microcirculation, reduced cerebral edema, and improved cerebral metabolism.[2,6] The HBO provides the stimulus necessary for a return to normal cell functioning in those areas of suppressed neuronal activity. As a result of improved circulation and metabolism, patients may recover some brain function.

The HBO therapy has been successfully used in the past to treat brain injury.[2] Recently, there has been a growing interest in using HBO therapy to treat children with CP. There are a multitude of anecdotal reports of treatment success using a variety of protocols. A review of the literature identified only one objective study which showed improvement in motor function and spasticity in children with CP who were treated with HBO.[7] The purpose of this study was twofold: (1) to determine if adjunctive HBO therapy improved functional capacity in

children with anoxic brain injury and (2) to identify the optimum number of treatments required.

Methods

Subjects. Nine volunteer subjects with a history of cerebral anoxic injury participated in this study. Eight of the subjects had varying degrees of CP and one was a near-drowning victim 1 year prior to starting treatment. The CP subjects consisted of 1 boy and 2 girls with spastic diplegia, 3 boys and 1 girl with spastic quadriplegia, and 1 boy with hypotonic diplegia. Seven of the CP subjects had a history of perinatal complications, such as respiratory distress and seizures, consistent with central nervous system hypoxia, and ischemia. The mean age of the 8 CP subjects was 6.4 years (range 1.0 to 16.5 years). The near drowning subject was a 5.6-year-old female. Potential subjects were limited to children age one and older who were eligible for care in a military medical facility. Exclusion criteria included inability to maintain adequate oxygenation without assistance; history of recent thoracic surgery, cancer, or chronic asthma; previous HBO therapy; and age less than 12 months.

One potential subject was excluded during initial evaluation due to difficulty maintaining adequate oxygen saturation levels. One subject was removed from the study after 30 HBO treatments, when he developed a severe viral respiratory infection requiring hospitalization and ventilatory support. Prior to participation, informed consent was obtained from the parent or legal guardian of each child and each of the chamber inside attendants. The children continued their routine physical, occupational and speech therapy during the study. New treatment medications and modalities were prohibited during the study.

Procedures. The procedures followed were in accordance with all ethical standards as approved by the Institutional Review Board of the medical center. The same investigators conducted evaluations before, during, and after HBO treatment. Initial evaluations included an electrocardiogram and chest x-ray to identify disqualifying medical conditions and to serve as a baseline in the event of a medical problem during the study. Prior to treatment, pressure equalization (PE) tubes were placed in all subjects to decrease the risk of barotrauma. An otolaryngologist primarily using *OtoLAM™* assisted myringotomy inserted the PE tubes.

Pre-treatment evaluation included the Gross Motor Function Measure (GMFM) test, Modified Ashworth Scale (MAS), Functional Independence Measure for Children (WeeFIM), video exam, 24-hour time measure, parental questionnaire, and single-photon emission computed tomography (SPECT) scan. Testing was repeated every 20 treatments to the end of the study except for the SPECT scan and parental questionnaire which were completed at 40 and 80 treatments. The testing procedures consisted of the following:

- *Gross Motor Function.* The GMFM is designed to detect changes in gross motor function in children with CP.[8] The GMFM is an observational measure that evaluates motor function in five areas: lying and rolling, crawling and kneeling, sitting, standing and walking, running and jumping. Each item is scored on a 4-point scale: 0 = cannot initiate activity, 1 = initiates activity, 2 = partially completes activity, 3 = completes activity. This test was administered to all subjects primarily by a neurologist who had no other involvement in the study.

- *Spasticity Level.* Spasticity was evaluated using the MAS in all four extremities.[9] Spasticity was graded on a 0 to 4 scale with 0 being no increase in muscle tone to 4 being limb rigid in flexion or extension. Evaluations were done by the neurologist in conjunction with GMFM testing.

- *Functional Skills.* The WeeFIM instrument was used to evaluate basic living and functional skills.[10] It is modeled after the Functional Independence Measure for Adults and includes 18 items that measure performance across the domains of self-care, sphincter control, transfers, locomotion, communication, and social cognition.[11] Each item is scored on a 7-point scale ranging from 1 (total assistance, child performs little if any of task) to 7 (complete independence). The neurologist administered this test along with the GMFM and MAS.

- *24-Hour Time.* Parents were given a stopwatch and asked to record the total time spent providing care for their child during a 24-hour period. Parents were instructed to only count time spent in physical contact providing direct care, such as bathing, feeding, dressing, and providing therapy. The measure was repeated for two consecutive days and the average time used for analysis. All data were recorded during weekends (Saturday/Sunday), as this time

period was determined to be the least variable in weekly family activities.

• *Video Analysis.* Subjects were recorded on videotape to document the motor disorder to include extremity range of motion and gross motor skills (for example, rolling, sitting, crawling, standing, walking, reaching). An initial session was done prior to HBO treatment and then after every 20 treatments until the end of the study. Investigators analyzed the tapes at the end of the study and recorded changes.

• *Questionnaire.* An 8-item questionnaire was distributed to the parents to complete prior to starting treatment and following 40 and 80 treatments. The questionnaire included the following categories: (1) sitting in chair; (2) sitting on floor; (3) crawling; (4) walking; (5) reaching for/holding objects; (6) eating; (7) personal hygiene/bath and; (8) communication. A 5-point scale described in an earlier CP studywas used to score each item.[7] The scale ranged from 0 to 4 (0 = totally dependent, no participation; 1= partially dependent, participates but requires constant help throughout the activity; 2 = partially dependent, needs help only to finish activity; 3 = independent with some form of aid or compensation; 4 = completely independent). There were five additional yes/no questions that addressed changes in sleep pattern, bowel or bladder pattern, emotional state, muscle spasticity, and medication use. Parents were also asked to list all changes noted during HBO treatment.

• *Functional Imaging.* A Tc-HMPAO SPECT scan was completed on each subject prior to HBO treatment and following 40 and 80 treatments. The SPECT scan shows brain function based on uptake of the radioactive tracer documenting regional cerebral blood flow. A radiologist who was blinded to the clinical outcome of the study reviewed the scans.

Hyperbaric Oxygen Therapy. All subjects received 80 treatments in a 12-person multiplace hyperbaric chamber. The HBO protocol was 100% oxygen at 1.7 atmospheres absolute (ATA) for 60 minutes. The treatment schedule was once daily, Monday through Friday for 4 months. The hyperbaric chamber was pressurized with air and the patients received oxygen via a hood. A parent or designated guardian accompanied each child and served as the inside attendant.

Data Aanalysis. For data analysis, each subject served as his or her own control by using pre-treatment scores as the baseline for comparison. Data were analyzed at 20 treatment intervals looking for trends and statistical significance in those trends. The Friedman matched groups signed ranks test was used to determine improvement in patient outcomes as a function of number of treatments. The analysis was applied for each of the separate areas of the GMFM, MAS, and WeeFIM tests. A one-way repeated measures analysis of varience was used to assess differences in care-taking time. To illustrate the effectiveness of HBO treatments, raw scores were converted to mean percent of maximum performance for each measure and percent change for every 20 treatments relative to baseline. Analysis was performed on the seven CP subjects as a group, while the near-drowning subject was evaluated separately. The near-drowning subject was analyzed separately since it was determined that the specific type and severity of her injuries placed her in a separate population.

Results

The GMFM test results for each subject are shown in Table 1. The average improvement in total GMFM score from pre-treatment to each measurement interval was zero-20 = 26.7%, zero-40 = 45.6%, zero-60 = 48.0%, and zero-80 = 58.1%. Figure 1 shows the percent improvement from pre-treatment for each of the functional areas: (1) lying and rolling; (2) crawling and kneeling; (3) sitting; (4) standing; and (5) walking, running, jumping. The largest gains generally occurred at the first 20 treatments, with continued improvement to the end of the study. In analyzing each area separately, significant ($P<0.05$) improvements were shown for areas one, two, three, and five. Younger subjects showed greater improvement (mean=17.8%) compared to the older group (mean=5.2%) but this was not statistically significant, $P=0.21$.

Spasticity was evaluated in both the upper and lower extremities of all subjects using the MAS (Table 2). No change was seen in the majority of subjects. One of the younger children showed minimal improvement in the lower extremities, while one of the older subjects had an increase in upper extremity spasticity. Subject number six had a previous left lower extremity amputation, therefore no data were recorded for this site.

		Area 1 Treatment No.					Area 2 Treatment No.					Area 3 Treatment No.					Area 4 Treatment No.					Area 5 Treatment No.					Total Treatment No.				
Subject	Age	0	20	40	60	80	0	20	40	60	80	0	20	40	60	80	0	20	40	60	80	0	20	40	60	80	0	20	40	60	80
1	2.4	16	18	23	23	23	0	0	2	0	0	0	3	6	6	8	0	0	0	0	0	0	0	0	0	0	16	21	31	29	31
2	3.5	51	51	51	51	51	1	3	6	7	10	43	33	41	48	48	6	5	5	11	14	4	6	7	9	10	105	98	110	126	133
3	1.6	48	51	51	51	51	11	23	27	29	28	1	34	38	39	38	3	11	13	14	26	0	5	8	10	8	63	124	137	143	151
4	1	44	49	49	51	51	3	4	4	5	13	1	17	17	16	20	1	11	10	11	8	0	0	0	2	4	49	81	80	85	96
5	14	49	50	50	51	51	7	19	22	24	24	32	39	41	42	45	2	2	2	2	5	1	0	3	3	3	91	110	118	122	128
6	12.3	10	5	7	7	7	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	10	5	7	7	10
7	16.8	4	4	5	4	5	0	0	0	0	0	6	9	9	9	6	0	0	0	0	0	0	0	0	0	0	10	13	14	13	11
Mean		31.7	32.6	33.7	34	34.1	3.1	7	8.7	9.3	10.7	11.9	19.3	21.7	22.9	24	1.7	4.1	4.3	5.4	7.6	0.7	1.6	2.6	3.4	3.6	49.1	64.6	71	75	80
SD		20.7	22.5	21.4	22	21.8	4.3	9.8	11.1	12.2	11.7	17.9	16	17.8	19.6	19.4	2.2	5	5.3	6.3	9.7	1.4	2.7	3.6	4.3	4.1	39.2	50.1	53.4	57.9	61.2
Maximum		51	51	51	51	51	42	42	42	42	42	60	60	60	60	60	39	39	39	39	39	72	72	72	72	72	264	264	264	264	264

Table 1. Individual Results for the GMFM Test

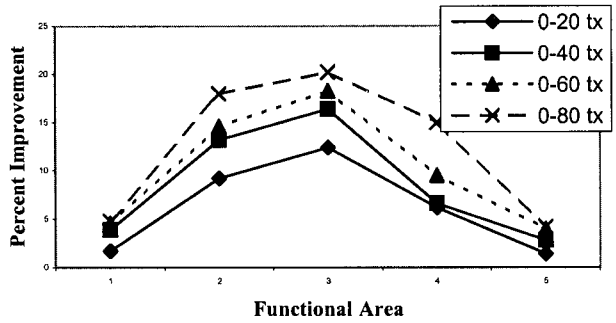

Fig 1. Percent improvement of GMFM score (based on % of maximum potential score) for each functional area by measurement interval.

Table 3 summarizes the evaluation of basic living and functional skills using the WeeFIM. The group as a whole showed only minimal improvement by the end of treatment. However, considerable differences were noted between the two age groups. Averaged across all six test measures at the end of the study, the younger children demonstrated a 58.6% improvement in total score. In contrast, the older group recorded a 6.7% decrease. This difference was found to be marginally significant (P=0.07). Figure 2 shows the percent improvement from pretreatment for each of the evaluated areas: (1) self care; (2) sphincter control; (3) transfers; (4) locomotion, (5) communication; and (6) social cognition. Most of the improvement in skills occurred during the last 20 HBO treatments. The largest gains involved locomotion skills, but these were not statistically significant.

Table 4 shows the total time parents spent providing care for their child during a 24-hour period. The overall results indicate a significant (P=0.03) reduction in the amount of time required. The biggest gains occurred at 20 treatments, with the general trend continuing as more treatments were administered. However, there were large individual variances ranging from 43.9% more time needed to an 81.9% time reduction at 80 HBO treatments. Thus, none of the pair-wise comparisons between time intervals approached statistical significance.

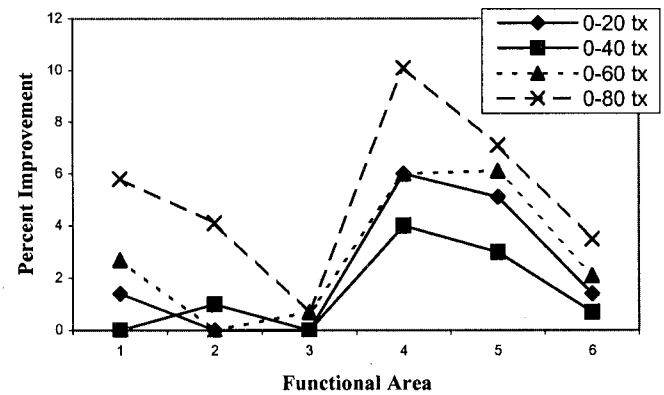

Fig 2. Percent improvement of WeeFIM score (based on % of maximum potential score) for each functional area by measurement interval.

		Left Upper Extremity Treatment No.					Right Upper Extremity Treatment No.					Left Lower Extremity Treatment No.					Right Lower Extremity Treatment No.				
Subject	Age	0	20	40	60	80	0	20	40	60	80	0	20	40	60	80	0	20	40	60	80
1	2.4	3	3	4	4	4	3	3	4	4	4	3	3	4	3	4	3	3	4	3	4
2	3.5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	1.6	2	1	1	1	1	1	1	1	1	1	3	2	2	2	1	2	2	2	2	1
4	1	1	1	1	1	1	2	1	1	2	2	2	1	1	1	1	2	2	2	2	2
5	14	1	2	3	3	3	1	2	3	3	3	3	4	4	4	4	3	4	4	4	4
6	12	4	4	4	4	4	4	4	4	4	4						4	4	4	4	4
7	17	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Mean		2.1	2.1	2.4	2.4	2.4	2.1	2.1	2.4	2.6	2.6	2.5	2.3	2.5	2.3	2.3	2.6	2.7	2.9	2.7	2.7
SD		1.6	1.6	1.7	1.7	1.7	1.6	1.6	1.7	1.6	1.6	1.4	1.6	1.8	1.6	1.9	1.4	1.5	1.6	1.5	1.7

Table 2. Individual Results for the MAS

		Treatment No.					Percent Change			
Subject	**Age**	0	20	40	60	80	0-20 tx	0-40 tx	0-60 tx	0-80 tx
1	2.4	18	18	18	18	18	0	0	0	0
2	3.5	28	41	30	40	51	46.4	7.1	42.9	82.1
3	1.6	20	26	31	37	42	30	55	85	110
4	1	19	21	22	23	27	10.5	15.8	21.1	42.1
5	14	28	27	25	25	25	-3.6	-10.7	-10.7	-10.7
6	12.3	27	23	24	23	23	-14.8	-11.1	-14.8	-14.8
7	16.8	18	19	19	19	19	5.5	5.5	5.5	5.5
Mean		22.6	25	24.1	26.4	29.3	10.8	7	17.1	29.8
SD		4.8	7.8	5	8.6	12.4				
Maximum		126	126	126	126	126				

Table 3. Summary Scores for the WeeFIM Test with the Percent Change Relative to Baseline

		Treatment No.					Percent Change			
Subject	**Age**	0	20	40	60	80	0-20 tx	0-40 tx	0-60 tx	0-80 tx
1	2.4	458	622	665	653	659	35.8	45.2	42.6	43.9
2	3.5	210	79	119	85	73	-62.4	-43.3	-59.5	-65.2
3	1.6	443	167	129	196	80	-62.3	-70.8	-55.8	-81.9
4	1	759	730	723	682	605	-3.8	-4.7	-10.1	-20.3
5	14	226	199	170	154	138	-11.9	-24.8	-31.9	-38.9
6	12	251	176	193	127	95	-29.9	-23.1	-49.4	-62.2
7	17	510	249	287	237	240	-51.2	-43.7	-53.5	-52.9
Mean		408.1	317.4	326.6	304.9	270	-26.5	23.6	-31.1	-39.6
SD		197.6	252.1	257.5	252.5	254.1				

Note: negative percent indicates time reduction

Table 4. Individual Results of Time Spent (Minutes) Providing Care in a 24-Hour Period

Two of the investigators reviewed the videotapes at the end of the study. Four subjects (57%) had some improvement in range of motion, with no improvements beyond 60 HBO treatments. All three subjects in the older age group demonstrated improved range of motion. Three subjects (43%) displayed improved gross motor function. All three were in the younger age group. The videos were rated as unchanged for the remaining subjects.

The results of the parent questionnaire are illustrated in Figure 3. The average scores for the seven subjects ranged from 0.1 to 2.4, with no statistically significant improvements. Most improvements occurred by 40 HBO treatments. Parents reported essentially no change in the area of personal hygiene while eating skills were most improved.

Parents provided additional information by answering the yes or no portion of the questionnaire. Sleep patterns improved for two subjects while becoming disrupted for two others. Two children began having routine bowel movements resulting in stool softeners

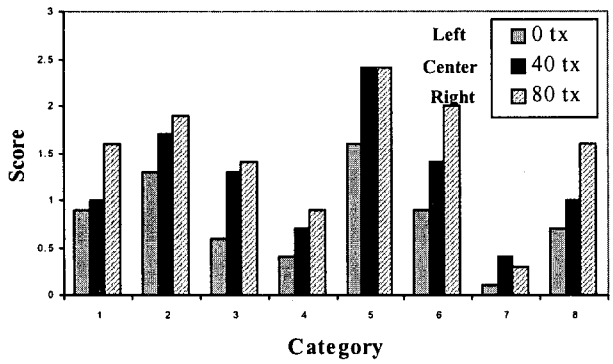

Fig 3. Responses of parents to an 8-item questionnaire.

being discontinued for one of them. After 2 to 3 weeks of HBO treatment, two of the subjects experienced personality changes, becoming more irritable and less tolerant. These changes resolved after 8 to 10 weeks of treatment. Five parents also reported a decrease in muscle spasticity and improved range of motion in their child, while one parent reported increased spasticity requiring an increase in medication. Overall, parents indicated continued improvement in their children through the end of the study.

Parents reported other improvements that were not measured in our assessment. Three children improved their ability to swallow, allowing them to have a greater variety of liquids and foods. The two subjects with strabismus had a reduction in severity, and the nystagmus in one subject resolved. One child who experienced frequent illnesses remained healthy during HBO treatment. One subject had complete resolution of a grade 3 vesicoureteral reflux, resulting in cancellation of her surgery.

The near-drowning subject showed little response to HBO treatment. The GMFM score improved 5.4% by 80 HBO treatments, with a zero score pre- and post-treatment for the areas of crawling and kneeling, standing, and walking, running, jumping. Spasticity remained at the maximum score of four during the entire study. Initial WeeFIM total score was 1.7% of maximum, with no improvement at the end of treatment. Parents reported a 14% reduction in total time spent providing care during a 24-hour period. Videotape review showed minimal improvement in range of motion throughout the study. Parents responded with a zero (totally dependent) score for all questions, pre- and post-treatment, on the questionnaire.

Discussion

This is the first study to collect serial data to objectively evaluate the effects of adjunctive HBO treatment for children with anoxic brain injuries. All subjects continued their routine therapy in addition to receiving HBO. In the CP group, progressive improvements were noted at each of the measurement intervals. Even with the small number of subjects, our findings demonstrated statistically significant improvements in gross motor function in four of the five areas on the GMFM test and in the total time spent by parents providing childcare. Additional improvement trends were noted in functional skills on the WeeFIM test and in the parent questionnaire results.

The near-drowning subject was analyzed separately because the mechanism of injury is significantly different from the CP subjects. Prior to injury, this subject had no obvious decrements in brain function. The acute, prolonged hypoxic event resulted in a large amount of cellular damage with minimal response to HBO treatment.

There are some risks associated with HBO treatment. The primary concern was injury (barotrauma) to the middle ear or sinuses due to daily exposure to pressure change. To eliminate the risk of middle ear injury, all subjects received PE tubes prior to starting treatment. Medical attendants were individually instructed on proper pressure equalization techniques and chamber pressurization was closely monitored to prevent problems. A low treatment pressure (1.7 ATA) with a short exposure (60 minutes) essentially eliminated the risk of oxygen toxicity in subjects. Other potential concerns included pneumothorax and risk of fire. None of the subjects exhibited any adverse symptoms during the study. We believe the benefits of HBO treatment for 60 minutes at 1.7 ATA outweigh the potential risks.

The SPECT scan results were omitted due to multiple procedural problems which were identified post-study. Scan results may be adversely affected by patient movement, patient position, and delays in imaging following tracer injection. The major complications we experienced included variation of head position during the scan process and the relationship between nuclear tracer

injection and scan time. Due to unforeseeable complications related to level of sedation, the time between tracer dose and scan varied from 20 to 60 minutes. Although multiple scans demonstrated improved brain blood flow, the procedural inconsistencies prohibited an accurate statistical analysis of the data.

The serial increases seen in the GMFM scores are considered true improvements from HBO treatment. The GMFM test has been validated as an accurate assessment of gross motor function in children with CP.[8] Since the subjects continued physical and occupational therapy during our study, some measurable improvement was expected. Two previous studies have documented improvement of 3.7% and 7.0% respectively in GMFM scores following intensive physical therapy over a 6 to 8 month period.[12,13] The subjects in our study received HBO treatment over a 4 to 5 month period with improvement in total score of 26.7% at 20 treatments, up to 58.1% at 80 treatments.

Our findings for the spasticity evaluations were much different than previously reported.[7] This is most likely due to a combination of factors. The MAS is a subjective tool that relies heavily on the experience of the evaluator and our neurologist had limited prior experience with this tool. Test reliability has been questioned, especially for lower extremity evaluations.[14] In addition, our score reflected overall limb spasticity, not specific muscle groups. Three subjects had pre-treatment upper extremity scores of zero or one indicating low levels of spasticity, making it difficult to detect improvement.

The WeeFIM instrument was selected to objectively evaluate changes in basic daily living and functional skills. Although the test has not been validated specifically for CP patients, reliability has been shown for children under age 7 with developmental disabilities.[10] Improvement trends were noted in each of the six evaluated areas, but were not statistically significant. The lack of significance was most likely due to the small number of subjects combined with the age and medical condition of some subjects. Three of the seven subjects exceeded the designated age range of the test. Two of these subjects showed a decrease in test scores while the third showed only minimal improvement. The lack of test reliability in older subjects may explain the contrast in scores noted between the younger and older groups.

A 24-hour time measurement was an additional objective tool used to assess improvement. Parents were given a stopwatch and told to activate it each time they provided care for their child. Total time was recorded for two consecutive 24-hour periods. Testing was conducted only on weekends to reduce variability. As the subject's functional and motor skills improved, we expected to see a reduction in time demands on parents. Significant reductions were noted in six out of seven subjects, with a timesaving of 1¼ to 6 hours per day. Although the size of the time reduction may be affected by a parent reporting bias, a time savings did occur. Parents indicated this time savings was important because it provided additional time for other family members and issues. As expected, larger gains occurred in older subjects since younger children generally require more time and attention.

There was some variability in test scores based on age. In general, younger subjects demonstrated a better response to treatment. The mechanism of injury in CP subjects involves a gradient of hypoxia producing a range of cellular effects, from inactivity to cell death.[3,4] As with any injury, persistent ischemia/hypoxia often results in progressive tissue loss. Early correction of hypoxia limits injury effects, and in brain tissue, provides the stimulus necessary for activation of suppressed neurons.[2,6] Therefore, prospects for improvement may be greater in younger children with shorter periods of hypoxia.

An important consideration is whether or not there was true improvement in daily functioning in these children. Both investigators and parents independently observed multiple functional improvements throughout the study. Many of these changes were a result of improved muscle tone and control. This included improved eating and swallowing ability, ambulation, and fine motor control. In addition, observers noted improved cognitive function and verbal skills, improved bladder and bowel control, and a decrease in strabismus and nystagmus. As a result of the changes, the time required for parental care of the children was reduced. The degree of improvement varied among subjects, as did the number of HBO treatments needed to elicit change. Functional improvements continued in several children to the end of the study. Overall, the quality of daily living appeared to improve for the majority of the children and their families.

The study findings suggest that adjunctive HBO

therapy may improve functional capacity in children with CP but not near drowning when treatment is delayed. We were unable to identify an optimum number of treatments, since improvements were noted to the end of the study. We recognize that there are several methodological limitations to the study that include small sample size, lack of a control group, and potential observer bias. In addition, we do not know the long-term effects of this treatment. Further research is needed with large patient populations and follow-up studies to determine the true potential of HBO treatment for children with cerebral anoxic injury.

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