

An ongoing study of different hyperbaric pressures & use of 100% oxygen or ambient air, for Early Medical Intervention Therapy in children with Cerebral Palsy (CP)

Dr. Arun Mukherjee, MBBS, MD (Med)
Director, UDAAN for the Differently Abled,
A-59 Kailash Colony, New Delhi, India
www.udaan.org

About us:

We started the “Foundation for Spastic & Mentally Handicapped Persons” (FSMHP, Regd. in 1994) a non-profit therapy center for children with various types of brain-dysfunction related disabilities (Neurodevelopmental Delay). Our aim is to give an unbiased open minded try to all therapies claimed and found, at least in pilot studies, to be useful and affordable. Since June 2001, we have been investigating the effects of various advanced medical interventions for helping these children, of which Standard Therapy, supplemented by HBOT, has stood the test of time as cost-effective choice. Our main activity center is called “UDAAN” (pronounced urran). It is a Hindi (Indian language) word meaning flight, symbolizing the Flight of the Spirit of Freedom inherent in the heart of every child, even a special need child.

Classical Management of CP

The classical management of Standard Therapy, given as target-oriented, need-based and customized one-to-one sessions of at least half an hour each of Physiotherapy, Occupational therapy, Special Education and Speech Therapy. Besides these, we have seen the emergence of some exotic techniques based on above including Peto technique, NDT (Neuro-Developmental Therapy), Bobbath technique, etc.

Objective of our Study:

We want to derive the best physical, cognitive, other CNS & psychosocial outcomes within the possibilities of neural function left after the original brain injury. After 8 years of providing only Standard Therapy at UDAAN, we realized that mere Standard Therapy did not prove itself to be sufficient. We were no doubt getting significant improvement in body functions, but it was slow and there was limited improvement in the inherent cognitive and intellectual progress of the child, because we were only tackling the body and not the brain.

There is a widespread misconception in the medical and paramedical fraternity that brain repair is not possible. However, we found a large number of papers supporting the notion that Hyperbaric Oxygen Therapy, provided as a supplement to Standard Therapy, children with CP who were carefully selected, documented and had SPECT Scan proven ischemic penumbra of injury, would indeed show faster and a significant degree of neurodevelopment as compared to that achievable with Standard Therapy alone. Unfortunately not many are indexed in “Free Internet Medline”. Most are available on the dozens of other “*****Lines” in the US National Library of Congress, available only on payment per article, and hence rarely sought out.

Evolution of existing HBOT for CP in India

In June 2001, UDAAN pioneered in India the study of use of HBOT (1.75 ATA 100% O₂ in a Multiplace Chamber) as supplement to Standard Therapy (OT + PT + Special Education + Speech Therapy) for CP children. We decided that this would be an ongoing

study of CP children given only Standard Therapy (Batch A) versus HBOT 40 sessions once a day, plus Standard therapy (Batch B), in children with CP. The children were selected after detailed assessment of severity by the Occupational Therapist, Special Educator and Speech Therapist, plus SPECT Scan of brain to study degree of Ischemic penumbra.

By mid 2004, International Authorities like Dr. Paul Harch guided us to lower the HBOT pressure to 1.5 ATA for better effect. By that time we had completed long term follow up of 60 CP children. We thus started our Batch C using 1.5 ATA HBOT with 100% Oxygen, 40 sessions, plus Standard Therapy.

A year later, encouraged by the data published in the Collet article in The Lancet, we acquired a soft chamber to provide room air compressed to 0.3 ATA above prevalent atmospheric pressure (1.3 ATA Hyperbaric Air Therapy or HBAT). We then started our Batch D giving 1.3 ATA HBAT 40 sessions plus Standard Therapy.

All four groups belong to an ongoing observational open, non-randomized parent chosen mode UDAAN Multimode Early Medical Intervention Therapy study of CP in children.

Inclusion Criteria

- Children with all types of C.P. (Most were between 1 to 5 years, oldest up to Teen age, mean age 3.5 to 4.87 years)
- Either Sex
- Any I.Q. level
- Pre-HBOT SPECT Scan showing presence of recoverable penumbra IN ALL test subjects.
- Those living in Delhi or willing to live in Delhi for 6 - 8 months within reasonable distance of UDAAN to facilitate daily transportation

Exclusion Criteria

- Uncontrolled Epilepsy
- Uncontrolled Bronchospastic and/or E.N.T. disorders.
- Any Genetic Disorders
- Pervasive Developmental Disorders.

Grouping & Assessment

Every child received matching Standard Therapy

Batch – A: n=20; Standard Therapy only

Batch – B: n=60; Standard Therapy plus initially 40 sessions of 1.75 ATA HBOT with 100% Oxygen, one session a day

Batch – C: n=24; Standard Therapy plus initially 40 sessions of 1.50 ATA HBOT with 100% Oxygen, one session a day

Batch – D: n=24; Standard Therapy plus initially 40 sessions of 1.30 ATA HBAT with room air, one session a day

Assessments done every 2 months

Physical Assessment

We used standard scales like GMFM, Modified Ashworth, BERI VMI, etc., but for statistical purpose, GMFM data were analyzed.

GMFM Measurements: Baseline, 4 months & 6 months, and now-a-days, 8 months

Statistical evaluation: By a Bio-statistician trained at the prestigious All India Institute of Medical Sciences, Delhi

Statistical Methods used by our Statistician

- Chi Squared Test for Categorical Data
- Non Parametric Wilcoxon Mann Whitney Test for 2 Groups
- Non Parametric Kruskal Wallis Test for more than 2 Groups
- Non Parametric Wilcoxon Signed Rank Test for two different time periods

Assessments other than Physical

Cognitive abilities (Special Education) assessments are always a problem in CP due to combination of intellectual impairment & physical inability in the children. Hence, based on our long experience with various scales, we developed a modified scale of 22 objective parameters for cognitive changes (Special Education) based on standard scales like FACP, Vineland, BASIC MR, Portage, etc. Each of the parameters was subdivided into 5 achievable grades of improvement. It is customized to measure smaller differences in Cognitive skills at 2 month intervals.

We also managed to do serial videos of most of the children for our records.

Each child getting any form of hyperbaric therapy was assessment of fitness for HBOT by a Pediatrician and ENT Surgeon. Parents were counseled in detail about all pros and cons of HBOT, their informed consent obtained for this experimental therapy and then only were they referred to the Multiplace HBOT center at a tertiary care hospital.

Even though many children availed of HBOT in our project, many parents could not stay in Delhi beyond HBOT therapy duration. We have limited our analysis only to those children who stayed with us and availed of our Standard Therapy throughout the 6 to 8 months of follow up, so that there would be no variable on that aspect of management.

Results

Age Cross Tabulation:

- No significant difference in Mean Age between the four batches (Non-parametric Kruskal-Wallis Test: $p > 0.06$)
- No significant difference in Age Distribution between the four groups (Pearson Chi-Square Test: $p > 0.2$)

Sex Cross Tabulation:

- No significant difference between the four batches in Sex ratio (Pearson Chi-Square Test: $p > 0.6$)

GMFM Scores

- Based on percentage change from baseline, all four batches improved significantly within their own groups based on the Non Parametric Test; Wilcoxon Signed Ranks Test (at 6 months, $p < 0.001$ for all four batches)

GMFM percentage change from baseline to 6 months, between control and Hyperbaric groups, using Non Parametric Mann Whitney Test.

- 1.30 ATA HBAT Vs Control: 1.30 ATA significantly better ($p < 0.005$)
- 1.50 ATA HBOT Vs Control: 1.50 HBOT significantly better ($p < 0.001$)
- 1.75 ATA HBOT Vs Control: 1.75 HBOT significantly better ($p < 0.001$)

GMFM Absolute Scores to compare 1.3 ATA HBAT with the two HBOT batches using NPar Tests: Mann-Whitney Test

- No significant difference between 1.3 ATA HBAT and 1.5 ATA HBOT at 6 months ($p = 0.316$ NS)
- No significant difference between 1.3 ATA HBAT and 1.75 ATA HBOT at 6 months ($p = 0.099$ NS)

Cognitive Percentage Improvement in Control vs. the three Hyperbaric groups using Mann Whitney Test

- 1.30 ATA HBAT superior to Control at 6 months ($p < 0.001$)
- 1.50 ATA HBOT superior to Control at 6 months ($p < 0.05$)
- 1.75 ATA HBOT superior to Control at 6 months ($p < 0.005$)

Special Education Cognitive improvement in the three Hyperbaric groups compared using Non-Parametric Tests - Mann-Whitney Test .

- No significant difference between 1.3 ATA HBAT and 1.5 ATA HBOT at 6 months ($p > 0.7$ NS)
- No significant difference between 1.3 ATA HBAT and 1.75 ATA HBOT at 6 months ($p > 0.4$ NS)

Discussion

This study was done on parent preference and economic affordability of the hyperbaric regimen. The 40 sessions of either HBOT costs \$1500 and HBAT costs \$900. This amount may be relatively small by US standards but mean a lot in India. Besides that, the quality of Standard Therapy remained the same, with all children being treated at UDAAN by the same set of therapists using the same techniques and the same equipment for the same duration of time a day for the same length of study. All four groups had matching children as far as age, sex, types and severity of lesion were concerned. We used the then-prevalent 1.75 ATA HBOT to begin with and completed long-term follow up on 60 CP children before being guided to change to 1.5 ATA HBOT. Soon after we started a parallel batch using 1.3 ATA hyperbaric air group based on the Lancet study.

We have excluded children who were not under constant observation and Standard Therapy under our control at our center, so that treatment bias should not creep in. Using these limited options, which were the best we could have done under prevailing conditions in our country, we observed that there was statistically greater improvement achieved by all three hyperbaric batches as compared to the control group (Batch A). However, intergroup comparisons between the three hyperbaric batches failed to show that any one batch was statistically superior to the other batches, though the two regular HBOT batches had a minor statistically non-significant trend in their favor over low pressure HBAT as far as motor (GMFM) changes were concerned. Similarly, in Special education / Cognitive parameters, all three hyperbaric batches showed a statistically significant improvement over the control non-hyperbaric batch, but there was no statistically significant difference in improvement scores between the three hyperbaric batches, as in the case of GMFM score. However, this time, there was a non-significant trend in favor of low pressure HBAT over regular HBOT as far as cognitive (Special education) changes are concerned.

We tried to investigate why these non-significant trends occurred.

Dr Julian Whitaker, M.D spoke at the 6th Int. Symp. on Hyperbaric Oxygenation and the Future of Healing, July 24 - 26, 2008, Torrance, California, USA, that HBOT outcomes may be improved by adding a little carbon dioxide to the pure oxygen used. He mentioned that Hyperoxia-induced hypocapnia narrows the blood vessels and reduces blood flow to the brain. It activates regions of the brain that control autonomic functions and floods the body with potentially harmful hormones and neurotransmitters. He

suggested that the addition of CO₂ to the gas mixture may diminish these responses and could reduce adverse effects of 100% O₂.

The motor pathways start from neurons in the highly vascular cortex of brain. All nerves bunch together to form the low vascularity Internal Capsule. Ischemic injury resulting in tissue edema and/or inflammation has a tendency to involve this area. Vasoconstriction produced by 100% oxygen HBOT may be superior in reducing blood flow and thus tissue edema and inflammation, to reduce the compression features in the Internal capsule to restore its function faster. Cognitive function is a different ball game altogether. Many interactive centers for Intellectual / Cognitive Functions, sight, sound, touch, temperature, vibration, pain, smell, emotional elements, as well as many Neuro-Endocrine systems scattered all over the brain interact in a wide-area-network, to give us the final end result of our intellect, memory, response, psychosocial behavior, attentiveness and following of command. Each center has to function at an optimum level to coordinate this work.

100% Oxygen HBOT-induced vasoconstriction may reduce function in some normal areas to upset the chain of events that work in tandem to develop our Cognitive abilities. HBAT using the atmosphere-like mixture we are accustomed to (vasoconstricting oxygen and vasodilating carbon dioxide), may prove more useful, as it would help revive ischemic zones without hampering function of normal areas.

Our 1.3 ATA HBOT regimen may have used this factor inadvertently to show the trend in favor of low pressure HBAT over higher pressure HBOT in cognitive improvement. With our ongoing study, we should have a more clear answer in the years to come.

Conclusions

Overall, all 3 Hyperbaric therapy plus Standard Therapy regimens are equivalent in showing a statistically significant improvement over Standard Therapies only in improving Motor and Cognitive skills in children with cerebral palsy.

100% O₂ HBOT (1.5 & 1.75 ATA) is slightly though Non-Significantly better than 1.3 ATA HBAT in improving GMFM Scores of motor function restoration.

1.3 ATA HBAT is slightly though Non-statistically superior to 100% O₂ HBOT (1.5 & 1.75 ATA) in improving Cognitive skills, which were found with an almost similar incidence in majority of children with cerebral palsy who took part in our study.

Possibly, more experience with CT-SPECT Fusion Scans could in future show the way as to which regimen could possibly work cost-effectively better in which variety of brain SPECT Scan pattern.

Tolerance to hyperbaric therapy was very good in the 128 children with long term follow up studied, as well as more than 3 dozen children who only came to us for hyperbaric therapy and then went back to carry out Standard Therapy in their home town, and was no different from the control group.

A few relapses of epilepsy in children with recent history of fits, was also seen in Controls. There was no claustrophobia in the children, though some mothers did complain of it. There were no behavioral problems inside chamber. No child deteriorated from hyperbaric therapy.

Bases on our ongoing data so far, we believe that the use of Hyperbaric Therapy is justified in properly selected young children with Clinical and SPECT Scan proven ischemic pathology, and that 1.3 ATA is a justifiable option to parents who cannot afford the high-cost of the more-studied HBOT, and yet wish to get an equivalent degree of improvement in the quality of life of their kids.