

Title: Hyperbaric Therapy-Based Multimode Therapy for children with Cerebral Palsy

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INTRODUCTION

Cerebral Palsy (CP):

Abnormalities of tone are an integral component of many chronic motor disorders of childhood. These disorders result from dysgenesis or injury to developing motor pathways in the cortex, basal ganglia, thalamus, cerebellum, brainstem, central white matter or spinal cord. The major damage is to the developing fetal / neonatal brain, mostly affecting the poorly vascularized Internal Capsule, Descending Cerebro- and Cerebello- Spinal tracts, thus affecting various motor functions. When the injury occurs in children before 2 years of age, the term Cerebral Palsy (CP) is often used.

Management of CP

The classical management of CP is Standard Therapy comprising individualised, need based and target-oriented Physiotherapy, Occupational therapy, Special Education and Speech Therapy. These are often offered as exotic management techniques such as Peto technique, NDT (Neuro-Developmental Therapy), Bobbath technique, etc. Down at heart, they are all specialised forms of Standard Therapy to derive the best physical and psychosocial outcomes within the possibilities of neural function left after the original brain injury.

Hoping that these standard therapies alone can solve the problems of the CP child is like hoping that changing the tyres and lubricating the wheels and axles of a car will make it run better when its engine is choked with carbon deposits. We need to repair the engine if the fault is in the engine: it is as simple as that.

There are dozens of papers in world literature, unfortunately not indexed in “Free Internet Medline” but in other more than 100 “*Lines” in the US National Library of Congress, that are available only on payment per article, and hence rarely sought out. They carry many reports on CP children treated with Hyperbaric Oxygen Therapy, showing improvement and increase in serial GMFM scores over time that were five to ten times faster than that achieved in the best centres of standard therapies.

UDAAN for the Disabled

UDAAN for the Disabled is a non-profit organization, recognized and partially aided by the Government of India. We are offering standard therapies since 1994 to children affected by various forms of Neurodevelopmental disabilities, in which CP predominates. Since 2001, we started a research project to study the benefits of HBOT-based multimode therapy of CP. We have a control batch of CP children that did not receive HBOT, as well as batches that received HBOT in a Multiplace rigid chamber either at 1.75 ATA (till July 2004) or 1.5 ATA (after July 2004) with 100% oxygen delivered by an Amron mask. There is a fourth batch that received mild pressurized air (with **no** additional oxygen supplementation either with a Concentrator or oxygen cylinder) at 1.3 ATA using the largest size OxyHealth soft portable chamber (since 2006).

The study is a prospective open non-randomised study, with batches decided by the parent based on their own convenience and financial status. It is an ongoing study. Hence, our database is growing by the year. This article represents data as available till June 2008.

Evolution of existing HBOT based Multimode Therapy for CP in India

June 2001

UDAAN pioneered in India the study of 1.75 HBOT at 100% O₂ as supplement to Standard Therapy (OT + PT + Special Education + Speech Therapy) for CP children.

March 2003

The first UDAAN paper on the use of HBOT in CP (Control 15 vs Test 15) was presented at the Annual Conference of Indian occupational Therapy Assoc. at Bangalore (Amit Sethi and Arun Mukherjee) and won the best scientific paper award. This was later reported in

July 2003

3rd Int. Symposium on HBOT & the Brain Damaged Child (Florida): Presented interim data on 20 CP children given only Standard Therapy vs. 20 matching Test group of 20 CP Children given additional HBOT (40 sessions of 1.75 ATA with 100% O₂). Trend favored the HBOT group on all parameters.

July 2004

4th Int. Symp. on HBOT (Florida): Presented data on 39 CP children given 40 sessions of HBOT at 1.75 ATA, with statistically significant improvement over the batch given only Standard Therapy (n=20) .

Dr. Paul Harch advised us to shift down to 1.5 ATA for better results. We did as advised.

July 2006

5th Int. Symp. on HBOT (Florida): Presented ongoing long term (6 to 8 months) study data of 84 CP children given supplemental HBOT (*sub-group analysis of 1.5 & 1.75 ATA not done*) Vs. 20 on Standard Therapy alone.

Data on interim pilot study on 7 given 1.3 ATA Hyperbaric Air also shown but not included in analysis.

July 2008

6th Int. Symp. on HBOT (Torrance CA): Presented data on 128 CP children who completed at least six months of follow up, after receiving only Standard Therapies (n=20), or standard therapies supplemented by (a) regular 100% O₂ HBOT at 1.75 ATA (n=60), (b) regular 100% O₂ HBOT at 1.5 ATA (n=24), or (c) HB-Air at 1.3 ATA using room air only (n=24).

Materials and Methods

Selection Criteria

Inclusion Criteria

- All types of CP in children aged mostly between 1 to 5 years, oldest up to Teen age
- Either Sex
- Any I.Q. level
- Pre-HBOT SPECT Scan showing presence of recoverable penumbra in 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

Every child received matching Standard Therapy at the same venue by the same group of therapists, using the same protocol, same equipment, and the same duration of 6 to 8 months.

- Batch – A: No hyperbaric therapy
 - Batch – B: 40 sessions of 1.75 ATA HBOT with 100% Oxygen during 1st two months
 - Batch – C: 40 sessions of 1.50 ATA HBOT with 100% Oxygen during 1st two months
 - Batch – D: 40 sessions of 1.30 ATA HBAT with room air during 1st two months
1. The Hyperbaric groups also received CP Specific Acupuncture one session a day for 60 sessions as part of multimode therapy, added from 5th month onwards, after giving HBOT / HBA enough time to exert its effects.
 2. Assessments done every 2 months
 3. Data analyzed for **Percentage Change from Basal to 4 and 6 Months.**

Physical Assessment

- Standard Scales like GMFM scale are always used. We also use other relevant scales where needed, like Modified Ashworth, BERI VMI, etc. The analytical data is based on the GMFM Scale.
- 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

Special Educational and Speech Therapist's assessments are always a problem in CP due to combination of intellectual disability & physical impairment 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)

Evolved from standard scales like Vineland, Help Check list; RUTTH GRIFFITH; REEL; FAB & BASIC MR. Each parameter has been divided into 5 achievable grades of improvement. These grading have been customized to measure smaller differences in Cognitive skills at 2 month intervals.

UDAAN Study Timeline

Protocol - Standard Therapy

6 days/week, one-to-one basis, ½ Hr each daily of

1. Physiotherapy
2. Occupational Therapy
3. Special Education
4. Speech Therapy

Assessment of fitness for Hyperbaric Therapy

Pre-HBOT SPECT Scan was done in just about every child to show ischemic brain lesion. Each child had to undergo medical fitness by a pediatrician and an ENT specialist to ensure safety at hyperbaric conditions. Neurological opinion was sought in children with fits, and where needed, dose of anti-epileptic therapy was slightly increased during the HBOT phase to minimize risk of fit relapse.

Protocol Hyperbaric Oxygen Therapy Regimen

HBOT was done in a multiplace chamber using 15 minutes to pressurize, 15 minutes to depressurize, and 60 minutes at pressure with 100% Oxygen given through an Amron mask.

The children received one session of HBOT a day x 40 sessions during 1st two months. The pressure used was 1.75 ATA from 2001 to July 2004, which was subsequently reduced to 1.5 ATA as per guidance received from our mentor, Dr. Paul Harch.

Hyperbaric Air Therapy Regimen

HBAT was done in a non-ASME-PVHO compliant OxyHealth soft chamber (their largest chamber size used) as part of our research protocol, at 1.3 ATA using non-enriched room air, in a dedicated air-conditioned room with filtered air. This batch duplicates the batch wrongly and repeatedly referred to as “Placebo” by Collet, the lead author of the landmark Canadian study of HBOT in CP (*Collet, J.P., Vanasse, M., Marois, P., Amar, M., Goldberg, J., Lambert, J. et al. (2001) Hyperbaric oxygen for children with cerebral palsy: A randomized multicentre trial. The Lancet, 357, 582-586*). Each child received one session a day x 40 days during first 2 months.

Protocol of Acupuncture

One 45-minute session a day for 60 working days, from 5th month onwards, after benefits of HBOT were observed. A trained qualified Acupuncture Therapist offers it. All usual aseptic and antiseptic techniques are followed, and no complications have occurred since 2001. We also use Laser Acupuncture where needed. The therapy is always done in close consultation with our Occupational Therapy Dept, with reference to case-to-case physical disabilities.

Observations

Age Group Cross tabulation

GROUP	N	MIN	MAX	RANGE	MEAN Age	S.D.	MEDIAN	SE OF MEAN
Control	20	1.0	17.0	16.0	3.5	3.49	3.00	0.78
1.3	24	1.5	9.0	7.5	4.87	2.16	5.00	0.44
1.5	24	1.0	13.0	12.0	4.33	3.14	3.0	0.64
1.75	60	1.0	12.0	11.0	4.22	2.47	4.0	0.24

Non-Parametric Kruskal-Wallis Test: $p > 0.06$ (NS)

Age Range Cross tabulation

GROUP	<=2 YR	3-4 YR	5-6 YR	7-8 YR	>8 YR	TOTAL
Control	8 (40)	9 (45)	2 (10)	0 (0)	1 (5)	20
1.3	4 (16.7)	5 (20.8)	10 (41.7)	3 (12.5)	2 (8.3)	24
1.5	7 (29.2)	9 (37.5)	3 (12.5)	2 (8.3)	3 (12.5)	24
1.75	15 (25)	24 (40)	12 (20)	6 (10)	3 (5)	60

Pearson Chi-Square test: $p > 0.02$ (NS)

Sex Division Cross tabulation

GROUP	FEMALE	MALE	TOTAL
Control	7 (35%)	13 (65%)	20
1.3	5 (20.8%)	19 (79.2%)	24
1.5	5 (20.8%)	19 (79.2%)	24
1.75	18 (30%)	42 (70%)	60

Pearson Chi-Square test $p > 0.2$ (NS)

Conclusion: no significant difference in Age or Sex distribution across the four groups

Motor Changes, from baseline to 4 & 6 months in GMFM Scores

GROUP	% CHANGE 0 - 4 MT MIN & MAX. MEAN + SD P =	% CHANGE 0 TO 6 MT MIN & MAX. MEAN + SD P =
Control n=20	Min: 1.3; Max 29.9 Mean: 5.99 + 7.6 p < 0.001	Min: 2.5; Max: 59.9 Mean: 11.95 + 15.2 p < 0.001
1.3 n=24	Min:0.0; Max: 164.1 Mean: 19.41 + 34.1 p < 0.001	Min: 2.53 Max: 281.5 Mean: 37.3 + 58.5 P < 0.001
1.5 n=24	Min: 2.44;Max: 194.1 Mean: 22.7 + 33.5 p < 0.001	Min: 4.41; Max: 358.5 Mean 39.1 + 62.9 p < 0.001
1.75 n=60	Min: 0.58; Max: 59.1 Mean 18.3 + 14.9 p < 0.001	Min: 1.53; Max: 118.5 Mean: 37.1 + 30.0 p < 0.001
1.5+1.75	Min: 0.58; Max: 194.2 Mean 19.9 + 23.3 p < 0.001	Min: 1.53; Max: 358.5 Mean: 37.8 + 30.0 p < 0.001

Non Parametric Test

Wilcoxon Signed Ranks Test

Conclusion: All four groups improved statistically significantly within their own groups.

Comparative GMFM changes

P VALUE OF % CHANGE IN GMFM FROM BASELINE TO:	4 MT	6 MT
1.3 vs. Control	p < 0.001 HS	p < 0.005 HS
1.5 vs. Control	p < 0.001 HS	p < 0.001 HS
1.75 vs. Control	p < 0.001 HS	p < 0.001 HS

All three Hyperbaric Groups were significantly superior to Control Group.

Absolute Value Changes in GMFM Scores

Group	0 mt Min & Max. Mean + SD	4 mt Min & Max. Mean + SD	6 mt Min & Max Mean + SD
Control n=24	Min:12.1; Max: 53.6 Mean: 29.6 + 13.0	Min: 12.5; Max: 54.3 Mean: 31.0 + 12.8	Min: 12.9; Max: 55.0 Mean: 32.4 + 12.3
1.3 n=24	Min:6.8; Max: 65.5 Mean: 31.2 + 14.7	Min: 20.5; Max: 69.4 Mean: 36.7 + 13.2	Min: 24.0; Max: 71.8 Mean: 38.3 + 13.1
1.5 n=24	Min: 4.12; Max: 70.8 Mean: 34.7 + 15.4	Min: 12.1; Max: 81.9 Mean 39.6 + 15.2	Min: 18.9; Max: 86.5 Mean: 42.8 + 15.2
1.75 n=60	Min: 13.5; Max: 81.5 Mean 32.6 + 11.7	Min: 17.4; Max: 63.7 Mean: 37.3 + 10.7	Min: 21.3; Max: 69.2 Mean: 42.10+ 10.3
1.5 +1.75	Min: 4.12; Max: 70.8 Mean 33.3 + 13.1	Min: 12.1; Max: 81.9 Mean: 38.1 + 12.5	Min: 18.9; Max: 86.5 Mean: 42.3 + 12.2

Using these values, the efficacy of 1.3 ATA HBA was compared to the two regular 100% oxygen based HBOT groups.

The comparative results were as follows, using Non-parametric Mann-Whitney Test:

1.3 ATA HBA vs. 1.5 HBOT:

At 4 months, difference **not significant** (p = 0.467)

At 6 months, difference **not significant** (p = 0.316)

1.3 ATA HBA vs. 1.75 HBOT

At 4 months, difference **not significant** (p = 0.601)

At 6 months, difference **not significant** (p = 0.99)

1.3 ATA HBA vs. 1.5 + 1.75 ATA HBOT

At 4 months, difference **not significant** (p = 0.509)

At 6 months, difference **not significant** (p = 0.126)

COGNITIVE CHANGES

Special Education Cognitive tests by Absolute values

Group	0 mt Min & Max. Mean + SD	4 mt Min & Max. Mean + SD	6 mt Min & Max. Mean + SD
Control n=24	Min: 27; Max: 122 Mean: 48.6 + 27.4	Min: 27; Max: 122 Mean 58.5 + 28.4	Min: 27; Max: 125 Mean: 63.1 + 30.5
1.3 n=24	Min: 23; Max: 81 Mean: 38.4 + 15.4	Min: 29; Max: 88 Mean: 60.9 + 18.6	Min: 32; Max: 96 Mean: 67.4+ 21.7
1.5 n=24	Min: 26; Max: 124 Mean: 48.5 + 28.7	Min: 29 Max: 127 Mean 62.9 + 30.8	Min: 30; Max: 128 Mean: 67.6 + 30.7
1.75 n=60	Min: 26; Max: 128 Mean 48.0 + 28.1	Min: 29; Max: 130 Mean: 67.9 + 32.1	Min: 30 Max: 130 Mean: 75.1+ 33.3
1.5+1.75	Min: 26; Max: 128 Mean 48.1 + 28.1	Min: 29; Max: 130 Mean: 66.4 + 31.6	Min: 30; Max: 130 Mean: 73.1 + 32.6

Based on these values, we tested the changes in the two Hyperbaric Oxygen Therapy groups as compared to changes in the 1.3 ATA Hyperbaric Air group

The comparative results were as follows, using Non-parametric Mann-Whitney Test:

1.5 ATA HBOT group

1.5 ATA HBOT group was **not statistically superior to the 1.3 ATA HBA** group, with p > 0.7 at 4 months and p > 0.7 at 6 months.

1.75 ATA HBOT group

1.75 ATA HBOT group was **not statistically superior to the 1.3 ATA HBA** group, with p > 0.7 at 4 months and p > 0.4 at 6 months.

1.5 + 1.75 ATA HBOT group

The combined 1.5 ATA + 1.75 ATA HBOT group was **not statistically superior to the 1.3 ATA HBA group**, with p > 0.8 at 4 months and p > 0.6 at 6 months.

Cognitive Percentage Improvement

Group	% Change 0 - 4 mt Min & Max. Mean + SD	% Change 0 – 6 Mt Min & Max. Mean + SD
Control (n=20)	Min:0.0; Max: 121.9 Mean: 24.4 + 29.7	Min: 0.0; Max: 165.56 Mean: 34.9 + 41.6
1.3 (n=24)	Min:4.9; Max: 157.1 Mean: 65.8 + 40.4	Min: 11.1; Max: 185.7 Mean: 83.6 + 48.2
1.5 (n=24)	Min:0.0 Max: 69.3.8 Mean: 34.7 + 20.2	Min: 0.0; Max: 96.6 Mean 47.2 + 26.5
1.75 (n=60)	Min: 0.78 Max: 167.7 Mean 49.8 + 42.,3	Min: 1.56; Max: 219.35 Mean: 69.5 + 55.7
1.5+1.75 (n=84)	Min: 0.0; Max: 167,7 Mean 45.6 + 37.9	Min: 0.0; Max: 219.4 Mean: 63.3 + 50.1

Using these values, the three Hyperbaric groups were compared to the Control groups. The comparative results were as follows, using Non-parametric Mann-Whitney Test:

1.3 ATA HBA group

1.3 ATA HBA group was statistically superior to the Control, with $p < 0.001$ at 0 to 4 months, and $p < 0.001$ at 0 to 6 months.

1.5 ATA HBOT group

1.5 ATA HBOT group was statistically superior to the Control, with $p < 0.05$ at 0 to 4 months, and $p < 0.05$ at 0 to 6 months.

1.75 ATA HBOT group

1.75 ATA HBOT group was statistically superior to the Control, with $p < 0.005$ at 0 to 4 months, and $p < 0.005$ at 0 to 6 months.

DISCUSSION

Efficacy

All FOUR Groups showed significant improvement with the therapy received at UDAAN. However, all three hyperbaric groups were significantly superior to the Control group at both 4 and 6-month follow up.

GMAE Trends

There was a statistically significant improvement recorded by all three hyperbaric groups as compared to the control group. No significant difference between the three Hyperbaric Groups. We may need a much bigger database than 128 CP children to see a significant difference. We are working towards it with our ongoing study.

The change in GMFM absolute scores after 6 months of therapy was 0.67 in Control, 1.18 at 1.3 ATA, 1.35 at 1.5 ATA and 1.6 at 1.75 ATA. These results are similar to the Lancet study and show that hyperbaric therapy doubles the improvement rate improvement compared to non-Hyperbaric therapy regimens, with no significant difference between the individual hyperbaric regimens used.

Cognitive Trends

The Cognitive tests done by the Special educators, using our own modified scale based on available internationally recognized scales adapted to measure smaller changes in Cognitive

improvements, showed no significant difference between the three Hyperbaric Groups. We may need a still bigger database to come to see a significant difference.

Why the non-significance between HBAT & HBOT

Let us study with an open mind

Tissue Oxygenation

The regular HBOT chambers rely on pure oxygen source (oxygen cylinders or piped hospital supply). They have independent air-cooling mechanisms to maintain a comfortable temperature inside during the procedure.

Normal tissue fluid Oxygen saturation = 0.3%. Regular HBOT, using a rigid chamber, at 1.5 to 1.75 ATA, with 60 minutes at 100% pure Oxygen, achieves tissue fluid Oxygen saturation of about 2 to 3 ml /100 ml, representing a 7 to 10 fold rise, or, almost a 700% rise. However, the use of a hood based close circuit also ensures that there is no inhalation of Carbon Dioxide. Hence, its level in tissue fluid and blood remains very low.

Carbon dioxide is the most potent stimulator of respiratory effort, besides causing vasodilatation to ensure normal tissue perfusion, which influences many neuro-endocrine and other mechanisms in the brain and body.

Thus, a typical HBOT chamber ensures tissue and blood oxygen concentration extremely higher than physiological levels, combined with intense vasoconstriction induced by highly unbalanced oxygen (vasoconstrictor) to carbon dioxide (vasodilator) ratio in blood and tissue fluid.

The low-pressure (1.3 ATA) OxyHealth Soft Hyperbaric chamber used by us compresses normal room air to 1.3 ATA, to achieve a tissue fluid Oxygen saturation of approximately 0.4 - 0.5 ml /100 ml, or 1/3 rd to 1/2 fold rise = 33 to 50 % increase. This is achieved by compressing normal room air that does not have any imbalance in its oxygen to carbon dioxide ratio, which is what our physiology is used to, in order to maintain physiological blood vessel patency and other neuro-hormonal regulatory balances within our systems.

Is a 33% rise in tissue Oxygen level enough?

How physiologically significant is a 33% change in our internal milieu of tissue oxygenation as produced by 1.3 ATA Hyperbaric therapy?

- Presume that a patient has fever with temperature of 105° F. We use an acetaminophene (paracetamol) tablet to lower temperature by only 6%. The temperature is now **normal**.
- A patient develops high diastolic BP of 105 mm Hg. We use an appropriate anti-hypertensive drug to lower blood pressure by only 30%. The BP is now **normal**.
- A patient develops acute respiratory or metabolic derangement, which acidifies his blood and decrease blood pH to 7.0. We use appropriate IV Fluids, Nutrition and Drugs to increase the blood pH by 6 %, which brings his blood pH back to about 7.4 or **normal**.

NOW, how significant is a 33% change in our internal milieu?

How could HBAT be non-significantly, though marginally, superior to regular HBOT on Cognitive parameters?

Compressed air heats up. While it is no problem in cold climates, it is a big problem in climate-wise hot countries like India.

When we started using such a low-pressure soft chamber in 2006, besides the additional problem of keeping the piped air dust free to ensure no problem to the already-weak special need child as well as prolong the life of the high-efficiency air filters attached to the air compressors, the high heat developed inside the chamber was intolerable.

We solved this problem by centrally air-conditioning the building to 25° C, and constructing an enclosed small cabin inside the complex with its own additional air-conditioner that

further cleaned and cooled down the cabin to 16° C. This achieved a physiologically balanced, clean and comfortable temperature atmosphere inside the soft chamber. However, we are now realizing that having a centrally closed air-conditioned building does lead to some degree of carbon-dioxide recirculation. In addition, the further enclosed cabin, which contains the chamber as well as its compressor, causes a slightly greater carbon-dioxide recirculation.

What is the effect of this slightly higher carbon dioxide level on brain physiology?

We were a little surprised to see that though both motor and cognitive changes were statistically equivalent in all three Hyperbaric groups, there was a statistically non-significant trend in favor of regular HBOT over low pressure HBAT as far as motor (GMFM) changes were concerned, whereas in contrast, there was a non-significant trend in favor of low pressure HBAT as far as cognitive changes are concerned.

In his presentation at the 6th International Symposium on Hyperbaric Oxygenation and the Future of Healing, July 24 to 26, 2008, Torrance, California, USA, (www.hbot2008.com) Dr Julian Whitaker, M.D., (*IMPROVING HBOT OUTCOMES BY NORMALIZING CO2 LEVELS*) suggested that a growing body of research suggests that breathing 100% O₂ at room pressure has adverse effects and that increasing carbon dioxide (CO₂) levels obviates these effects. 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.

Studies reveal that the addition of CO₂ to the gas mixture greatly diminishes these responses and could reduce adverse effects of 100% O₂. Standard practice of 100% O₂ ventilation needs to be revisited and methods for reducing hypocapnia explored-both at room pressure and HBOT. These include modifications to gas mixtures, breathing and rebreathing devices, and breath holding techniques.

This is what we inadvertently achieved in our enclosed HBAT cabin. The slightly higher CO₂ levels inside the HBAT soft chambers were altering physiology in ways that need further study, since motor controls are relatively simple brain functions whereas cognitive and psycho-social behavior are very complex multi-region based neural functions, that are regulated by a whole host of neuro-endocrine systems, that could be affected by changes in vascular supply even though they may lie in non-ischemic zones. We must also remember that the Human Body Physiology works **within quite narrow physiological margins, and, during ill health, nature usually requires only mild to moderate changes in internal milieu to change the prognosis in favor of the patient.**

What this means

Based on our experience, we believe 1.5 or 1.75 ATA HBOT with 100% O₂ is slightly though Non-Significantly better than 1.3 ATA HB-AIR as regards motor recovery in children with cerebral palsy while 1.3 ATA HBAT with room air is slightly though Non-statistically superior to regular 100% oxygen based HBOT for improving cognitive and psycho-social abilities. Overall, they balance out in improving the prognosis of the child significantly as compared to children receiving only standard therapy.

1.3 ATA HB-Air is statistically Non-Inferior to 1.5 or 1.75 ATA HBOT with 100% oxygen though it costs roughly half to provide.

Possibly, more experience with CT-SPECT Fusion Scans could in future show the way as to which regimen will possibly do cost-effectively better in which brain SPECT Scan pattern, involving cognitive/temporal lobes or the motor areas of cerebral cortex and internal capsule.

Tolerance

Our experience on tolerance is based on a database of 84 CP children given a minimum of 40 sessions of HBOT at 100% Oxygen and 24 matching CP children treated with a minimum of 40 sessions of 1.3 ATA HBAT using room air, compared to 20 matching CP children (Control) who received the same Standard Therapy but no Hyperbaric Therapy in any form.

- A few children with recent history of fits had relapse of epilepsy, but its incidence was similar to the rate of fits in Control children. We stopped therapy for 7 to 10 days, and could complete the course in all except one child, in the 1.5 ATA group.
- His/her own mother or relation usually accompanies the CP child inside the chamber. No case of claustrophobia was seen in the children (perhaps due to their cognitive impairment), though some mothers or relations did have some such problem. Our Nurse on duty accompanied their children inside the chamber in such cases.
- There were no significant behavioral problems inside chamber, including some children with autism, who were not a part of this particular project.
- We have been doing HBOT since 2001 and HBAT since 2006. During this period, no deterioration was noticed in any child treated so far.

Chamber problems

Regular Monoplace HBOT chambers pressurize with 100% oxygen. If they start using room air to give less costly 1.3 ATA HBAT, the condensing moisture could play havoc with the inside chamber materials and sealing which were designed to use dry pure oxygen from a dedicated oxygen source.

The Multiplace chambers simultaneously treat many types of patients, and not just CP. Different indications require different pressures, often exceeding 1.5 ATA. Hence providing the less costly 1.3 ATA in such chambers is not cost effective or feasible

Both types of regular HBOT provide 100% pure dry oxygen to the patient. Thus the patient does not receive physiologically necessary levels of carbon dioxide. Problems associated with carbon dioxide levels need to be studied in future. There may also be respiratory problems later on in children receiving dry air for 1.5 hours.

The 1.3 ATA soft HBAT chambers on the other hand, provide the physiological levels of oxygen and carbon dioxide mixture, and may be better at maintaining intracranial neuro-hormonal controls. However, they supply humid air, at least in our setting, which condenses inside the chamber. The chamber needs to be wiped clean after each round, and aerated periodically in-between sessions.

Our suggestions for soft chambers:

1. We normally have a tidal breath volume of 500 ml, and breathe up to about 20 times per minute. Hence, the chamber must have a flow rate of 10 liters per minute per person, to ensure normal oxygen supply. Since the chamber normally has a child and a relation, rarely the nurse also, we need a minimum flow rate of 30 liters/minute. The Oxyhealth chamber we use has a flow rate of 50 liters/minute.
2. There should be a dehumidifier inline, before the compressor, with airflow rates matching that of the compressor. The dehumidified and compressed air can be used to achieve lower humidity inside the HBAT chamber.
3. The flexible pipe from the compressor to the chamber is quite long. We could take a small fridge, and modify it to have an inlet and outlet hole on one wall, through which the majority of the pipe can be put inside the chamber to be cooled thoroughly before it opens inside the chamber. That would minimize air-conditioning costs and even do away with the need for a dedicated room
4. The HBAT room containing the chamber should have a small exhaust fan, with its air inlet opening onto a pipe whose other end is brought down to open in a funnel like

fashion close to the twin exhaust valves of the soft chamber. This will reduce the recirculation of stale air inside the air-conditioned room and chamber and help maintain the CO₂ levels closer to physiologically normal inside the HBAT chamber.

What next?

- How many can afford HBOT at its present cost level even in the economically advanced USA? Not a great many, except in the states where Medicaid has allowed re-imburement as a follow up of the Steele child court case in Georgia in 2006.
- Now think how many can afford costly regular HBOT in India and other similar not so developed countries which do not have any reimbursement for “experimental HBOT” in CP children? The soft chambers are “Not ASME-PVHO” compliant.
- Do we tell them: “Either go in for regular HBOT only, or Get Lost?”
- We need the option of an economical monoplace HBAT chamber that can deliver 1.3 ATA room air at an economical rate, which can run even on a small Electrical generator (because electricity load-shedding is endemic in countries like ours) with a dehumidifier AND an air cooling device INLINE.
- Such an equipment, used by trained personnel under medical supervision, in properly investigated, selected and adequately followed up cases, should not need permission from Dept. of Explosives, Dept. of Drugs and the Fire Safety guys because NO FIRE-SAFETY NORMS ARE VIOLATED AND NO EXPLOSIVE OXYGEN IS USED.
- The pressure used in such low pressure chambers is less than the pressure differences experienced in any commercial airline (0.5 ATA down when ascending and the same up while descending to land). The pressure increase is equal to that experienced when diving into a standard swimming pool to a depth of only 10 feet or 3 meters.

Our Dilemma

What pressure do we recommend to a particular child? That is a hard decision we must take, especially as the much more affordable 1.3 ATA gives statistically similar benefit at almost half the cost, which many more parents in the less economically affluent segments can afford. We would categorically like to clarify that we are NOT RECOMMENDING any particular chamber, but merely discussing different pressure effects in Indian Children, with their lower body weight and metabolic activity, with our experience limited to regular HBOT at 1.5 ATA and 1.75 ATA, and also at 1.3 ATA inside an OxyHealth soft chamber, with their limitations and benefits, in CP children.

We do not, repeat, DO NOT, advocate the use of 100% Oxygen or an oxygen concentrator with NON-ASME PVHO chambers, as we have no experience with it nor have any plans to do so in future.

The mHBOT data we have shown have been with compressed room air only. In fact, the notice on the side of the chamber clearly states that these chambers are not recommended by their manufacturer to be inflated with Oxygen.

Our position

Our data in 128 CP children treated and followed up for 6-8 month is not enough to make an authoritative recommendation even though our preliminary data suggest that improvements seen with Hyperbaric Therapy in **all it's three tested forms** is very encouraging, and we should continue the study further.

We believe that we require more supportive data to show that the use of 1.3 ATA may be an option to parents who cannot afford the higher cost of 1.5 ATA, to get a fair degree of improvement in the quality of life of their kids. We also need to develop protocols to select the children who would definitely do better on the low-pressure regimen. It is possible that the CP child with greater motor dysfunction will be slightly better off with regular HBOT

while the ones with significant cognitive impairment will do better with low pressure HBAT. Only time will tell us a more definitive answer. Our ongoing research should have more data on this aspect in another 2 to 3 years.

Conclusions

We have carried out an ongoing open non-randomized controlled prospective study of management of CP children with intensive one-to-one standard therapies, supplemented in 60 children with 1.75 ATA HBOT, in 24 CP children with 1.5 ATA HBOT and in 24 CP children with 1.3 ATA HBAT.

The four groups were matching in age, age distribution, sex distribution and initial severity. They were assessed at 4 and 6 months. Most children also had serial video recordings also. All three hyperbaric therapy groups induced significant improvement over the Control group in Cognitive & Speech / Communication parameters within 4 months. The early response as compared to motor response could be due to the shorter intra-cranial axons responsible, which re-myelinate faster after HBOT.

The Cognitive and Speech / Communication skill changes appeared to be permanent during our longer-term follow-up of 6 to 8 months or more.

Improvements in Physical (GMFM) Parameters reach significance after 4th months, though our clinical impression is that it peaks after 6 to 8 months. The greater response time required for clinically significant motor achievements could be due to the longer time needed to remyelinate the long Pyramidal tract from brain to lower spinal motor neurons. The gains in Physical Controls appear to be permanent

Re-spasticity occurs at limbs due to reduced ability of spastic muscles to lengthen on par with normal muscles during bone lengthening as per age related growth. Intensive OT/PT till at least 21 years of age may reduce extent of re-spasticity in those children who are doing it.

We showed at the 5th Symposium on HBOT (Florida) in 2006 that the preferred age for HBOT in CP is 1-4 years, before brain development, dendritic arborization, synaptic development, cerebral sphingomyelin & cholesterol concentrations complete. However, encouraging statistically significant improvements was also seen older children, due to their higher level of understanding, cooperation and self-motivation.

Our data suggests that a minimum of 4 months, preferably 6 months, of follow up is needed to show significant cognitive, and later, motor improvements.

Just as a normal child needs up to 4 years for his full Neuro-development, so does a CP child given HBOT, whose "TIME" starts six months after completing HBOT, when remyelination is complete.

How many HBOTs?

We suggest that parents carry on intermittent HBOT (40 sessions at a time) as long as the GMFM development curve shows significant upward deviation (more than about 1 point per month).

Our Final Conclusion

CP is a multifactorial ischemic brain pathology with motor deficiencies, besides variable degrees of cognitive, sensory, communication and visual deficiencies.

Based on the data we have gathered so far, we feel that in the medical intervention therapy of CP children receiving intensive Standard Therapy with supplemental Hyperbaric Therapy gives a statistically significant benefit as compared to children receiving only similar Standard Therapy.

Also that 1.3 ATA Low pressure Hyperbaric Air Therapy is **Statistically Not Inferior to** Regular HBOT at 1.5 / 1.75 ATA using 100% oxygen.

Further study over the next 2 to 3 years may shed more light on this evidence.