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The effect of hyperbaric oxygen in prolonged coma. Possible identification of marginally functioning brain zones.

ABSTRACT.- The outlook for a patient with vegetative coma is not good,as such patients rarely recover. Positive clinical outcomes from hyperbaric oxygen (HBO) therapy in many acute head injury cases experimentally and clinically led to this trial in 17 vegetative comas due to post-head injury with HBO. The response was significant enough to warrant further study of the use of HBO for this condition. It is felt that the results suggest that HBO identifies marginally functioning zones which may respond to prolonged HBO treatment. The author wishes to express his gratitude to Joseph Gelety, M.D., Center for Neurological Services, Ft.Lauderdale, Florida and to F.W. McGehee, HBO Center of Houston, Houston, Texas for their cooperation in the treatment of certain of these patients and allowing publication of data.

KEY WORDS-Hyperbaric oxygen therapy-Coma-Head injury.

The outlook for a patient with prolonged vegetative state is difficult to determine during the first two weeks following onset of the acute event. After that time, as Posner[1] has noted, if no recovery ensued, the prognosis becomes uniformly poor. Of twenty-four such individuals who survived one month only five were alive at the end of the year; three remained permanently vegetative, and the other two had overwhelming neurological deficits as well as incapacitating mental impairments. Reports of other authors generally indicate similarly poor outlook for patients still in the vegetative state after one month[2]. There is virtually no mention in the literature of any type of therapeutic modality that could be employed to salvage these patients. This report describes treatment with hyperbaric oxygen (HBO) of seventeen such patients previously classified as "hopeless".

Materials and Methods

A.) SUBJECTS: Seventeen closed head injury patients in prolonged coma were randomly selected to receive HBO treatment, (See Table 1). The ages ranged from four (4) to sixty-three (63) years, mean 23, with 10 males and 7 females. Table one indicates the interval from onset of coma to the initial HBO treatment with a range from one month, eleven days, to twenty-two months, twenty-four days, the average being seven months thir teen days. All patients had at least one CT scan and one

Table one. - *Summary of clinical date*

Case	Age	Interval from coma to study	Diagnosis	Status at time of study
1	63	1mo. 26days	L. Subdural Hematoma	Akinetic mutism
2	4	18 mos. 6 days	L. Ventricular Bleeding	Akinetic mutism
3	8	1 mo. 11days	R. Parietal Contusion	Akinetic mutism
4	7	10 mos. 11days	R. Subdural Posterior Parietal Hematoma	Akinetic mutism
5	10	22 mos. 24days	Linear Fracture of Occipital Region with Extension to Foramen of Magnum	Vigil Coma
6	18	4 mos. 12days	Brain Stem Injury	Akinetic Mutism
7	21	2 mos. 27days	Cerebral Contusion, Intracerebral hemorrhage	Vigil Coma
8	25	11 mos.	Intracerebral and Ventricular bleeding	Moderate Com
9	29	13 mos. 26days	Fracture L. Temporoparietal bone	Vigil Coma
10	23	2 mos. 26days	Brain Stem Injury; Left Subdural Hematoma	Akinetic Mutism
11	24	1 mo. 25days	Brain Stem Contusion	Vigil Coma
12	21	16mos.	Brain Stem Injury	Vigil Coma
13	35	9weeks	Cerebral Contusion	Akinetic Mutism
14	26	60days	Brain Stem Hemorrhage	Vigil Coma
15	19	58days	Brain Stem Contusion	Akinetic Mutism
16	18	6mos.	Cerebral Contusion	Akinetic Mutism
17	22	55days	Subdural Hematoma, Left Frontal Parietal	Akinetic Mutism

EEG. Those patients whose CT scan showed excessive ventricular enlargement were excluded. All patients had abnormal EEGs but none were flat or completely disorganized. Fourteen patients required respirator care some time after their initial hospitalization. Six patients were diagnosed as brain stem injuries. One patient had a history of seizures and was on medication at the time of the accident.

B.) METHODOLOGY: The patients received from 40 to 120 exposures of HBO in a monoplace chamber over a 20-90 day period. This varied from one to two treatment hours per day at pressures of 1.5-2 ATA.

All patients were administered the Glascow Coma Scale (GCS) pre and post-HBO, the results of which are seen in Table Two.

Case Histories

Case 15: This 19-year-old female received a brain stem injury in an automobile accident. She was comatose with decerebrate posturing. Five days after admission she developed Cheyne-Stoke type respiration and had a tracheotomy. Four months and five days later she was discharged with an N/G tube for feeding and virtually no neurological change. The tracheotomy was removed during the next six days. When she started HBO on the seventh day her eyes were open spontaneously and seeming to focus, her pupils were equal and reactive, and she was decerebrate to pain. Her private duty nurse stated she was able to utter appropriate words at times: i.e. pain, hurt etc. After 60 exposure to HBO she had improvement as listed in Table Three.

Case 17: This 22-year-old female had a head injury on April 24, 1981. She was examined in the emergency room of a hospital and released.There days later she was returned to the hospital in a comatose state with akinetic mutism. The diagnosis at that time was subdural hematoma. A CT scan showed lack of visualization of the ventricular system with a midline shift left to right and evidence to suggest subdural hematoma of the left frontal area of the frontal parietal. An evacuation of the subdural hematoma was performed. Four days later the patient required a tracheotomy. At that time a cerebral angiogram showed an epidural mass inferior to the left parietal lobe flap in a rather semicircular or semi-lunate configuration. A left epidural hematoma evacuation was done. The patient remained in an akinetic mutism state. Two and a half months later a CT scan showed possible left hemispheric infarction, post-surgical skull changes, and no subdural hematoma. The brain density appeared normal except for an equivocal wedge shaped low density in the left parietal lobe area. A portion of this was thought to possibly represent artifact. Fifty-five days after the injury the patient began HBO treatment. After 30 days she was responding to instructions, able to walk a few steps, and showing other improvement. The final results after 100 treatments are shown in Table Three.

Results

There were increasing levels of improvement with continued HBO treatment in most patients. For example during the initial treatment some could follow simple commands, i.e. "close your eyes", which they could not do previously. Subsequent treatment led to responses involving more complex commands, i.e. "say Hi", "stand", "show me five fingers", etc. In most patients improved GCS scores reflected the general level of clinical improvement that was noted. However, in five patients, the coma score remained unchanged or slightly improved, while the patients were felt to be improved from their pre-treatment status. These changes reflected changes of a qualitative nature which did not yield themselves readily to computation on the GCS, i.e. increased levels of total limb movement and further degrees of movement.

It is highly significant that the above documented improvements have persisted over a period of up to four years without lessening. Such continued benefit is in contrast to the treatment benefits noted in acute stroke[3] patients who are being evaluated for EC/IC by-pass surgery with HBO. Very often only transient improvements are seen in this group of patients unless continued treatments are administered[4]. There seems to be a cumulative effect of additional responses with HBO at the appropriate pressures.

No adverse treatment effects from HBO were noted during the treatment. No convulsive seizures were observed due to hyperoxia and no neurobehavioral changes such as Korsakoff syndrome were noted. No deaths were recorded in this group.

While admittedly we believe that the response noted in these patients might be due to "change" for random improvement, we do not feel that such is the case. Given the duration of the comatose state and the rare instances of improvement seen in such patients, we believe that HBO did, in fact, confer these gains.

Discussion

The use of and rationale for HBO in acute cerebral trauma has been well documented in the medical literature[2,3,4,5,6,7,8] and with the exception of the United States is widely used. The metabolic effect of HBO on Lactate, glucose, pH, regional cerebral blood flow studies and other parameters indicate in might be of value in the vegetative coma state[6]. Animal studies have shown that HBO contributes to reduction in mortality, morbidity, neuronal destruction and cerebral edema[2,4].

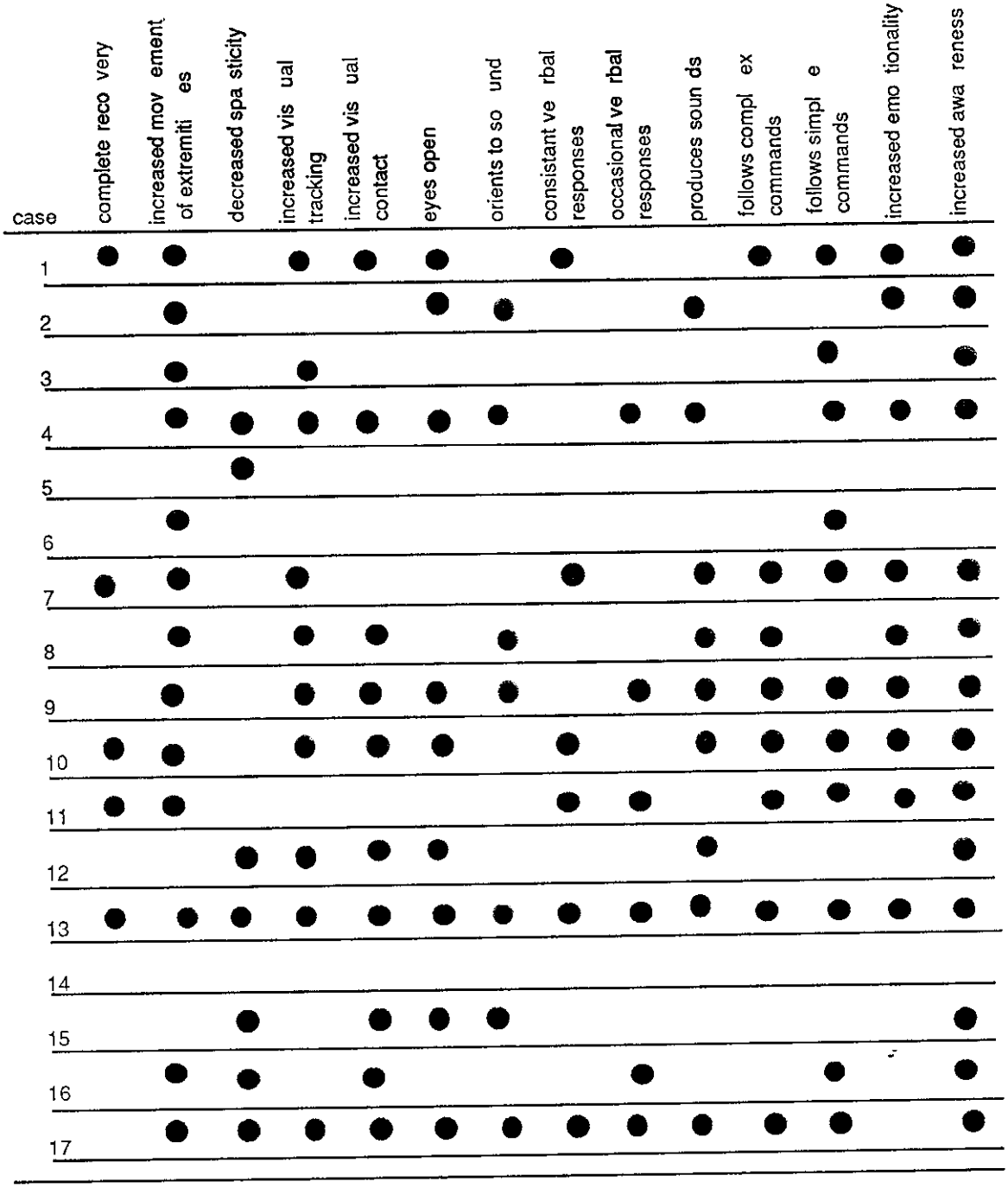
Holbach, Wassmann, and Kolberg, in an extensive controlled study of patients suffering from midbrain syndrome, found that those patients treated with intensive therapy plus HBO displayed substantial improvement both in survival time and rate. They concluded that with the addition of HBO, the syndrome was reversible to a large degree and that a high number of cases obtained a more complete cure. Tischenko[7] reported that the exposure of severely brain damaged patients to HBO resulted not only in a more rapid return to consciusness but an increased clearing of the psychotic state so frequently seen in patients recovering from prolonged coma as well. Further studies by Mogami et al[8]. included somewhat equivocal results in the acute state. While there was clinical, sometimes remarkable, improvement in 50 percent of the sixty-six patients exposed to HBO during treatment, most of these improvements were temporary in nature. A small percentage of these patients did, however, display permanent residual neurologic deficit. Interestingly, this same study also found a slight improvement in lactate pyruvate/ratio in cerebrospinal fluid. This led the authors to suggest that HBO might contribute to the repair of cerebral damage.

An important consideration in selecting patients for HBO is the question of the actual status of the residual neurons. It is known that the brain requires minimal oxygen and glucose to survive. It is assumed that some oxidative glycolyis is certainly going on even at the comatose level. Yet, the relative degress of oxidative versus anerobic metabolism in prolonged vegetative states and long-standing coma is unknown. The assumption that all brain cells are dead has more or less been disproven by the works of Roski[9], Symon[10] and others. Roski et al reported restoration of vision even seven years after stroke with surgical anastomoses. One could postulate as Symon[10] did that there exists marginal cells or a "penumbra", cells in an environ-

Table Two.- *Summari of Coma Scores*

Case	PreHBO	PostHBO
1	5	15
2	8	11
3	8	11
4	7	12
5	5	7
6	8	11
7	9	15
8	8	12
9	12	13
10	5	12
11	11	15
12	5	9
13	8	14
14	4	4
15	5	9
16	8	11
17	2	12

Table Three.- *Summary of observation*



mental limbo that with proper internal mileau could be restored to some degree of function. This, in fact, constitutes the basis of our decision to treat these patients. It was felt that our results with HBO treatment cited above are consistent with isolating and identifying patients possessing marginal areas of brain function, that is, cells with potential reversibility of brain defect. As of yet it is not feasable to identify these patients by other methods.

Conclusion

In this study each patient served as his own control, and therefore it is not presented as a rigorous double-blind evaluation, but as an observation of lightenening of coma with exposure to HBO in patients who do not otherwise usually improve. It was felt that any treatment that would change the degree of coma, or make the patient amenable to rehabilitation would justify further study of the use

of HBO in prolonged coma. While the results of this were rewarding and encouraging, they cannot justufy the use of HBO as a panacea for vegetative coma.
The cases cited do show that HBO identifies potentially treatable marginal surviving brain zones, and along these lines clearly justifies additional investigational studies. Studies involving the use of evoked potential criteria in auditory , visual and somatosensory areas are being undertaken to determine if this might facilitate identification of those patients having marginal surviving neurons.

Riassunto

L'effetto dell'ossigeno iperbarico nel coma prolungato. Possibilità di identificare zone cerebrali marginalmente funzionanti.-
La prognosi di un paziente in coma vegetativo non é favorevole, dato che egli raramente recupera. Esiti clinicamente positivi conseguenti l'impiego dell'ossigenoterapia iperbarica (OTI) in molti casi di trauma cranico acuto rappresentano una prova sperimentale e clinica dei vantaggi di questa terapia in 17 casi di coma vegetativo trattati dall'Autore con (OTI).
La risposta era sufficientemente significativa per utilizzare ulteriori studi sull'uso dell'OTI in questa condizione. I risultati di questo studio sembrano suggerire che l'OTI identifica zone marginalmente funzionanti che possono rispondere a trattamento OTI prolungato.

PAROLA CHIAVE: Ossigenoterapia iperbarica - coma - trauma cranico.

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