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Hyperbaric Oxygenation as a Promising Pharmaceutical in Acute Cortical Hypoxia

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Abstract

Previous attempts to eliminate or correct the ischemic cascade due to acute 02 deprivation have included hypothermia, iv manatol and removable parts of the skull to reduce intra cranial pressure. Very limited success has resulted.

Lack of oxygen rather that of a low blood flow has been shown to be the etiology of the devastating effects of brain hypoxia resultant from three to five minutes of total 02 loss. Usually these changes are irreversible and may be caused by any acute brain insult initiating the ischemic cascade. Cerebral edema, reversal of calcium/potassium intracellular ratio as well as changes the lactic acid/pyruvate ratio along with a multitude of deleterious biochemical changes lead to severe neurologic consequences. High dose oxygen or hyperbaric oxygen adheres to all the gas laws of physics. Under such conditions free molecular oxygen is delivered directly to the cell for immediate metabolic use without energy exchange via tissues that will accept this drug (bone, urine, plasma, lymph and especially cerebral spinal fluid) even with compromised circulation.

Oxygen delivery has been shown to take place in the experimental animal study with total lack of blood yet all organs functioned normally. Documented effects in animal as well as clinical studies in acute ischemic thrombotic stroke, acute mid-brain injury and acute anoxic encephalopathy will be presented. The remarkable pharmacological properties seen with hyperbaric oxygenation alone may also open an avenue to potentiate other drugs especially Tissue Plasminogen Activator in acute stroke.

Introduction

Although gaseous in nature, oxygen used under pressure adheres to all the gas laws of physics. It has very distinct pharmaceutical properties that no other compound posses. O2 is the only reason we are on this planet. Normally when we take a breath we inhale 19-21% of oxygen, the rest being nitrogen and other inert gases. The oxygen immediately attaches to the hemoglobin molecule by way of the lung inspiration. It binds and is transported throughout the blood stream down to the capillary level. An energy laden process takes place delivering free molecular O2, to the cell for metabolism as all life takes place on a cellular level and not in the blood stream. Carbon dioxide is then picked up and exhaled through the lungs.

There has never been a pharmaceutical that will accomplish these outstanding results. The possibility of combining standard pharmaceuticals with hyperbaric oxygenation will open a new field of endeavor. Case reports trickling in from around the world have shown the use of hyperbaric oxygenation with tissue plasminogen (TPA) activator to be extraordinary. This would be very logical in the early stroke since the TPA will partially or fully dissolve the obstruction which would allow a normal amount of oxygen into the insulted area. Under hyperbaric conditions, excess oxygen would be available which would reduce localized cerebral edema and rectify the impending ischemic penumbra and promptly heal the temporarily injured area. Another area would be with intractable infections. As antibiotics are being more and more indiscriminately used, the day is approaching an era when not only resistance will occur but an era through which the organism will thrive upon the antibiotics.

Obviously, any trauma infection or lack of circulation ranging from stroke to gangrene will seriously interfere with the oxygen delivery by way of the blood stream. The tissue becomes hypoxic and may eventually die. This may happen suddenly or gradually with the phenomenon called apoptysis. The late Edward Teller PHD, the father of the hydrogen bomb one of the two geniuses of this century was a ten year patient and friend of Dr. Neubauer. He was one of Dr. Neubauer's greatest supporters to substantiate the use of high dose oxygen in the treatment of hypoxic areas in the body with particular reference to neurology. Dr. Teller received three thousand hyperbaric oxygenation treatments in a mono-placed chamber over a ten year period. Prior to his demise he functioned on a genius level until two days before his passing. Incidentally at the time the chamber was delivered Dr. Teller's home his wife had severe emphysema was bed ridden, twenty- four oxygen day demented, weighed seventy pounds and was given two months to live by the pulmonologist. No drugs had been effective in her recovery. She was gradually started on small doses of supplemental pressure oxygen and eventually gained thirty-six pounds. Medication then became effective and she had five wonderful years. She did however rely on oxygen as it became her life support. Should the attendant fail to give her one of her two treatments per day she would have wilted.

Since hyperbaric oxygenation enhances phagocytosis increases the immune system, causes neonangiogenesis is a scavenger-free radical and reduces any long term edema, such a combination of hyperbaric oxygen with certain antibiotic resistant

patients could be considered.

In Japan, hyperbaric oxygenation is routinely used in combination with low dose chemotherapy or radiation therapy. The results are greatly enhanced. This presentation is only to suggest a potent amelioration of many standard pharmaceuticals.

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Dr. Edward Teller, who was a Nuclear Physicist, understood well the role and utilization of oxygen. To quote Edward who said that "when oxygen is delivered under hyperbaric conditions, it is delivered to the cell free as molecular oxygen for immediate metabolic use without energy exchange even after compromised circulation". There are well known physiologic properties of oxygen under pressure in the acute and long-term injuries especially neurological but also pertaining to various chronic wounds, neuropathies, long standing bone infections or radiation problems.

There are a multitude of conditions in which hyperbaric oxygenation is effective particularly in multi-dimensional modes. Its uses in acute and long term situations, especially neurologic conditions is presented below.

Effects of Pressurized Oxygen in Acute Brain Insult:
Reduces cerebral edema & ICP
Limits the ischemic cascade
Reduces CNS lactate peak in hypoxia
Neutralizes toxic amines
Deaggragation of platelets
Increases Phagocytic activity of PMN cells (white blood cells)
Reduces Adhesiveness of WBCs to endothelium
Perfuses all tissue spaces
Life sustaining O_2 available via retrograde perfusion in absence of trickle phenomena
Delivers metabolically available O_2 without chemical energy transfer – *Enough to sustain life without blood*
Under pressure O_2 adheres to all the gas laws of physics

Page Three.....

Effects of Pressurized Oxygen in Acute Brain Insult(cont'd):

Displaces all other gases in the body:
N_2, CO
Follows the Law of Mass Action
Completely saturates hemoglobin
Increases plasma O_2 by 2000%
Dissolves in cerebrospinal fluid, lymph, bone and urine

Effects of Pressurized Oxygen in Long Term Brain Insults:
Reactivates idling neurons
Enhances plasticity
Efficiently elevates diffusional driving force for O_2 thereby increasing tissue oxygen availability
Promotes phagocytosis (internal debridement)
Ameliorates multiple biochemical changes
Restores the integrity of the blood brain barrier and cell membranes
Improves cell respiration, Reduces cell byproducts – cytokines
Promotes Neovascularization
Promotes Epithelization
Acts as scavenger of free radicals
Bacteriostatic effects, synergizes with certain antibiotics
Neutralizes certain Toxins: Clostridium, anaerobes
Stimulates the adaptive immune system, especially in elderly (mice)

There are 3 types of chambers:
The multi-place chamber will hold between 4 and 20 patients. This is pressured with air and the oxygen is delivered by way of mask or hood. These are effective but not as accurate as the next type of chamber which is the monoplace. This is an acrylic cylinder with full visibility and compressed with 100% oxygen. The third type entering the market is the portable Kevlar collapsible chamber capable at 1.35 ATA of air. The 02 may be increased within with a concentrator or with an E type of tank and mask. This has been approved only for high altitude sickness but certain remarkable results have been shown in CP, the brain-injured child, cosmetic surgery and long-term stroke. This is an extremely economical way and may be an interesting approach to the potentiation of pharmaceuticals.

Hyperbaric oxygenation alone is a multi plural potent pharmaceutical. It has many positive effects in salvation of life and is used extensively in decompression, carbon monoxide intoxication and various areas of wound care including osteomylitis and radiation damage. Newer aspects of its use are in the field of neurology both the acute stroke, traumatic brain injury, anoxic ischemic encephalopathy. The profound effects of this drug alone have been mentioned. The possibility of enhancing other pharmaceuticals is strongly suggested from the text.

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Hyperbaric Oxygenation as a promising pharmaceutical in acute cortical hypoxia

Franz Gerstenbrand M.D., Richard Neubauer M.D.

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Why Are We Here?

Oxygen!

Oxygen is the only reason we are on this planet

- Our environment is 19 – 21% Oxygen
- Lack of Oxygen for 3 to 5 minutes causes deleterious effects
- Pressurized Oxygen has physiological properties unmatched by any drug

Hyperbaric Oxygen Therapy is the use of 100% Oxygen at greater than atmospheric pressure

Pressurized O_2 adheres to all gas laws of physics

Henry's Law states there is a direct relationship between pressure and the amount of gas dissolved in solutes

Oxygen is a Pluripotent Drug Unmatched by any Pharmaceutical

Under pressure free molecular oxygen is delivered directly to the cell for immediate metabolic use without energy exchange even with compromised circulation.

Edward Teller, Ph.D.

Life Without Blood

A Major Breakthrough

Boerema I
J Cardiovasc Surg 1960;
133-146.

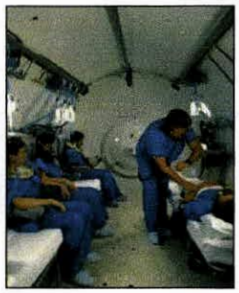
Pressurized Oxygen is a Drug With a Specific Dose for Each Diagnosis

- **Dose Equals**
  - **–Depth of Pressure**
  - **–Time (length) of Exposure**
  - **–Frequency**
  - **–Total Number of Treatments**

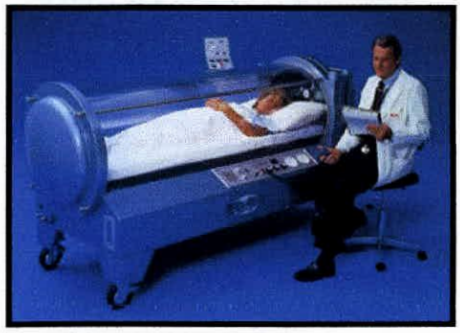
How Administered - Pressure Vessel

- **Multiplace Chamber**
- **Monoplace Chamber**
- **Low Pressure Portable Chamber**

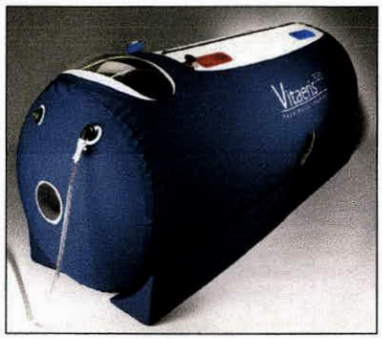
Multiplace Chamber



Monoplace Chamber



Low Pressure Chamber



Immediate Effects of HBOT

- Under pressure O_2 adheres to all the gas laws of physics
- Follows the Law of Mass Action
- Reduces cerebral edema & ICP
- Limits the ischemic cascade
- Reduces CNS lactate peak in hypoxia

Immediate Effects of HBOT

- Increases plasma O_2 by 2000%
- Dissolves in cerebrospinal fluid, lymph, bone and urine
- Life sustaining O_2 available via retrograde perfusion in absence of a trickle phenomena
- Delivers metabolically available O_2 without chemical energy transfer – *Enough to sustain life without blood*

Immediate Effects of HBOT

- Perfuses all tissue spaces
- Reduces Adhesiveness of WBCs to endothelium
- Neutralizes toxic amines
- Deaggragation of platelets
- Increases Phagocytic activity of PMN cells (white blood cells)

Long Term Effects of HBOT

- Reactivates idling neurons
- Enhances plasticity
- Efficiently elevates diffusional driving force for O_2 thereby increasing tissue oxygen availability
- Restores the integrity of the blood brain barrier and cell membranes

Long Term Effects of HBOT

- Improves cell respiration, Reduces cell byproducts – cytokines
- Promotes phagocytosis (internal debridement)
- Promotes Neovascularization
- Promotes Epithelization
- Acts as scavenger of free radicals

Long Term Effects of HBOT

- Bacteriostatic effects, synergizes with certain antibiotics
- Neutralizes certain Toxins: Clostridium, anaerobes
- Stimulates the adaptive immune system, especially in elderly (mice)
- Ameliorates multiple biochemical changes

If HBOT is so beneficial why is it not in general use?

- Lack of Knowledge
  - Not Taught in Medical School
- Lack of Facilities
- Expense
  - Nothing to be Patented

Would HBOT be worthy of consideration If a less expensive & more readily available delivery system were available to enhance current and future pharmaceuticals?

What is Needed?

- Basic research on humans
  - Extensive animal work in the literature
- Education
- Less expensive methodology
  - Portable inflatable chamber

The portable chamber is FDA approved to 1.3 ATA, thereby raising the inspired oxygen availability from 19% to 27%

HBOT may enhance the effectiveness of certain drugs & extend the longevity of the product

Results to Date

Synergizes with Various Antimicrobial Agents

- Aminoglycosides
- Sulfa
  - —Converts Bacteriostatic to Bactericidal
- INH - Isonicotinic Acid Hydrazide
- PAS – Para-Aminosalicylic Acid

HBOT currently used in combination with drugs

- Mexico & S. Africa – Stroke treated with TPA & HBOT - *Exceptional Results*
- Worldwide – CROM treated with HBOT & antibiotics

HBOT currently used in combination with drugs

- Japan, Mexico & S. America
  - —Cancer treated with Low dose Radiation, Chemo, Antibiotics & HBOT
- Anecdotal Reports – Cellulitis to Meningitis

Other Pharmaceutical Enhancements

Previous data has shown that photodynamics with vitamin C enhance its tumor killing ability and heating of blood has been tried with some positive results

Current Applications in Neurology

- TBI
- Stroke
- AIE
- Small Vessel Disease

Current Applications in Neurology

- Cranial Nerves 1-5-7-8-12
- MS
- Mitochondrial Disorders
- Parkinson's Disease

What is Needed?
(for severe cases only)

- Smaller portable
- Less Expensive
- Cost Effective
- Hyperbaric Air & Oxygen Chambers

Exceptional Clinical Experience

Edward Teller
1908 - 2003
"Father of the H Bomb"
Had over 3000 consecutive HBO Treatments 1 Hour @ 1.25 – 1.5ATA

Edward Teller, PhD
1905 – 2003
Father of the Hydrogen Bomb

- DX: Cardiovascular, small vessel disease
- Multiple medications
  - Coumadin
  - Coreg
  - Lasix
  - Proscar

Example: M. Teller

- Age: 77
- DX: COPD
- Bedridden, Demented
- Surface O_2 24 Hours
- Pulmonologist prognosis 2 Months
- Medication Refractive

Results with HBOT 2/ Day

- Lived an Additional 5 Years
- Normal Life
- Mentally Alert
- Weight Gain
- All Medications Effective

This is the first scientific suggestion that a drug may be enhanced with a change in atmospheric pressure and oxygen tension

"Here is Better than the Open Air : Take it Thankfully"

William Shakespeare
King Lear iii.6.1
1564 - 1616