Symposium on HYPERBARIC MEDICINE

Effects of Hyperbaric Oxygen on Anaerobic Organisms

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On the basis of their gaseous requirements, bacteria are divided into aerobes, obligate anaerobes and facultative anaerobes. The distinction lies chiefly in the response of the organism to molecular oxygen and carbondioxide. Dependence upon oxygen is due to the presence of cytochrome oxidase systems which provide a great part of the cell's ATP by ultimate reduction of molecular oxygen to water. Anaerobes are distinguished by their need for the exclusion of molecular oxygen from the growth medium. Probably, oxygen is toxic to these organisms because it is reduced by their flavoproteins to hydrogen peroxide which is toxic.

It is generally assumed that growth of anaerobe is facilitated by the lowering of the O - R potential in foci of necrosis produced by bacterial toxins, simple chemicals or by interruption of blood supply due to pressure and trauma. Concomitant secondarily infecting organisms, whether aerobes, or anaerobes induce similar changes in the O-R potential due to local proliferation or by destroying host tissue. Whatever be the reason the simple logic of providing oxygen in its hyperbaric state in cases of anaerobic infections has given fruitful results. Efficiency of treatment with hyperbaric oxygen has been demonstrated against clostridial infection specially those of gas gangrene and tetanus.

While noticing the inhibitory effect of HBO on anaerobic organisms, the question arose as to what would be the effect of hyperbaric oxygen on aerobic organisms. As early as 1878, Bert[3] had described the toxic effects of HBO on most of the living things including bacteria and yeasts. First clinical application was made in 1887 when a Spanish physician successfully used oxygen at pressure of 2 atmospheres in treating a youngman with pneumonia. Later, Bean[1] also cited several reports of its antimicrobial powers. Mc Allister and his colleagues[17] subjected strains of Pseudomonas pyocyanea, Staphylococcus aureus, Streptococci, Escherichia and Proteus organisms to oxygen at 1 atm and 2 atm and observed that the results varied with different microorganisms though Ps. pyocyanea, Staph. aureus and Escherichia coli were most affected. These appeared to be permanently altered by their exposure to HBO and failed to attain the appearance of the controls. HBO is bacteriostatic rather than cidal No significant change in antibiotic sensitivity pattern was observed. Similar observations were made by Hopkinson and Towers[13]

Ross and Mc Allister[20] investigated the possibility of producing significant aerobic bacterial inhibition in acutely infected animals without incurring the risk of oxygen poisoning Basically, the experiment demonstrated that working within the limits imposed by oxygen toxicity, HBO can exert a protective effect on the infected host provided the organism is sensitive to HBO and infection is located at a site where 2 atm of oxygen is attainable. In this study, the toxic effects of infection were due to direct bacterial invasion of blood and beneficial effects were explained from a direct contact between intravascular bacteria and high arterial oxygen tension.

Schreiner[21] studied the effect of HBO on antibiotic sensitivity of Staphylococcus. Out of a

large number of antibiotics used, penicillin and furadantin showed maximum response where sensitivity of organisms, as determined by conventional disc method, was greatly enhanced under HBO. However, minimum effective dose of penicillin in liquid culture, gave no indication of being effected. It was suggested that growth retardation by antibiotic is additive to but not potentiated by the bacteriostatic action of HBO. Bornside[3,4] and Brown et al[6,7] have conducted extensive studies on this problem and showed enhancement of activity of antibiotics like polymixin B against Ps. aeruginosa under HBO. Bornside and Nance[5] again showed augmentation of effect in experimental burns. However, hope of finding a good adjunct to treatment of aerobic infections in the form of HBO received a set back when it was postulated that unknown pathogenic nature of aerobic bacteria may be produced by this exposure that enhanced mortality rate[22,23]. Irvin et al[13,15] showed that response of broth cultures of Staph. aureus was dependent upon the depth of medium and, though a bactetiostatic effect was produced, a high proportion of organisms survived prolonged exposure. In vivo studies on animals infected with various bacteria showed no inhibition of organisms when treated with HBO[16]. The logical therapeutic applications thus appeared to be in the local treatmant of superficial infections[8] only. Clinical experience on the subject was limited. Sjack et al[25] reported 5 cases of osteomyelitis treated successfully with HBO. Perrins[19] also reported similar beneficial effects in 24 cases of osteomyelitis. Goulon et al[11] treated 5 cases of suppurative pseudo arthrosis but Meijne[18] did not get encouraging results with his cases. Progressive cutaneous gangrene, when treated with HBO, yielded the best results. Reduction in secondary wound infections has been observed in burn patients treated with HBO[14].

So far, most of the vitro experiments on bacterial cultures were done by exposure to prolonged and continuous HBO, the duration and intensity of such exposures far exceeding those which are therapeutically attainable. Brown et al[7] studied Staph. aureus and Ps. aeruginosa by exposing them for 60 minutes to 2 atm at 8 hourly intervals and observed that no morphological or culture variations occurred and that the effect of antibiotics used was unaltered under HBO.

We are, therefore, confronted with 2 relatively controversial situations, i.e.,

a) though prolonged exposures to HBO inhibit bacterial growth and alter their antibiotic sensitivity pattern the effects are negligible with short duration exposures,

b) irrespective of controversial results of 'in vitro' studies, therapeutic response of experimental animals/patients suffering from infections by aerobic organisms is always good when HBO is used as adjuvant to conventional treatment.

A possible mechanism for alteration in bacterial growth is the formation of superoxide ion inducing oxygen toxicity in bacteria[9,10]. Exposure to HBO increases intracellular super oxide dismutase causing an increased resistance of bacteria, and results in an increased resistance of bacteria to the lethal effects of HBO. Crucial factor is the actual oxygen tension reaching the bacteria which will be different in various situations. A more thorough study of this problem may give us certain ready-made profiles based upon which HBO treatment and simultaneous use of antibiotics in infection with different organisms can be attempted.

References

1. Bean, JW. Oxygen poisoning in micro organisms and its relation to the toxicity of oxygen at high pressure on mammalian tissue. J. Cell Comp. Physiol. 17 : 277, 1941 cited by Meijne, N.G. 1970.

2. Bert, P. La pression borometrique, recharches de experimentale. Paris. G. Masson. pp 867. 1878 cited by Meijne N. G. 1970.

3. Bornside, G.H. Exposure of Pseudomonas aeruginosa to hyperbaric oxygen : Inhibited growth and enhanced activity of polimixin S. Proc Soc, Exptl. Biol. Med., 125 : 1162, 1967.

4. Bornside, G. H. Enhancement of antibiotic activity against staphylococcus aureus by exposure to hyperbaric oxygen. Appl. Microbiol. 15 : 1020, 1967.

5. Bornside, G.H. and Nance, F.C. High pressure oxygen combined with antibiotics in the therapy of experimental burn wounds. In Antimicrobial Agents and Chemotherapy (Ed) G.L. Hobby. Bethesda. Md Am Soc. Microbiol, pp 497 - 500, 1968.

6. Brown , O R., Silverberg, R.G. and Huggett, D O. Synergism between hyper oxia and antibiotics for Pseudomonas aeruginosa. Appl. Microbiol. 15 : 260, 1969.

7. Brown, G. L., Thomson, P. D., Mader J.T , Hilten, J. G. Browne, M. E. and Wells, C. H. Effects of hyperbaric Oxygen upon S. Aureus, Ps. Aeruginosa and C. albicans. Aviat. Space Environ Med. 50 (7) : 717, 1979.

8. Brummelcamp. W. H. Hyperbaric oxygen therapy in recurrent progressive cutaneous gangrene in female patients. In Hyperbaric Medicine. Proceedings of the Third International Conference on Hyperbaric Medicine (Eds) I. Brown and B. Cox. Washington National Academy of of Sciences, 501, 1966.

9. Fridovich, I. The biology of oxygen radicals. Science. 201 : 875, 1978.

10. Gregory, G.M. and Fridovich, I. Induction of superoxide dismutase by molecular oxygen. J. Bacteriology. 114 : 543, 1973.

11. Goulon, M., Rapin, M., Lotournel, E., and Barois, A. Five cases of suppurative pseudarthrosis (Osteomyelitis) treated by hyperbaric oxygenation. In Proceedings of the Third International Conference on Hyperbaric Medicine (Eds.) I. Brown and B. Cox. Washington National Academy of Sciences. 565, 1966.

12. Grogan, J.B. The effect of hyperbaric oxygen on experimental infections. Arch. Surg. 92 : 740, 1966.

13. Hopkinson, W.I., and Towers, A.G. Effects of hyperbaric oxygen on some common pathogenic bacteria. Lancet, 2 : 1361, 1963.

14. Ikeda, K., Ajiki, H., Nagoa, H., Karino, K., and Sugh. S. Experimental and clinical use of hyperbaric oxygen in burns. In Proceedings of the Fourth International Conference on Hyperbaric Medicine (Eds.) J. Wada and T. Dua, Baltimore, Williams and Watkins. pp 377 1979.

15. Irvin T.T., Suwanagul, A., Norman, J.N. and Smith. G. The effect of hyperbaric oxygen on staphylococcus aureus. Surg. Gynae. Obstet. 125 : 1217, 1967.

16. Irvin, T. T. and Smith, G. Treatment of bacterial infections with hyperbaric oxygen. Surgery. 63 : 363, 1968.

17. Mc Allister, T.A., Stark, J M., Norman. J.N., and Ross, R.M. Hyperbaric Oxygen and aerobic micro organisms. Hyperbaric oxygenation. Proceedings of the Second International Congress. (Ed.) Iain Mc A. Ledingham, Pub. E & S Livingstone, Edinbergh pp 250-256, 1965.

18. Meijne, N.G. Hyperbaric Oxygen and its clinical value Pub. Charles C. Thomas. Springfield, Illinois, USA., pp 190-193, 1970.

19. Perrins, D.J.D., Mandsly, R.H. and Col. Will. M.R. OHP in the management of chronic osteomyelitis. In Proceedings of the Third International Conference on Hyperbaric Medicine (Eds.) I. Brown and B. Cox. Washington National Academy of Sciences, p 578, 1966.

20. Ross, R.M., and Mc Allister, T.A. Treatment of experimental bacterial infection with hyperbaric oxygen. Hyperbaric oxygenation. Proceedings of the Second International Congress. (Ed.) Iain Mc A Ledingham. Pub. E & S. Livingstone, Edinbergh. pp 257-262, 1965.

21. Schreiner, H.R. Quantitative evaluation of effects of hyperbaric oxygen and antibiotic drugs on staphylococcus. In : Hyperbaric oxygenation. Ledingham. I. Mc A. (Ed). Edinburgh and London, E & S Livingstone, p 267, 1965.

22. Slack, W.K, Thomas, D. A., Honson, G. C., Chou, H, Mandaly. E., and Colwell, M. Hyperbaric oxygen in Infection. In Proceedings of the Third International Conference on Hyperbaric Medicine (Eds.) I. Brown and B. Cox Washington. National Academy of Sciences 521, 1966.

23. Stark J. M , and Orr J. S. Letter to Editor, Lancet. 2 : 106, 1965.