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A prospective, randomized Phase II clinical trial to evaluate the effect of combined hyperbaric and normobaric hyperoxia on cerebral metabolism, intracranial pressure, oxygen toxicity, and clinical outcome in severe traumatic brain injury.

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Abstract

Object Preclinical and clinical investigations indicate that the positive effect of hyperbaric oxygen (HBO_2) for severe traumatic brain injury (TBI) occurs after rather than during treatment. The brain appears better able to use baseline O_2 levels following HBO_2 treatments. In this study, the authors evaluate the combination of HBO_2 and normobaric hyperoxia (NBH) as a single treatment. Methods Forty-two patients who sustained severe TBI (mean Glasgow Coma Scale [GCS] score 5.7) were prospectively randomized within 24 hours of injury to either: 1) combined HBO_2/NBH (60 minutes of HBO_2 at 1.5 atmospheres absolute [ATA] followed by NBH, 3 hours of 100% fraction of inspired oxygen [FiO_2] at 1.0 ATA) or 2) control, standard care. Treatments occurred once every 24 hours for 3 consecutive days. Intracranial pressure, surrogate markers for cerebral metabolism, and O_2 toxicity were monitored. Clinical outcome was assessed at 6 months using the sliding dichotomized Glasgow Outcome Scale (GOS) score. Mixed-effects linear modeling was used to statistically test differences between the treatment and control groups. Functional outcome and mortality rates were compared using chi-square tests. Results There were no significant differences in demographic characteristics between the 2 groups. In comparison with values in the control group, brain tissue partial pressure of O_2 (PO_2) levels were significantly increased during and following combined HBO_2/NBH treatments in both the noninjured and pericontusional brain ($p < 0.0001$). Microdialysate lactate/pyruvate ratios were significantly decreased in the noninjured brain in the combined HBO_2/NBH group as compared with controls ($p < 0.0078$). The combined HBO_2/NBH group's intracranial pressure values were significantly lower than those of the control group during treatment, and the improvement continued until the next treatment session ($p < 0.0006$). The combined HBO_2/NBH group's levels of microdialysate glycerol were significantly lower than those of the control group in both noninjured and pericontusional brain ($p < 0.001$). The combined HBO_2/NBH group's level of CSF F2-isoprostane was decreased at 6 hours after treatment as compared with that of controls, but the difference did not quite reach statistical significance ($p = 0.0692$). There was an absolute 26% reduction in mortality for the combined HBO_2/NBH group ($p = 0.048$) and an absolute 36% improvement in favorable outcome using the sliding dichotomized GOS ($p = 0.024$) as compared with the control group. Conclusions In this Phase II clinical trial, in comparison with standard care (control treatment) combined HBO_2/NBH treatments significantly improved markers of oxidative metabolism in relatively uninjured brain as well as pericontusional tissue, reduced intracranial hypertension, and demonstrated improvement in markers of cerebral toxicity. There was significant reduction in mortality and improved favorable outcome as measured by GOS. The combination of HBO_2 and NBH therapy appears to have potential therapeutic efficacy as compared with the 2 treatments in isolation. Clinical trial registration no.: NCT00170352 (ClinicalTrials.gov).

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