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Editors' Note: In "Hyperbaric oxygen: B-level evidence in mild traumatic brain injury clinical trials," Drs. Figueroa and Wright reviewed published clinical trials on the effect of hyperbaric oxygen therapy (HBOT) on mild to moderate traumatic brain injury/persistent postconcussion syndrome (mTBI/PPCS) and concluded that HBOT has therapeutic effects on mTBI/PPCS symptoms and can alleviate posttraumatic stress disorder symptoms secondary to a brain injury. Challenging the review, Drs. Hampson and Holm critique the claim that oxygen content of arterial blood plasma (oxygen dissolved in plasma) during hyperbaric exposure correlates with treatment response. They point out that arterial blood plasma oxygen content was not measured in any of the studies reviewed and that the authors presumably estimated the arterial blood partial pressure of oxygen from the calculated alveolar PO_2 using the alveolar gas equation and assumed that the participants had normal metabolism and pulmonary. They also suggest that the authors did not take into consideration the fact that the studies used different treatment times and numbers. Drs. Figueroa and Wright agree that PaO_2 was not measured in the published studies but assumed that study participants had normal metabolism and pulmonary function since they were cleared to be placed inside a pressure vessel. They also address the difference in time to HBOT exposure and stress that pressurized air is a biologically active agent, rendering the conclusions of inactivity or placebo effect in HBOT/TBI studies questionable. In the study "Autopsy validation of ^{123}I-FP-CIT dopaminergic neuroimaging for the diagnosis of DLB," Thomas et al. showed that ^{123}I-FP-CIT imaging in dementia is a valid and accurate biomarker for dementia with Lewy bodies (DLB) and that the high specificity compared with clinical diagnosis (20% higher) is clinically important. They also concluded that while an abnormal ^{123}I-FP-CIT scan strongly supports Lewy body disease, a normal scan does not exclude DLB with minimal brainstem involvement. Commenting on the study, Professor Abe notes that there are some patients with cognitive and behavioral dysfunction, but without parkinsonism for years. In such situations, he says that he cannot diagnose patients with DLB. In response, Thomas et al. clarify that about 25% of patients with DLB do not show features of parkinsonism. This is recognized in the consensus criteria for DLB, which do not require parkinsonism for diagnosis. They emphasize that DLB can be recognized despite a normal dopaminergic scan if other characteristic symptoms of DLB are present.

—Chafic Karam, MD, and Robert C. Griggs, MD

LETTER RE: HYPERBARIC OXYGEN: B-LEVEL EVIDENCE IN MILD TRAUMATIC BRAIN INJURY CLINICAL TRIALS

Neil B. Hampson, James Holm, Seattle: In their article, Drs. Figueroa and Wright[1] reported a reanalysis of hyperbaric oxygen's effect on mild traumatic brain injury and claimed that oxygen content of arterial blood plasma (oxygen dissolved in plasma) during hyperbaric exposure correlates with treatment response.

Arterial blood plasma oxygen content was not measured in any of the studies reviewed. The authors provided no details in the Methods, but undoubtedly estimated it from arterial blood partial pressure of oxygen (PaO_2, in mm Hg oxygen) by multiplying PaO_2 by the coefficient 0.0031 mL/mm Hg oxygen/dL. However, PaO_2 during hyperbaric exposure was not measured in the studies. It was presumably estimated from the calculated alveolar PO_2 using the alveolar gas equation and making the assumptions that these patients had normal metabolism (respiratory quotient) and pulmonary function (alveolar to arterial oxygen difference).

Not only were the authors attempting to correlate the response to a value several estimates or assumptions beyond anything actually measured, they ignored the fact that the studies used different treatment times and numbers. If total oxygen dose administered was calculated (partial pressure of oxygen breathed × minutes of hyperbaric exposure × treatment number), it would not correlate in any meaningful way with clinical response in the reported studies.

1. Figueroa XA, Wright JK. Hyperbaric oxygen: B-level evidence in mild traumatic brain injury clinical trials. Neurology 2016; 87:1400–1406.

AUTHOR RESPONSE: HYPERBARIC OXYGEN: B-LEVEL EVIDENCE IN MILD TRAUMATIC BRAIN INJURY CLINICAL TRIALS

Xavier A. Figueroa, Seattle; James K. Wright, Port Townsend, WA: We thank Drs. Hampson and Holm for commenting on our Views & Reviews article.[1] It is true that PaO2 was not measured in the published studies and assumptions were made regarding normal metabolism and pulmonary function of the study participants. This was a valid assumption, as all participants were cleared to be placed inside a pressure vessel and not excluded due to pulmonary or metabolic dysfunctions.

Drs. Hampson and Holm point out an important issue raised by other researchers, including Wolf et al.[2]:

"partial pressure of oxygen breathed × minutes in hyperbaric exposure × number of treatments" may turn out to be a more accurate measure of the effects of hyperbaria on total improvement. However, the effects of pressurized air, even accounting for the difference in time (300 minutes more in the Wolf et al. study vs all other studies compared),[1] demonstrate an improvement that is greater than pressurized pure oxygen for RPQ values. The effect does not vanish, although it is reduced, when total exposure time is included. The correlation is valid. The pertinent point is that pressurized air is a biologically active agent, rendering the conclusions of inactivity or placebo effect in hyperbaric oxygen therapy/traumatic brain injury studies questionable.

1. Figueroa XA, Wright JK. Hyperbaric oxygen: B-level evidence in mild traumatic brain injury clinical trials. Neurology 2016;87:1400–1406.
2. Wolf EG, Baugh LM, Kabban CM, Richards MP, Prye J. Cognitive function in a traumatic brain injury hyperbaric oxygen randomized trial. Undersea Hyperb Med 2015;42:313–332.

LETTER RE: AUTOPSY VALIDATION OF ^{123}I-FP-CIT DOPAMINERGIC NEUROIMAGING FOR THE DIAGNOSIS OF DLB

Kazuo Abe, Nishinomiya, Japan: The article by Thomas et al.[1] validated ^{123}I-FP-CIT dopaminergic neuroimaging for the diagnosis of autopsy-proven dementia with Lewy bodies (DLB). The authors depicted 3 patients with DLB who met pathologic criteria for Lewy body disease but had normal ^{123}I-FP-CIT imaging.[1] Although further description concerning severity of parkinsonism remains unclear, these patients may not have severe parkinsonism. Thus, the patients' dopaminergic neuroimaging may not be included in scans without evidence of dopaminergic deficit.

The diagnostic criteria by the Consortium on DLB seemed to weight existence of parkinsonism.[2] They defined DLB as a clinically defined syndrome consisting of a primary dementia characterized by visuoperceptual and executive dysfunction accompanied by prominent visual hallucinations, fluctuating attention, and parkinsonism.[3] However, in daily practice, we encounter patients with cognitive and behavioral dysfunction, but without parkinsonism for years. In such situations, we cannot diagnose patients with DLB. A certain percentage of patients have Lewy bodies only in the cerebrum, not in the brainstem. For accurate diagnosis of DLB, patients should be studied from psychiatric as well as neurologic viewpoints. Thomas et al.[1] suggested a future direction of clinical study for DLB.

1. Thomas AJ, Attems J, Colloby SJ, et al. Autopsy validation of ^{123}I-FP-CIT dopaminergic neuroimaging for the diagnosis of DLB. Neurology 2017;88:276–283.
2. McKeith IG, Dickson DW, Lowe J, et al; Consortium on DLB. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. Neurology 2005;65:1863–1872.
3. McKeith I. Dementia with Lewy bodies and Parkinson's disease with dementia: where two worlds collide. Pract Neurol 2007;7:374–382.

AUTHOR RESPONSE: AUTOPSY VALIDATION OF ^{123}I-FP-CIT DOPAMINERGIC NEUROIMAGING FOR THE DIAGNOSIS OF DLB

Alan J. Thomas, Johannes Attems, Sean J. Colloby, Newcastle Upon Tyne; John T. O'Brien, Cambridge; Ian McKeith, Newcastle Upon Tyne; Rodney Walker, London; Lean Lee, Epping; David Burn, Debra J. Lett, Newcastle Upon Tyne; Zuzana Walker, Epping, UK: Professor Abe raises the important issue of the involvement of Lewy body disease in the substantia nigra (SN) when making the diagnosis of dementia with Lewy bodies (DLB). It has long been known that, even later on in their illness, about 25% of patients with DLB do not show features of parkinsonism. This is recognized in the consensus criteria for DLB, which do not require parkinsonism for diagnosis. Patients with DLB can have normal dopaminergic imaging because, as with our 3 patients who also had no parkinsonism,[1] there is no significant involvement of the SN by Lewy body disease.

Importantly, abnormal dopaminergic imaging is only related to reduced number of SN neurons but not to striatal or neocortical Lewy body pathology[2]; hence, normal dopaminergic imaging is not at variance with the presence of high Lewy body pathology in limbic and neocortical areas (i.e., DLB). Clinicians should not rule out DLB as a diagnosis on the basis of a normal dopaminergic scan where other characteristic symptoms of DLB are present.

1. Thomas AJ, Attems J, Colloby SJ, et al. Autopsy validation of ^{123}I-FP-CIT dopaminergic neuroimaging for the diagnosis of DLB. Neurology 2017;88:276–283.
2. Colloby SJ, McParland S, O'Brien JT, Attems J. Neuropathological correlates of dopaminergic imaging in Alzheimer's disease and Lewy body dementias. Brain 2012;135:2798–2808.

Author disclosures are available upon request (journal@neurology.org).

CORRECTIONS

Escalation therapy for multiple sclerosis in Austria: Analysis of gender differences in the nationwide registry

The 2017 AAN Annual Meeting abstract "Escalation therapy for multiple sclerosis in Austria: Analysis of gender differences in the nationwide registry" by A. Karamyan et al.[1] was incorrectly published online after being withdrawn by the authors. The Abstract vendor regrets the error.

REFERENCE

1. Karamyan A, Guger M, Fertl E, Berger T, Sellner J. Escalation therapy for multiple sclerosis in Austria: analysis of gender differences in the nationwide registry. Neurology 2017;88:P2.404. Abstract.

The role of genetics in ethanol-induced cell death in the forebrain and brainstem

The 2017 AAN Annual Meeting abstract "The role of genetics in ethanol-induced cell death in the forebrain and brainstem" by A. Shokoohi et al.[1] was incorrectly published online after being withdrawn by the authors. The Abstract vendor regrets the error.

REFERENCE

1. Shokoohi A, Theberge E, Wu K, Balce K, Hamre K, Goldowitz D. The role of genetics in ethanol-induced cell death in the forebrain and brainstem. Neurology 2017;88:P3.201. Abstract.