CLINICAL PRACTICE

Blood-brain barrier integrity in a zolpidem-responder patient

N E Nyakale, R P Clauss, H W Nel, M M Sathekge

A 27-year-old neurologically disabled but fully conscious male zolpidem-responder patient was investigated for blood-brain barrier (BBB) dysfunction 5 years after a traumatic brain injury. A baseline single-photon emission computed tomography (SPECT) technetium-99m-labelled hexamethylpropylene amine oxime (^{99m}TcHMPAO) brain scan was performed and the patient was administered 10 mg zolpidem daily. The patient was rescanned 2 weeks later when ^{99m}TcHMPAO was injected 1 hour after zolpidem application. SPECT technetium-99m-labelled diethylene-triamine-pentacetic acid (^{99m}TcDTPA) BBB scans were also performed before and after zolpidem treatment. There was decreased uptake of ^{99m}TcHMPAO in the left frontoparietal brain region, left temporal region and left thalamus on baseline scanning; this improved within 1 hour after zolpidem treatment at the follow-up scan. The ^{99m}TcDTPA scan remained within normal limits before and after zolpidem treatment. The patient's neurological disabilities, especially coordination, speech and gait, improved markedly. The Barthel index remained normal, but the Tinetti falls efficacy scale improved from 21/100 to 15/100. The results implied that the underlying cause for the patient's long-term neurological disability and brain suppression was not due to a long-term dysfunctional BBB.

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Studies have documented improvements in brain-damaged patients following zolpidem treatment;[1-3] single-photon emission computed tomography (SPECT) technetium-99m-labelled hexamethylpropylene amine oxime (^{99m}TcHMPAO) brain scans have shown functioning in previously dormant areas of injured brain, sometimes many years post injury.[3] These dormant areas have no typical location, vary from patient to patient and have slow-wave rhythmic electrical activity which desynchronises after zolpidem treatment.[4] Neurotransmitter abnormalities, including γ-aminobutyric acid (GABA) depletion via chronic blood-brain barrier (BBB) dysfunction, have been proposed as the cause for dormancy. Other considerations include leakage into the cerebrospinal fluid or inadequate neurotransmitter production.[2]

We report for the first time a zolpidem-responder patient investigated for chronic BBB dysfunction 5 years after traumatic brain injury. The BBB was investigated using an intravenous hydrophilic radio-tracer – technetium-99m-labelled diethylene-triamine-pentacetic acid (^{99m}TcDTPA) which is kept outside of the brain by a normally functioning BBB, but penetrates it upon disruption following acute traumatic brain injury, stroke, brain tumour or infection.[5]

Case description

A 27-year-old man sustained a left-sided head injury during a car accident in September 2005. Initially comatose, he regained full consciousness after 3 months, but remained neurologically disabled, walking with difficulty and a limp due to severe muscle spasms. He had poor co-ordination, short-term memory impairment, and impaired speech, especially in consonant pronunciation. He had decreased confidence in performing daily activities and withdrew socially.

In February 2011, upon initiation of treatment with 10 mg oral zolpidem daily, the patient's movement, coordination and gait improved markedly. His muscle spasms decreased and only a minimal limp remained. His speech improved, especially in the pronunciation of 's' and 'r'. He became more confident in daily activities and his family reported an increase in his social participation. His Barthel index was normal before and after zolpidem treatment. The patient's Tinetti falls efficacy scale improved from 21/100 to 15/100. On baseline brain SPECT scan prior to zolpidem treatment there was a decreased uptake of ^{99m}TcHMPAO in the left frontoparietal region, left temporal region and left thalamus. Marked improvement within 1 hour after zolpidem treatment was demonstrated at a follow-up scan 2 weeks later (Fig. 1, a and b). Results of the ^{99m}TcDTPA BBB scan remained within normal limits before and after zolpidem treatment

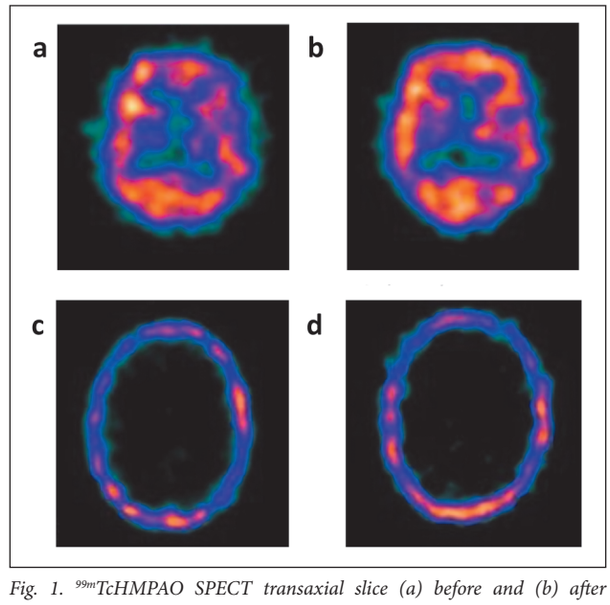

Fig. 1. ^{99m}TcHMPAO SPECT transaxial slice (a) before and (b) after zolpidem, and ^{99m}TcDTPA SPECT transaxial slice (c) before and (d) after zolpidem.

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(Fig. 1, c and d). The baseline ^{99m}TcHMPAO scan showed a focally deficient cerebral blood flow that improved after zolpidem treatment, but the ^{99m}TcDTPA scan remained normal. There was therefore no evidence of a BBB leak in the patient 5 years after brain damage.

Conclusion

This case confirms previous findings of clinical and cerebral blood flow improvements with zolpidem treatment in a patient left neurologically disabled after brain damage. Long-term brain suppression and dormancy, reversible with zolpidem, was not attributed to long-term BBB dysfunction in the patient.

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