Amantadine

Pharmacologic strategies have been advocated to enhance the neurorehabilitation of persons with severe traumatic brain injury. Dopaminergic pathways have been felt to play a significant role in arousal. Employing single case design methodology we present the case of a survivor of severe traumatic brain injury who appeared to have a dose dependent response to the pro-dopaminergic medication amantadine. Further research is necessary to clarify the role of pharmacotherapy in the improvement of functional outcome.

Amantadine acts as a nicotinic receptor antagonist, dopamine receptor agonist and non-competitive N-Methyl-D-aspartate receptor antagonist. Amantadine is a long-known drug, originally approved for treatment of influenza A and Parkinson`s Disease. It has been proven effective in improving vigilance after traumatic brain injury. The underlying mechanisms remain largely unknown, albeit anti-glutamatergic and dopaminergic effects might be most relevant. With limited evidence of amantadine efficacy in non-traumatic pathologies, the aim of our study is to assess the effects of amantadine for neuroenhancement in non-traumatic neurointensive patients with persisting coma.

Methods: An investigator-initiated, monocenter, phase IIb proof of concept open-label pilot study will be carried out. Based on the Simon design, 43 adult (neuro)intensive care patients who meet the clinical criteria of persisting coma not otherwise explained and < 8 points on the Glasgow Coma Scale (GCS) will be recruited. Amantadine will be administered intravenously for five days at a dosage of 100 mg bid. The primary endpoint is an improvement of at least 3 points on the GCS. If participants present as non-responders (increase < 3 points or decrease on the GCS) within the first 48 h, the dosage will be doubled from day three to five. Secondary objectives aim to demonstrate that amantadine improves vigilance via alternative scales. Furthermore, the incidence of adverse events will be investigated and electroencephalography (EEG) will be recorded at baseline and end of treatment.

Discussion: The results of our study will help to systematically assess the clinical utility of amantadine for treatment of persisting coma in non-traumatic brain injury. We expect that, in the face of only moderate treatment risk, a relevant number of patients will benefit from amantadine medication by improved vigilance (GCS increase of at least 3 points) finally leading to a better rehabilitation potential and improved functional neurological outcome. Further, the EEG data will allow evaluation of brain network states in relation to vigilance and potentially outcome prediction in this study cohort.

Trial registration: NCT05479032 [1)]

1)
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