Letter to the Editor

Does Neuroprotection Still Have a Role in Injured Brain Following Aneurysmal Subarachnoid Haemorrhage?

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I read with great interest the study by Akçıl et al. (1), reporting the results of a preliminary study aimed to assess the neuroprotective role of amantadine in neurocognitive function in patients with aneurysmal subarachnoid haemorrhage (SAH). The authors hypothesised that amantadine, a N-methyl-D-aspartate receptor (NMDA) receptor antagonist widely studied in patients with traumatic brain injury (TBI), ameliorates cognitive dysfunction following SAH. In this preliminary study, 12 patients with aneurysmal SAH were included and divided in two groups: group A received amantadine for 30 days after admission along with the standard treatment for SAH, and group C received only the standard treatment. Neurocognitive function was evaluated using the Coma Recovery Scale-Revised and Disability Rating Scale on the first and fifth days and third and sixth months after admission. The primary endpoint was to compare the effects of amantadine in combination with the standard treatment with those of the standard treatment alone on neurocognitive function over 6 months. They found that amantadine administration along with the standard treatment improved the recovery compared with the standard treatment alone.

The authors should be complimented for highlighting the neuroprotective role of amantadine in SAH. Neuroprotection has been considered for many years as an alternative strategy to limit the extent of irreversible damage to neuronal cells after brain injury, including aneurysmal SAH (2). Neuroprotectants disrupt the cellular, biochemical and metabolic processes that lead to brain injury and encompass a wide and continually expanding array of pharmacological interventions. An ideal addition to the SAH treatment armamentarium would be a well-tolerated neuroprotective agent that has the ability to reduce arterial vasospasm and delayed ischaemic neurological deficit. Several drugs have been developed that have the potential to limit cerebral vasospasm and delayed ischaemic neurologic deficit, thus improving patient outcomes (3). However, although numerous agents that can prevent arterial narrowing and/or block the excitatory cascade of events leading to ischaemic neuronal death in experimental conditions have been proposed, there is no pharmacological agent proven to improve patient outcomes in the clinical practice.

Although this study by Akçıl et al. (1) was well-designed and adequately performed, the exciting results may put amantadine at the risk of being labelled as a 'miracle drug' before appropriate information on its biological action, underlying mechanism and therapeutic window is assessed, similar to the cases of other drugs previously investigated as neuroprotectants (4). All the currently available information on the efficacy of amantadine is derived from experimental investigations and TBI clinical studies. Translation of such information from a different clinical scenario to the treatment of patients with SAH would be misleading because the interaction and influence of amantadine on physiological variables as well as with other drugs commonly used in patients with SAH are unknown. Second, the time window, dose and duration of treatment warrant further studies. The results by Akçıl et al. (1) act as a stimulus for further investigations and suggest that further phase II studies must be performed to determine the safety, optimum tolerated dose, therapeutic time window and treatment duration of amantadine in the current clinical setting.

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Author's Reply

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Dear Editor,

We are grateful to the reader for her/his interest and well interpretation of our study results. Neuroprotection after aneurysmal subarachnoid haemorrhage is still being studied; unfortunately, the results of clinical studies are not as satisfying as those of experimental ones (1). We used amantadine with the standard treatment and found that patients' neurocognitive outcomes were better than those obtained with the standard treatment alone. Furthermore, we did not observe any side effects of amantadine in our patients during the study period. We underline that an indispensable part of the aneurysmal subarachnoid haemorrhage treatment is the prevention of re-bleeding and management of increased intracranial pressure, vasospasm, delayed ischaemic deficit and hydrocephalus. Neuroprotective strategies, such as amantadine administration, should be used only as an adjunct to the standard treatment. This study is still underway, and we desire to share the results after we reach an appropriate sample size according to power analysis. As the reader, we emphasise the need for more studies with larger sample size to determine the safety, optimum tolerated dose, therapeutic time window and treatment duration of amantadine after aneurysmal subarachnoid haemorrhage.

Sincerely…

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