Editorial

A New and Promising Perspective on Neuroprotective Agents in Stroke Management

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Neuroprotective agents have long been proposed to be effective in the management of stroke. These agents have been evaluated experimentally in a myriad of studies. However, satisfying results have not been achieved, and translation of these findings from bench to bedside has failed so far. These studies have examined many different strategies in the animal models of stroke which are classically divided into those that halt ischemic cascades such as thrombolytic agent use, sodium and calcium channels blockers, and potassium channel modulators, or those that decrease reperfusion damage including, free radicals scavengers, anti-inflammation therapies, therapeutic hypothermia and barbiturate use [1, 2].

Despite some positive results in the experimental phase and laboratory, unfortunately, these agents have failed to yield significant results in the clinical trials. This is also known as "reproducibility crisis". There appears to be some reasons justifying why these agents are effective in the laboratory but are futile in the clinic. First, the preclinical studies are biased, many of which have been performed in an uncontrolled condition with an urge to publish the results. Second, some of these studies are not well-designed and have either small sample size or problems with the methods reporting. Third, there is a publishing bias which discourages publishing negative results [2, 3]. For example, in an analytic study by Macleod et al. the authors concluded that unblindness of the animal studies in this field have led to the overestimation of the efficacy of interventions with neuroprotective agents [4].

In a recent study by Llovera et al. the authors tried to overcome these issues by designing an animal study similar to randomized, placebo-controlled multicenter clinical trials which is merely called preclinical randomized controlled trial (pRCT) [5].

On the other hand, additional factors contribute to the issues mentioned above and dampen neuroprotective agents efficacy in the clinic. It is possible that the most efficacious neuroprotective agent might not be a "single compound", but rather a combination of neuroprotective strategies [6]. Namely, in a new registered and ongoing multicenter randomized clinical trial (ESCAPE NA-1), neuroprotective agent is being administered intravenously in a single dose in selected acute stroke patients treated by endovascular revascularization. In this study, the design was improved by the use of NA-1 in acute phase during elimination of occlusion in special stroke patients with appropriate salvageable tissue [7]. In other trials, neuroprotective agent is applied in the early phases of probable stroke cases when the patients are transferred by the emergency department personnel and before administration of thrombolytic agents or endovascular thrombectomy. Researches about the targeted use of neuroprotective agents in the penumbra or ischemic tissue are also on the go and may lead to the promising results shortly [8].

The mentioned trials are just some of the new approaches that are being tried to address the major pitfalls we are facing with, in this field. Generally, despite disappointing results in this research area in the past years, it seems that promising results will be accomplished soon.

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