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Reply to: "An update on statins: Pleiotropic effect on intracerebral hemorrhage"

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To the Editor,

We thank Chen et al. for their interest in our paper [1]. As several studies reported that statin alleviates inflammation reactions and has an anti-oxidative effect, such benefit is a major component of our hypothesis that statin contributes to mortality reduction after intracerebral hemorrhage (ICH) in our real-world data. The animal model used a similar design of continuing/discontinuing statin as our study did, and the result gave a good laboratory evidence of a pleiotropic effect after ICH. We appreciated the authors' effort to prove that continuing simvastatin after ICH has a potential neuroprotective effect and promote hematoma resolution in the animal model [2,3].

Several animal studies reported many mechanisms to explain the potential neuroprotective effect of statin. Simvastatin treatment significantly alleviated polymorphonuclear neutrophils (PMNs) brain-infiltration and the subsequent neuroinflammatory reaction after ICH, in part by accelerating peripheral PMNs apoptosis by disorganizing the expression of apoptotic related proteins [4]. Perihematomal edema (PHE) is considered a radiological surrogate for secondary injury and local inflammation and it is independently associated with mortality and poor functional outcomes in ICH patients [5]. Higher neutrophil–lymphocyte ratio (NLR) is independently associated with the progression of PHE [5], and peripheral neutrophil modulation may also be involved in the neuroprotective effect of continuing statin for ICH. In terms of the effect of statin in promoting hematoma resolution, one study showed that simvastatin significantly enhanced brain hematoma absorption, alleviated hydrocephalus, and improved neurological recovery after experimental intraventricular hemorrhage [6], another study showed simvastatin also accelerates hematoma resolution after ICH in a PPAR gamma-dependent manner [7].

Moreover, enough preclinical and clinical data exist implicating the immune pathways and inflammatory cells as mediators of secondary brain damage and outcome predictors. Like several animal studies, this animal model gave the same results on the benefit of statin after ICH, partly by reducing the inflammation reaction and promoting hematoma resolution. However, such animal models always reflect iatrogenic hematoma, and we do not know whether similar benefits exist on patients with spontaneous ICH, even most clinical spontaneous ICH associated with underlying diseases or vascular abnormality. We agree that there is a need for further investigations to provide mechanistic insights into the underlying molecular and cellular links, characterize the specific role of leukocytes subsets, and identify potential targets for ICH treatment. Therefore, we would like to share our real-world experiences compatible with Dr. Chen's opinions.

Conflict of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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