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CNS lymphatic drainage blockade exacerbates cerebral vasospasm and cerebral injury following subarachnoid hemorrhage and partially reversed by Ginkgo biloba extract.**Arunkumar Prasad³, Bao-liang Sun^{1,2}, Xuan Wang^{1,2}, Li Jia^{1,2}, Li-li Jia^{1,2}, Xi-chang Liu^{1,2}, Zi-cui Cheng^{1,2}, Ming-feng Yang², Cheng-bi Zheng³, Lei-lei Mao², Cun-dong Fan², Zong-yong Zhang², Da-wei Li² and Xiao-yi Yang^{1,2}**¹Affiliated Hospital, Taishan Medical University, China²Key Lab of Cerebral Microcirculation in Universities of Shandong (Taishan Medical University), Taian³Taishan Medical University, China;

Recent studies suggest that CNS lymphatic drainage pathway to extracranial lymph compartments may play an important role in the removal of substances in the brain and cerebrospinal fluid (CSF). After the onset of subarachnoid hemorrhage (SAH), large amount of macromolecular substances, such as cellular lysates, proteins, peptides, were accumulated in the brain tissue and CSF, which contribute to cerebral vasospasm and cerebral injury. The present experiment was carried out to investigate the possible role of cerebral lymphatic drainage pathway in the development of cerebral vasospasm and related cerebral injury and the influence of Ginkgo biloba extract. Wistar rats were used in the experiment and animals were divided into different groups. SAH models were replicated by double cisternal injection of autologous arterial hemolysate. In some animals the main cerebral lymphatic drainage way out being blocked (cerebral lymphatic blockade, CLB). Two different constituents, Ginkgolides and Ginkgo flavone, were given as interventions. It was found that SAH reduced the drainage of Evans blue-labeled albumin (EBA) from the brain to the olfactory bulbs, cervical lymph nodes and abdominal paraaortic lymph nodes. A kinetic analysis of 125I-labeled human serum albumin (125I-HSA), a cerebrospinal fluid (CSF) tracer, showed that the clearance rate of macromolecules in the CSF was significantly reduced after SAH. Furthermore, SAH reduced the diameters of basilar artery (BA) and increased thickness of BA. Prominent cerebral injury was found after induction of SAH. The spasm of BA and cerebral injury were partially antagonized by Ginkgolides and Ginkgo flavone. It was concluded that cerebral lymphatic drainage pathway exerts intrinsic protective effects against cerebral vasospasm and cerebral injury by removal of macromolecular substances in the brain and subarachnoid spaces. Ginkgolides and Ginkgo flavone may alleviate the exacerbated cerebral vasospasm and cerebral injury following SAH by CLB.

Key words: subarachnoid hemorrhage; lymphatic drainage; cerebral vasospasm; cerebral injury; Ginkgolides; Ginkgo flavone

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