



The unique action of nicorandil on cerebral circulation

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To the Editor:

Kotoda et al. [1] demonstrated that the intraperitoneal 1 mg/kg nicorandil without affecting systemic hemodynamics causes the increase in cerebral blood flow (CBF), which is canceled by either an ATP-sensitive K⁺ channel (KATP) antagonist glibenclamide or a non-selective nitric oxide synthase inhibitor N^G-nitro-L-arginine (L-NAME). They concluded that nicorandil produces the enhancement in CBF, which is probably induced via both the nitric oxide pathway and KATPs [1]. We would like to add several discussions regarding the conclusion. First, the systemic administration of L-NAME causes the reduction of CBF at the range of –20 to –40%, which is mediated by the nitric oxide synthase inhibition [2]. The CBF possibly remains unchanged within the baseline in the animals exposed to the systemic L-NAME, which results in the CBF reduction, in combination with the vasodilation induced by nicorandil. Therefore, there seems no evidence to conclude that nicorandil increases CBF via the enhanced levels of nitric oxide since Kotoda et al. [1] did not examine the effect of L-NAME alone on the naïve CBF and that of the nitric oxide inhibitor in combination with glibenclamide on increased CBF by nicorandil. On the other hand, the activation of nitric oxide synthase might be possible by the application of a KATP opener in the artery

of rodents [3]. Second, whether nicorandil produces cerebral arterial dilation via KATPs is still unclear in animals. Indeed, the agent does not induce dilation of rat anterior cerebellar artery [4], and it causes relaxation via nitric oxide pathway, but not KATP activation, in the canine basilar artery [5]. Therefore, the CBF enhancement by nicorandil is most likely to be mediated by mechanisms such as the increased cardiac output resulting from systemic vasodilation other than that originated from vasorelaxation in the brain. Collectively, we would like to await the additional study to verify the role of nicorandil in the cerebral circulation.

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Compliance with ethical standards

Conflict of interest Hiroyuki Kinoshita is a consult of IMI Co. Ltd, Koshigaya, Saitama, Japan.

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