Atorvastatin Attenuates Quinolinic Acid-Induced Seizures and Hippocampal Cell Death in Mice via Akt phosphorylation and Glutamate Uptake

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Statins are cholesterol-lowering agents due to the inhibition of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Recent studies have shown statins possess pleiotropic effects which appear to be independent from its cholesterol-lowering action. In this study, we investigated whether atorvastatin would have protective effects against hippocampal cell death promoted by quinolinic acid (QA)-induced seizures in mice. Mice were pretreated with Atorvastatin (1 or 10 mg/kg) or vehicle (saline, 0.9 %), orally, once a day for seven days before the i.c.v. QA infusion (36.8 nmol/site). Atorvastatin treatment with 1 mg/kg/day did not significantly prevent QA-induced seizures (13.34 %). However, administration of atorvastatin 10 mg/kg/day prevented the clonic and/or tonic seizures induced by QA in 29.41 % of the mice. Additionally, administration of atorvastatin 10 mg/kg/day significantly prevented QA-induced cell death in the hippocampus. Atorvastatin treatment promoted an increased Akt phosphorylation, which was sustained after QA infusion in both convulsed and non-convulsed mice. Moreover, atorvastatin pretreatment prevented the reduction in glutamate uptake into hippocampal slices induced by QA i.c.v. infusion. These results show that atorvastatin attenuated QA-induced hippocampal cellular death involving the Akt pathway and glutamate transport modulation. Therefore, atorvastatin treatment might be a useful strategy in the prevention of brain injury caused by the exacerbation of glutamatergic toxicity in neurological diseases such as epilepsy.

Key words: atorvastatin, quinolinic acid, glutamate, seizures

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