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Role of nitric oxide in the anticonvulsant effects of acute atorvastatin treatment in mice

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Background and Aims: In addition to lowering the serum level of cholesterol, statins (e.g. atorvastatin) have neuroprotective and anti-excitotoxic effects. There is also some evidence that nitric oxide (NO) pathway plays a crucial role in the effects of atorvastatin on vascular system. In the current study, alteration of the seizure threshold was investigated in acute atorvastatin treatment . Moreover, nitrergic system involvement was evaluated.
Methods: This study was performed on male NMRI mice weighing 20–30 g. Two methods of maximal electroshock (MES) and intraperitoneal administration of PTZ were used to assess the seizure susceptibility. Doses of atorvastatin, 1, 5, 10 and 20 mg/kg in electroshock method and 5, 10 and 20 mg/kg in PTZ method were administered orally by gavage 30 minutes before seizure induction. To examine the role of nitric oxide, non effective doses of L-NAME (L-NG-Nitro-L-arginine methyl ester hydrochloride), a non selective inhibitor of nitric oxide synthase (5 mg/kg), or aminoguanidine, a selective inducible nitric oxide synthase inhibitor (100 mg/kg), were administered 30 minutes before atorvastatin and 60 minutes before electroshock or PTZ.
Results: Acute atorvastatin (1, 5, 10 and 20 mg/kg) treatment decreased the incidence of tonic seizure and death in electroshock-induced seizure model. Also it was shown that acute atorvastatin (10 mg/kg) treatment increased the clonic seizure threshold in pentylenetetrazole-seizure model. Acute L-NAME or aminoguanidine administration prevented the anti-convulsant effect of atorvastatin in electroshock-induced seizure model. Moreover acute L-NAME or aminoguanidine administration decreased the enhanced clonic latency of clonic seizure threshold induced by atorvastatin in pentylenetetrazole model in mice.
Conclusions: Anti-convulsant effect of atorvastatin was demonstrated in two seizure models. Nitric oxide release, probably through inducible nitric oxide synthase at least in part is responsible for this effect.

Keywords: Atorvastatin; Convulsion; Mice; Nitric oxide