Effects of the PDE5-inhibitor vardenafil in a mouse stroke model.

Abstract:
Recent experimental studies in rodents suggest that treatment with inhibitors of phosphodiesterase type 5 (PDE5) (tadalafil, sildenafil, zaprinast) not only increases cerebral blood flow but also improves functional recovery after stroke. Here, we investigated in a mouse model of stroke the effects of vardenafil on survival, functional outcome and lesion size after experimental stroke. Mice were subjected to experimental stroke by occlusion of the middle cerebral artery (MCAO) for 45 min. A group of mice received vardenafil (twice 10 mg/kg body weight per day orally over 14 days) starting 3 h after MCAO. Control animals received the vehicle only. Survival, body weight, and behavior were monitored over 4 weeks and brain lesions were measured by T2-weighted MRI, hematoxylin/eosin -- as well as GFAP-staining of cryostat sections, subsequently. The mortality in MCAO-operated animals amounted to 45% until day 10 after stroke and no significant difference in survival between the vardenafil- and vehicle-treatment groups was observed. Compared to sham-operated animals, MCAO-operated mice from both treatment groups demonstrated a significant weight loss until day 5 and regained their body weight by day 14 after ischemia. There was no significant difference between the vardenafil and vehicle-treated MCAO groups. In behavioral studies (sucrose consumption and pole test), analyzing sensorimotor functions as well as a
parameter of depression-like symptoms, we observed no significant effect of vardenafil treatment on functional recovery in our model of stroke. Although we observed a trend towards less hemispherical atrophy in the vardenafil compared to the vehicle-treated group four weeks after MCAO our data do not suggest a functionally relevant CNS-tissue protective or regenerative effect in murine stroke.