The aim of the present study was to evaluate the efficiency of combination of hyperbaric oxygen (HBO) and an antioxidant on permanent focal cerebral ischemia. Male Wistar rats underwent permanent middle cerebral artery occlusion (MCAO). Then, animals were randomly assigned to one of four groups: the control group (n=9) received no treatment, HBO group (n=9) was treated for 90 min at 2.5 absolute atmosphere for 3 days, the U-74389G group (n=8) received single U-74389G injection (3 mg/kg), the HBO + U-74389G group (n=8) received both HBO and U-74389G treatments. Treatments were initiated within the first 10 min after MCAO. After 3 days, the infarct volumes in rat brains were measured. The infarct ratios were 25.6 +/- 6.5 % for the control group, 21.9 +/- 6.4 % for the HBO group, 15.7 +/- 5.7 % for U-74389G group and 12.5 +/- 3.8 % for HBO + U74389G group. The infarct volumes were significantly reduced in rats treated with U-74389G (p<0.05) and combination therapy (p<0.05). HBO failed to reduce infarct volume significantly. We concluded that 1) U-74389G is more beneficial than HBO on permanent MCAO in rats, and 2) a combined therapy failed to significantly improve infarct volume more than either single treatment.