**BACKGROUND:** Stroke is one of the most common causes of death and the leading cause of disability in adults. Cerebral ischemia/reperfusion injury causes cerebral edema, hemorrhage, and neuronal death. AIMS: In post-ischemic reperfusion, free radical production causes brain tissue damage by oxidative stress. Pregabalin, an antiepileptic agent was shown to have antioxidant effects. The aim of this study was to evaluate the neuroprotective and antioxidant effects of pregabalin on ischemia and reperfusion in rat brain injury. STUDY DESIGN: Animal experimentation. METHODS: Male Wistar rats weighing (250-300 g) were randomly divided into six groups, each consisting of 6 rats: control (C), pregabalin (P), ischemia (I), pregabalin + ischemia (PI), ischemia + reperfusion (IR) and ischemia + reperfusion + pregabalin (PIR). Rats were initially pre-treated with 50 mg/kg/d pregabalin orally for two days. Then, animals that applied ischemia in I, PI, IR and PIR groups were exposed to carotid clamping for 30 minutes and 20 minutes reperfusion was performed in the relevant reperfusion groups. RESULTS: NR2B receptor levels were significantly lower in the PIR group in comparison to the IR group. In the PIR group, Thiobarbituric acid reactive substance (TBARS) level had statistically significant decrease compared with IR group. Glutathione peroxidase (GSH-PX) levels were also significantly increased in the PIR group compared with I, IR and control groups. In the PI and PIR groups, catalase (CAT) levels were also significantly increased compared with I and IR groups (p=0.03 and p=0.07, respectively). CONCLUSION: Pregabalin may protect the damage of oxidative stress after ischemia + reperfusion. This result would illuminate clinical studies in the future. KEYWORDS: Cerebral ischemia; ischemia-reperfusion; neuroprotective effects; pregabalin