Abstract

Targeting newly identified damage pathways in the ischemic brain can help to circumvent the currently severe limitations of acute stroke therapy. The activity of 12/15-lipoxygenase was increased in the ischemic mouse brain, and 12/15-lipoxygenase co-localizes with a marker for oxidized lipids MDA2. This co-localization is also detected in the brain of a human stroke victim. A novel inhibitor of 12/15-lipoxygenase, LOXBlock-1 protects neuronal HT22 cells against oxidative stress. In a mouse model of transient focal ischemia, the inhibitor reduces infarct sizes both 24 hours and 14 days post stroke. Even when treatment is delayed until at least four hours after onset of ischemia, LOXBlock-1 is protective. Furthermore, LOXBlock-1 does not worsen outcomes in a mouse model of intracerebral hemorrhage, suggesting it is safe. This study establishes inhibition of 12/15-lipoxygenase as a viable strategy for first line stroke treatment. Additional models of ischemia will be discussed.

Relevant References

