

**Evaluation of the Anti-Oxidant Activity of the Combination of Minocycline Plus N-Acetylcysteine in a Mouse Model of Traumatic Brain Injury**

Traumatic brain injury (TBI) is often fatal or debilitating and leads to chronic disease. With an estimated prevalence of 1.5 million TBIs per year in the United States, the lack of pharmaceutical options to treat TBI is burdensome to individuals, their families, and society. Thus, research on pharmacotherapies for TBI treatment is especially necessary and relevant. As oxidative damage is fundamental in the pathophysiology underlying TBI, drugs aimed at combating this damage have shown to be effective in extensive preclinical studies done in the Bergold laboratory. The goal of this study was to better understand the pharmacodynamics of the combination of minocycline (MINO) and N-acetylcysteine (NAC) compared to the individual drugs in a mouse model. We examined reduced glutathione levels using the GSH/GSSG-Glo™ assay in uninjured animals following 3 days of treatment with saline, MINO, NAC, or MINO+NAC. We also measured microglial activation in mice following closed head injury and treatment with saline, MINO, NAC, or MINO+NAC. Activation of microglia was assessed by immunofluorescence labeling using ionized calcium-binding adaptor molecule 1 (Iba-1) with cell nuclei labeled with DAPI. We found that treatment with MINO+NAC resulted in significantly higher levels of reduced glutathione than saline-treated mice ( $p < 0.05$ ), whereas mice treated with MINO or NAC alone did not have statistically significantly higher levels of reduced glutathione than saline-treated mice. The data we collected was suggestive of a possible synergistic relationship, which would provide further support for the use of MINO plus NAC in combination. Additionally, we found that injured mice treated with MINO plus NAC had significant lower levels of activated microglia in the contralateral thalamus than saline-treated mice ( $p < 0.05$ ). By increasing our understanding of these drugs alone and in combination, these experiments furthered our insights into treatment for TBI in humans.