**Combination of Lidocaine and IL-1Ra Is Effective at Reducing Degradation of Porcine Cartilage Explants**

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**Purpose:** Posttraumatic inflammation following joint injury, like articular fracture, contributes to the development of arthritis, and the administration of interleukin 1 receptor antagonist (IL-1Ra) is a potential intervention to mitigate this response. It is currently known that IL-1Ra mitigates cartilage degenerative changes induced by IL-1$\alpha$ and that lidocaine is used for local pain management in acute joint injury. Intra-articular delivery of both drugs in combination would be a novel and possibly disease-modifying treatment. However, it is not known if the interaction with lidocaine at clinical concentrations (1%) would alter the efficacy of IL-1Ra to protect cartilage from the catabolic effects of IL-1. We hypothesized that the treatment of articular cartilage with IL-1Ra in combination with a clinically relevant concentration of lidocaine (1%) will inhibit proteoglycan loss due to IL-1$\alpha$ equally to IL-1Ra alone.

**Methods:** Fresh porcine cartilage explants were harvested, challenged with IL-1$\alpha$, and incubated for 72 hours with IL-1Ra or a combination of IL-1Ra and lidocaine. The primary outcome was total sulfated glycosaminoglycan (sGAG) release. Additional experiments assessed the effect of premixing and storage temperature of IL-1Ra and lidocaine on sGAG release.

**Results:** The combination of IL-1Ra and lidocaine was as effective as IL-1Ra alone at inhibiting IL-1$\alpha$-mediated sGAG release. Regardless of the time point at which IL-1Ra and lidocaine were premixed or storage temperature prior to adding to explants, IL-1Ra and lidocaine significantly decreased total sGAG release to control levels and was not significantly different from IL-1Ra alone.

**Conclusion:** Our hypothesis was supported, and results indicate IL-1Ra and lidocaine combination treatment for inflammatory cartilage injury with IL-1$\alpha$ are not inferior to IL-1Ra treatment alone. Further, the combination is stable when reagents are stored in advance of administration at varying temperatures, providing clinically relevant information about storage of medications. The combination of IL-1Ra and lidocaine is equally as efficacious as IL-1Ra treatment alone in mediating biologic cartilage injury due to IL-1$\alpha$ in an explant model of the acute inflammatory state. The ability to premix and store this drug combination for intra-articular delivery may provide a novel treatment following joint injury to provide pain relief and block inflammation-induced catabolism of joint tissues.