Ibuprofen Impairs Capsulolabral Healing in a Rat Model of Anterior Glenohumeral Instability

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Introduction: Anterior glenohumeral dislocations frequently result in injury to the glenoid labrum and capsule. The failure of these soft tissue restraints to sufficiently heal can lead to persistent shoulder instability. In order to study capsulolabral healing, our group has developed a novel rat model of shoulder instability. In previous work with this model, we found that immunohistochemical expression of the pro-inflammatory cytokines IL-1β and TGF-β1 were increased in the tissues of injured compared to uninjured animals. [1] Therefore, we hypothesized that downregulating this initial inflammatory response may inhibit healing of the labrum and capsule to the glenoid. Although nonsteroidal anti-inflammatory medications (NSAIDs) have been shown to impair fracture, tendon, ligament, and enthesis healing, the effects on capsulolabral healing are unknown. The purpose of this study was to determine the effect of ibuprofen, a commonly used NSAID, on the healing glenoid labrum and capsule after glenohumeral dislocation in a rat model.

Methods: Sixty-six rats had surgically induced anterior-inferior labral tears and anterior glenohumeral dislocation. The animals were assigned to either a control group with normal drinking water (n=32) or an experimental group with ibuprofen drinking water (n=31). The animals in the experimental group were given water mixed with an ibuprofen suspension and consumed an average 30mg/kg per day. Animals were euthanized at two and four weeks postoperatively. Fourteen animals were excluded due to infection (n=1) and persistent irreducible dislocation (n=13). Three specimens from each group (total of 12 animals) underwent H&E staining and were examined for density of inflammatory cells, organization of collagen, and healing. The remaining thirty-seven specimens underwent biomechanical testing (Figure 1) on both the injured (right) and uninjured (left) limb using a custom-designed tensile testing apparatus. The glenohumeral joint was fixed at 45° of abduction and neutral rotation. Prior to final clamping, the humerus was manually centered in the glenoid and a compressive axial load was placed. Anterior to posterior cyclic laxity fatigue was performed for 100 cycles at a frequency of 1Hz and a load of 3.64% of the weight of the rat. Monotonic loading with anterior humeral translation was then performed until either failure or complete displacement of the humeral head anterior to the glenoid (7mm). The data between experimental groups was tested for normality with the Kolmogorov-Smirnov test and the statistical analysis was performed with the two-tailed student’s t-test. The uninjured limb groups were compared with the Mann-Whitney U test. A matched comparison between the injured and uninjured limbs was performed utilizing the Wilcoxon test.

Results: Maximum Load: Within the NSAID groups, maximum load increased from 2 to 4 weeks post injury (5.70 ± 1.88 N and 8.43 ± 1.79 N, p < 0.01). At 2 weeks, the maximum load was lower in the NSAID compared to the control group (5.70 ± 1.88 N and 7.78 ± 2.23 N, p < 0.05). In the matched comparison between injured and uninjured limbs, the maximum load was significantly decreased in the injured limb.
of the 2 week NSAID group (5.70 ± 1.88 N, 7.47 ± 3.02 N, p < 0.01). There were no differences in maximum load within the control group.

Stiffness: Terminal capsular stiffness increased from 2 to 4 weeks in both the NSAID (1.30 ± 0.16 N/mm versus 0.96 ± 0.14 N/mm, p < 0.001) and the control groups (2.08 ± 0.42 N/mm versus 1.13 ± 0.49 N/mm, p < 0.01). At 4 weeks, the NSAID group had decreased stiffness as compared to the 4 week control group (1.30 ± 0.16 N/mm and 2.08 ± 0.42 N/mm, p < 0.001). When comparing the uninjured limbs in the NSAID and control groups, there were no significant differences in maximum load, initial stiffness, or terminal stiffness.

Discussion: In a novel rat model of glenohumeral instability, the post-injury administration of ibuprofen resulted in decreased biomechanical properties of the healing glenoid capsulolabral complex. Capsular stiffness and maximum load increased with time after injury indicating some healing of the capsule and labrum. However, statistically significant differences in maximum load and capsular stiffness were observed, with NSAID treated animals having decreased maximum load at 2 weeks and decreased capsular stiffness at 4 weeks post injury. A matched pair analysis of injured to uninjured limbs supported the findings of impaired healing in the NSAID treated animals. These findings demonstrate that the use of NSAIDs after glenohumeral dislocation may impair capsulolabral healing and should be limited or avoided to optimize glenohumeral stability.

Significance: In this study, a novel rat model was developed to investigate capsulolabral healing in glenohumeral instability. NSAIDs were found to impair capsulolabral healing after surgically induced shoulder dislocation. The findings of the current study may have important implications for the use of NSAIDs after shoulder dislocation and labral repair.
Terminal Capsular Stiffness

- Control
- NSAID

P < 0.01

N/mm

Time

2 wks

4 wks

Load Curve

Max Load

Dislocation

Terminal Capsular Stiffness

Capsular Laxity

Displacement (mm)