Low-Intensity Pulsed Ultrasound Accelerates and a Nonsteroidal Anti-inflammatory Drug Delays Knee Ligament Healing

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FROM ABSTRACT

Background:
Low-intensity pulsed ultrasound and nonsteroidal anti-inflammatory drugs are used to treat ligament injuries; however, their individual and combined effects are not established.

Hypotheses:
Low-intensity pulsed ultrasound accelerates ligament healing, a nonsteroidal anti-inflammatory drug delays healing, and the nonsteroidal anti-inflammatory drug inhibits the beneficial effect of low-intensity pulsed ultrasound.

Methods:
This study used 60 adult rats with acutely injured medial collateral ligaments, who were treated with either nonsteroidal anti-inflammatory drugs (NSAIDs) or with low-intensity pulsed ultrasound (LIPUS).

Results:
After 2 weeks of intervention, ligaments treated with low-intensity pulsed ultrasound were 34.2% stronger, 27.0% stiffer, and could absorb 54.4% more energy before failure than could ligaments that were not treated.

Ligaments from the NSAID group could absorb 33.3% less energy than could ligaments from the LIPUS group.

Conclusions:
Low-intensity pulsed ultrasound accelerated but did not improve ligament healing, whereas the nonsteroidal antiinflammatory drug delayed but did not impair healing.

When used in combination, the beneficial low-intensity pulsed ultrasound effect was cancelled by the detrimental nonsteroidal anti-inflammatory drug effect.

Clinical Relevance:
Low-intensity pulsed ultrasound after ligament injury may facilitate earlier return to activity, whereas nonsteroidal anti-inflammatory drugs may elevate early reinjury risk.
THESE AUTHORS ALSO NOTE:

“Ligament injuries pose substantial problems for athletes, both acutely in terms of time lost from participation and chronically in terms of joint laxity and degenerative joint disease.”

“The major goal of clinicians when treating acute ligament injuries is to return athletes to their preinjury level of function, ideally in the shortest time possible and without compromising tissue-level healing.”

“Ultrasound therapy is used after acute ligament injury in an attempt to accelerate healing. In a recent survey, 95% of physical therapists reported using ultrasound when managing acute ligament injuries.”

The traditional use of ultrasound has “minimal scientific evidence to support a beneficial effect” and “reviews of its effects have repeatedly concluded that there is insufficient evidence to support the current application of ultrasound.”

Consequently, a new direction for ultrasound using low-intensity pulsed ultrasound (LIPUS) therapy has shown significant clinical benefit on injured tissue.

Low-intensity pulsed ultrasound uses an intensity of no more than 100 mW/cm² (.1 W/cm²).

“Although NSAIDs have become somewhat synonymous with the management of acute injuries, their efficacy has yet to be proven.” This is of particular concern in view of recent research indicating potential detrimental tissue effects of NSAIDs.

Recent research shows that the use of COX-2 inhibitors reduce acute ligament healing.

“The aim of the current study was to investigate the individual and combined effects of LIPUS and an NSAID (a selective COX-2 inhibitor) on acute ligament healing in an animal model. It was hypothesized that LIPUS would accelerate repair, the NSAID would delay repair, and the NSAID would inhibit the beneficial influence of LIPUS, as determined via tests on ligament mechanical properties.”

In this study, the celecoxib [Celebrex] dose used was equivalent to that used clinically to treat acute pain in humans.

The ultrasound used was set at 100 mW/cm², and introduced daily for 20 minutes, 5 d/wk.

Animals were sacrificed and assessed at 2 weeks, 4 weeks, and 12 weeks.

“All surgical defects were bridged with scar tissue at the time of dissection.”
DISCUSSION

“Based on tests of ligament mechanical properties, LIPUS had a beneficial effect on healing, whereas the NSAID had a negative effect.”

LIPUS refers to pulsed-wave ultrasound that is equal to or lower than 100 mW/cm². “This intensity is categorized as low, relative to the range that is commonly used in physical therapy (0.5-2 W/cm²).”

LIPUS has shown significant beneficial effects when applied to injured connective tissues.

Clinical trials have shown LIPUS to accelerate the rate of fracture repair in the tibia, radius, and scaphoid by 30% to 38% and to stimulate union in 86% of fractures displaying nonunion.

The current study confirms that LIPUS accelerates ligament healing.

At 2 weeks, LIPUS–treated ligaments were 34% stronger than non-treated ligaments. “This improvement may conceivably allow earlier return to sport and/or prevent reinjury during initial healing.”

LIPUS may mechanically stimulate reparative fibroblasts, inducing their proliferation and production of collagen.

In this study, NSAIDs were found to have a “negative effect on ligament healing.”

Nonsteroidal anti-inflammatory drugs reduce inflammation by reducing the formation of prostaglandins from arachidonic acid, but they also inhibit the synthesis of connective tissues.

NSAIDs have been “shown to have a negative effect on ligament healing.”

[Important]

This study demonstrates that NSAID use after acute ligament injury delays ligament healing.

“Because LIPUS and the NSAID had opposing effects that were approximately equal in magnitude, their combined effect is equivalent to the introduction of no intervention at all.”

“The results of the current study suggest that LIPUS may be used clinically after acute ligament injury to facilitate earlier return to activity, whereas NSAIDs should be avoided, as they may elevate early reinjury risk.”
“In addition, the data suggest that combined LIPUS and NSAID intervention should not be used during early ligament healing, as the NSAID negated the beneficial LIPUS effect.”

In summary, this study found LIPUS accelerated ligament healing, whereas an NSAID delayed impair healing.

“When used in combination, the beneficial LIPUS effect was cancelled by the detrimental NSAID effect.”

These findings support a theoretically sound argument for the use of LIPUS and nonuse of an NSAID after acute ligament injury.

KEY POINTS FROM DAN MURPHY

1) The traditional use of ultrasound (using .5-2 W/cm²) probably does not improve the timing or quality of the healing of injured ligaments.

2) Using low-intensity pulsed ultrasound at an intensity of no more than 100 mW/cm² (< .1 W/cm²) significantly accelerates the healing of acutely injured ligaments.

3) Using NSAIDs, especially COX-2 inhibitors (Celebrex in this study) reduces acute ligament healing and has a negative effect on ligament healing.

4) Nonsteroidal anti-inflammatories inhibit the synthesis of connective tissues.

5) NSAID use after acute ligament injury delays ligament healing.

6) NSAID intervention should not be used during early ligament healing because they delay healing and elevate early re-injury risk.

7) This study shows that injured ligaments heal with scar tissue.