Preventing Bone Loss Improves Tendon-Bone Healing in a Canine Model

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ABSTRACT

Studies have shown that tendon insertion site injuries can lead to bone loss. Following tendon-bone repair, bone loss can lead to widening of the repair tunnel. This widening may negatively affect the establishment of a strong tendon-bone interface, leading to recurrence of failure. Our goal was to suppress bone loss after insertion site repair using alendronate in an attempt to prevent the decrease in biomechanical properties. Flexor digitorum profundus tendons were injured and repaired into bone tunnels in the distal phalanx in seven canines. Dogs received a daily oral dose of alendronate. Dogs also received a local dose of alendronate in the bone tunnels of either the second or fifth digit at the time of surgery. Insertions were evaluated at 21 days for mechanical properties and bone mineral density. Our data indicated that tendon to bone healing can be improved by preventing bone loss. We showed that: 1) alendronate prevents the bone loss which occurs after tendon to bone repair and 2) prevention of bone loss leads to significantly improved mechanical properties. This effect may be because there is a more stable surface for tendon-bone integration or because there is less inflammatory tendon degradation in the bone tunnel.

INTRODUCTION

Studies have shown that tendon and ligament insertion site injuries can lead to bone loss, as evidenced by reduced bone mineral density (BMD) [e.g., 1, 2]. Following ligament-bone or tendon-bone repair, bone loss can lead to widening of the osseous repair tunnel. This widening may negatively affect the establishment of a strong tendon-bone interface, leading to recurrence of failure. We previously showed, in a canine model, significant bone loss and decreased mechanical properties in the first 21 days after flexor tendon insertion site injury and repair [1, 3]. Our goal in this study was to suppress bone loss after insertion site repair using alendronate (a bisphosphonate) [e.g., 4] in an attempt to prevent the decrease in biomechanical properties. We hypothesized that: 1) systemic alendronate would reduce bone loss and lead to improved biomechanical properties, and 2) the addition of a local dose of alendronate would further suppress bone loss and lead to further improvement in biomechanical properties.

METHODS
Animal model: Flexor digitorum profundus (FDP) tendons were injured and repaired into bone tunnels in the distal phalanx in seven canines using an established method [3]. Each dog had the second and fifth FDP tendons injured and repaired. The FDP was approached via a lateral incision and the tendon transected sharply at its insertion. The cut tendon end was grasped using a 4-strand modified Becker stitch. A 5mm deep x 3mm diameter hole was drilled at the base of the distal phalanx. Two needle holes were drilled through these holes and tied over the dorsal surface of the toenail, pulling the tendon stump into the bone tunnel. To eliminate confounding effects from the loading environment, the repaired tendons were cut proximally to remove all loads from the distal phalanx repair site. Post-operatively forelimbs were subjected to passive motion rehabilitation. Dogs received a daily oral dose of alendronate (2mg/kg). Dogs also received a local dose of alendronate in the bone tunnels of either the second or fifth digit at the time of surgery. The local dose was administered by filling the bone tunnel with alendronate (2mg/ml), waiting two minutes, and then performing the repair [5]. Due to the high affinity of alendronate to bone mineral, 2 minutes was considered sufficient for local delivery [5]. With this paired study design, each animal received a systemic dose plus a local dose of alendronate in one repair and a systemic dose alone in the second repair.

Assays: Dogs were sacrificed at 21 days, dissected, and tendon-bone specimens were pulled in uniaxial tension until failure [1, 3]. Historical control data consisting of the identical injury and repair with no administration of alendronate were used for comparison (repair only at time zero and repair only at 21 days [3]). Bone mineral density (BMD) of the distal phalanx was assessed at the insertion site using peripheral quantitative computed tomography (pQCT; Stratec) [1, 3].

Statistics: Groups were compared using an analysis of variance (ANOVA) followed by a Fisher’s least squares differences post-hoc test. The ‘Systemic Alendronate’ group was compared to the ‘Systemic + Local Alendronate’ group using a paired t-test. Mechanical testing failure modes were compared using a Chi-square test.

RESULTS

Alendronate was effective in preventing the bone loss in the distal phalanx over the initial 21 days of healing. The BMD for the repair alone group was 71% of control, while the BMD of the systemic alendronate group was 94% of control (Figure 1, Table 1). The BMD for the systemic plus local alendronate group was 104% of control (Figure 1, Table 1). The BMD of the distal phalanges of dogs treated with alendronate was not significantly different from the BMD at time zero.

The suppression of bone loss led to an improvement in the biomechanical properties observed over the first 21 days (Figure 2, Table 1). Both systemic alendronate and systemic plus local alendronate were effective in significantly increasing ultimate tensile load compared to repair alone at 21 days (Figure 1, Table 1). Without treatment, the ultimate load was only 42% of the initial, time-zero level. With systemic alendronate treatment and systemic plus local alendronate treatment, the ultimate load was 78% and 69% of control, respectively. Alendronate treatment did not significantly affect stiffness compared to repair alone (Figure 3, Table 1). All three injury groups had significantly lower stiffness values compared to the repair at time zero. At 21 days, stiffness reached 63% of control for the repair only group, 63% of control for the systemic alendronate treatment group, and 46% of control for the systemic plus local alendronate treatment group. Surprisingly, the local application of alendronate had a significantly detrimental effect on stiffness compared to systemic alendronate alone. Elongation at 20 Newtons was not significantly different between any of the groups (Table 1). Failure mode was significantly different when comparing alendronate treatment to repair alone (Table 2). There was a lower incidence of suture pull through (PT) in alendronate treated dogs, suggesting less tendon degeneration.
**Figure 1**- Bone loss was reduced by systemic administration of alendronate and further reduced by the addition of local alendronate. a: p<0.05 compared to ‘Repair Only (0d)’, b: p<0.05 compared to ‘Repair Only (21d)’, c: p<0.05 compared to ‘Systemic Alendronate’, d: p<0.05 compared to ‘Systemic + Local Alendronate’.

**Figure 2**- The attenuation of bone loss coincided with increased ultimate load, suggesting that preventing bone loss may enhance insertion healing strength. a: p<0.05 compared to ‘Repair Only (0d)’, b: p<0.05 compared to ‘Repair Only (21d)’, c: p<0.05 compared to ‘Systemic Alendronate’, d: p<0.05 compared to ‘Systemic + Local Alendronate’.
Figure 3- Alendronate treatment did not have an effect on the stiffness of the repair. Local administration of alendronate had a detrimental effect on stiffness compared to systemic administration alone. a: p<0.05 compared to ‘Repair Only (0d)’, b: p<0.05 compared to ‘Repair Only (21d)’, c: p<0.05 compared to ‘Systemic Alendronate’, d: p<0.05 compared to ‘Systemic + Local Alendronate’.

Table 1- Biomechanical properties were improved with the administration of alendronate. However, the addition of local administration had a detrimental effect on stiffness. ANOVA: analysis of variance, LSD: Fisher’s least squares differences test post-hoc test. Differences between groups [0d: Repair Only (0d), 21d: Repair only (21d), S: Systemic alendronate, L: Systemic + Local alendronate] indicated for p<0.05.

Table 2- Failure mode differed significantly in the alendronate groups compared to the repair only (21d) group. SB: suture break, PT: suture pull through tendon.

DISCUSSION

These data indicate that tendon to bone healing can be improved by preventing bone loss. We showed that,

1. Alendronate prevents the bone loss which occurs after tendon to bone repair, presumably by suppressing osteoclast activity.
2. Prevention of bone loss leads to significantly improved mechanical properties. This effect may be because there is a more stable surface for tendon-bone integration or because there is less inflammatory tendon degradation in the bone tunnel.
ACKNOWLEDGMENTS

The authors thank Dr. John Dalton for assisting on the tendon-bone surgical repairs. NIH R01 5R01AR033097. Alendronate provided as a gift from Merck & Co.

REFERENCES


