The effects of alendronate on tibial bone tunnel enlargement: an experimental rabbit model

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Introduction: Anterior cruciate ligament (ACL) reconstruction with free tendon grafts to be fixed in bone tunnels is a popular procedure in orthopaedic knee surgery. Among the related complications, tunnel enlargement has been reported in recent years. Tunnel enlargements were found to be an early process produced first by the pendulum movement of the drill bit and heat necrosis, enhanced by a non-specific inflammatory reaction. However no definite causes have been demonstrated for bone tunnel enlargement. Alendronate inhibit osteoclast-mediated resorption with inhibition of the mevalonate pathway in osteoclasts. Previous study has shown that alendronate prevent bone loss and improves tendon-bone repair strength in a canine model (1). Therefore, we make a hypothesis that alendronate prevent bone tunnel enlargement. Aim of this study is to investigate the effects of alendronate on bone tunnel enlargement after tendon transplantation model in the rabbit.

Material and Methods: Ethical approval was obtained from Animal Care Committee of University of the Ryukyus. A total of 51 skeletally mature male Japanese white rabbits (Japan SLC, Shizuoka, Japan) from 28 to 32 weeks in age were used in this study (weight: 3.2-3.6 kg). The rabbits were divided into two groups with 24 animals in each group: control group and alendronate group. Alendronate (0.8mg/kg) was administered systemically during the operation. Operations were performed according to the procedure reported by Rodeo et al (2). The long digital extensor tendon graft was dissected at the origin of the femur and the tendon was sewn with a baseball stitch at proximal end by use of a polyester suture. A 2.1-mm diameter hole was drilled parallel to the joint line at the proximal tibia. The graft was then inserted and routed through the bone tunnels via the holding sutures. The rabbits were allowed free cage activities after surgery. The rabbits were euthanized at 0 (baseline), 3 and 6 weeks postoperatively, with 12 rabbits participating each time point. At each time point, eight tibia-tendon complexes were harvested for evaluation of bone tunnel area used for micro-CT (micro-C-40; Scanco Medical, Figure 1) and trabecular bone mineral density used for pQCT (XCT Research SA+Stratec Medizintechnik GmbH, Pforzheim, Germany); the other four were used for histological evaluation with bone histomorphometry on fluorescence labeling. The data were analyzed with JMP software. Differences between groups were established with Mann-Whitney U tests. The mean difference was significant at the 0.05 level. The mean difference was significant at the 0.05 level. The data were analyzed with JMP software.

Results: The tunnel cross-section area was 3.54mm² at time 0, 5.03mm² at 3 weeks, 4.23mm² at 6weeks in control group and 3.65 mm² at 3 weeks, 2.39mm² at 6weeks in alendronate group. Alendronate group was significantly smaller than control group (P<0.01; 3weeks, P<0.05; 6weeks, Figure 2-A). The trabecular bone mineral density was 179.7mm² at time 0, 174.2mm² at 3 weeks, 206.6mm² at 6 weeks in control group and 215.5 mm² at 3 weeks, 208.1mm² at 6 weeks in alendronate group. Alendronate group was significantly higher than control group at 3 weeks (P<0.05, Figure 2-B). Histologically, eroded surface was 37.0% at 3weeks, 52.1% at 6 weeks in control group and 18.7% at 3weeks, 47.3% at 6 weeks in alendronate group. Alendronate group was significantly smaller than control group at 3 weeks (P<0.05, Figure 3-A). Osteoclastic surface was 10.4% at 3weeks, 14.5% at 6 weeks in control group and 3.7% at 3weeks, 8.9% at 6 weeks in alendronate group (Figure 3-B). The number of minishealing which is regarded as bone formation occurred on quiescent bone surfaces without preceding bone resorption (Figure 4) was 0 at 3weeks, 0.7 at 6 weeks in control group and 7.4% at 3weeks, 7.3 at 6 weeks in alendronate group (Figure 3-C). It was detected that there is lower osteoclastic activities and more trabecular minishealing in alendronate group than control group.

Discussion: The present study demonstrated that alendronate prevented bone tunnel enlargement and increased trabecular bone mineral density at 3 weeks. In addition, we observed trabecular minishealing in alendronate group more frequently than in control group. It was suggested that the mechanism of suppression of bone tunnel enlargement relates to osteoclastic activities and minishealing which occurred in the
tendon-bone interface by alendronate. The long-term effects of alendronate on tunnel enlargement must be studied before clinical use is recommended.

Significance: The treatment with alendronate might reduce bone resorption on bone-tendon interface and suppress bone-tunnel enlargement.

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References:
1) Thomopoulos S; Alendronate prevents bone loss and improves tendon-to-bone repair strength in a canine model. J Orthop res. 2007
2) Rodeo SA.; Tendon-healing in a bone tunnel; A biomechanical and histological study in the dog. J Bone J Surg. 1993

Figure 1. Three-dimenisional image reconstructed from micro-CT
(A) alendronate group, (B) control group

Figure 2. (A) Bone Tunnel area, (B) Trabecular bone mineral density

Figure 3. (A) Eroded surface, (B) Osteoclastic surface, (C) The number of minishealing

Figure 4. the evidence of minishealing; the combination of fluorochrome labeling and a smooth cement line