Validation of the Osteopenia Sheep Model for Orthopaedic Biomaterial Research

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Published in:
55TH ANNUAL MEETING OF THE ORTHOPAEDIC RESEARCH SOCIETY

Publication date:
2009

Document version
Publisher's PDF, also known as Version of record

Citation for published version (APA):
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Introduction: Currently, majority orthopaedic prosthesis and biomaterial researches have been based on investigation in normal animals. In most clinical situations, most patients do not have a normal bone quality that in many cases are due to osteoporosis (OP) even in osteoarthritic joints. Although a variety of ovariectomized (OVX) animals has been used to study osteoporosis, there is a great need for suitable large animal models with adequate bone size that closely resemble osteoporosis in humans.

This study aimed to validate glucocorticoid-induced osteopenia sheep model for orthopaedic implant and biomaterial research. We hypothesized that a 7-month GC treatment together with restricted diet but without OVX would induce osteopenia.

Materials and Methods: Eighteen female sheep were randomly allocated into 3 groups: group 1 (GC-1) received GC treatment (0.60 mg/kg/day methylprednisolone) for 7 months, group 2 (GC-2) received the same treatment for 7 months, and further observed for 3 months without GC; and group 3 served as the control group, and left untreated for 7 months. The sheep were housed outdoors in paddocks, and received restricted diet with low calcium and phosphorus (0.55% calcium and 0.35% phosphorus) and hay.

After sacrifice, cancellous bone specimens from the 5th lumbar vertebra, bilateral distal femur, and bilateral proximal tibia, and cortical bone samples from midshaft femur were micro-CT scanned (vivaCT 40, Scanco Medical AG., Switzerland) to quantify their 3-D microarchitectural properties(2). The cancellous bone samples were then tested compressively (MTS Systems Co., USA), and cortical bone samples after demineralized were tested in tensile to determine their mechanical properties. Serum biomarkers for bone formation (osteocalcin) and resorption (crosslaps) were determined. The results were analyzed statistically, and p<0.05 was considered significant.

Results: After 7 months of GC treatment, vertebral cancellous bone volume fraction was reduced by 36%, trabecular thickness by 30%, and cortical bone samples from midshaft femur were micro-CT scanned (vivaCT 40, Scanco Medical AG., Switzerland) to quantify their 3-D microarchitectural properties(2). The cancellous bone samples were then tested compressively (MTS Systems Co., USA), and cortical bone samples after demineralized were tested in tensile to determine their mechanical properties. Serum biomarkers for bone formation (osteocalcin) and resorption (crosslaps) were determined. The results were analyzed statistically, and p<0.05 was considered significant.

Discussion: The present study evaluated the effects of GC-treatment alone on the development of the microarchitecture and mechanical properties of the cancellous bone and cortical bone. The dose used corresponds to concentrations in earlier experimental studies, however in combination with OVX(1).

Our data demonstrated the GC treatment affects cancellous bone and cortical bone. 7 month GC-treatment on density and microarchitecture of cancellous bone are comparable with those observed in human after long-term GC-treatment. Moreover, we have shown that bone strength and microarchitecture of cancellous bone recover after 3 months further observation without GC. Osteocalcin was significantly reduced after 7 months but a rebound phenomenon was observed after 10 months. This suggests that a prolonged administration of GC is needed for a long-term observation to keep osteopenic bone.

In conclusion, after 7 months of GC treatments with restricted diet, the microarchitectural characteristics, mechanical competence, mineralization of the bone tissues, and suppression of bone formation markers were similar to osteoporosis-related changes in humans. A prolonged GC treatment is needed for a long-term observation to keep osteopenic bone. This model resembles long-term GC treated OP model, and might be useful in pre-clinical studies.


Acknowledgement: Danish Research Agency (SSVF-22-04-0705).

Cancellous bone of vertebra

Cortical bone of midshaft femur

Fig. 1. 3-D reconstruction of cancellous bone (upper) and midshaft cortical bone (lower). Significant changes in cancellous bone were seen.

Fig. 2. Microarchitectural & mechanical properties of sheep vertebral cancellous bone & femur midshaft cortical bone, and serum biomarkers. Data are presented as mean (SD). Significant differences are indicated.