

Evaluation of osteoprotegerin and tumor necrosis factor- α changes in synovial fluid and serum in dogs with osteoarthritis: An experimental study

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Abstract

Osteoarthritis (OA) is a progressive and degenerative condition of the articular cartilage and other joints' structures. It is essential to diagnose this condition as early as possible. The present study was conducted to measure the Osteoprotegerin (OPG) and Tumor Necrosis Factor- α (TNF- α) levels in synovial fluid and serum samples of dogs with experimental cruciate ligament rupture as a model of OA. In the present study, four adult (~ 20 months), large (weighing ~ 18 kg), mixed breed, male clinically healthy dogs were selected to investigate the effect of experimental OA, on OPG and TNF- α as a way of early detection of OA. OPG and TNF- α were measured in synovial fluid and serum on days 0, 14, 28, 90 and 180 after the surgical transaction of the cranial cruciate ligament in one stifle joint. Statistical analysis of the results showed that there was a significant increase in the concentrations of TNF- α in both synovial fluid and serum. Serum level of OPG showed a reduction before and two weeks after surgery and remained steady for the rest of the study period. Synovial fluid levels of OPG had no wide fluctuation throughout the study. OPG had constant levels at the beginning of experiment and increased at final stage. In conclusion, TNF- α could be used in both synovial fluid and serum as a way of early detection of OA.

Key words: Osteoarthritis, Osteoprotegerin, Tumor necrosis factor α , Synovial fluid

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References

- Amin, A. (1999). Regulation of tumor necrosis factor- α and tumor necrosis factor converting enzyme in human osteoarthritis. *Osteoarthritis and Cartilage*, 7: 392-394.
- Botha-Scheepers, S.; Watt, I.; Slagboom, E.; de Craen, A.; Meulenbelt, I.; Rosendaal, F. et al. (2006). A2 innate production of tumor necrosis factor- α and interleukin-10 is associated with progression of knee osteoarthritis. *Osteoarthritis and Cartilage*, 14: S17-S18.
- Clements, D. (2006). Arthrocentesis and synovial fluid analysis in dogs and cats. *In Practice*, 28: 256-262.
- Ding, M.; Odgaard, A. and Hvid, I. (2003). Changes in the three-dimensional microstructure of human tibial cancellous bone in early osteoarthritis. *The Bone & Joint Journal*, 85: 906-912.
- Felson, D.T. and Neogi, T. (2004). Osteoarthritis: is it a disease of cartilage or of bone? *Arthritis & Rheumatology*, 50: 341-344.
- Fernandes, J.C.; Martel-Pelletier, J. and Pelletier, J.P. (2002). The role of cytokines in osteoarthritis pathophysiology. *Biorheology*, 39: 237-246.
- Fujita, Y.; Hara, Y.; Nezu, Y.; Schulz, K.S. and Tagawa, M. (2006). Proinflammatory cytokine activities, matrix metalloproteinase-3 activity, and sulfated glycosaminoglycan content in synovial fluid of dogs with naturally acquired cranial cruciate ligament rupture. *Veterinary Surgery*, 35: 369-376.
- Goldring, S. and Goldring, M. (2006). Clinical aspects, pathology and pathophysiology of osteoarthritis. *Journal of Musculoskeletal Neuronal Interaction*, 6: 376.
- Goldring, S.R. and Goldring, M.B. (2004). The role of cytokines in cartilage matrix degeneration in osteoarthritis. *Clinical Orthopaedics and Related Research*, 427: S27-S36.
- Hayami, T.; Pickarski, M.; Zhuo, Y.; Wesolowski, G.A.; Rodan, G.A. and Duong, L.T. (2006). Characterization of articular cartilage and subchondral bone changes in the rat anterior cruciate ligament transection and meniscectomized models of osteoarthritis. *Bone*, 38: 234-243.
- Kadri, A.; Ea, H.; Bazille, C.; Hannouche, D.; Liote, F. and Cohen-Solal, M. (2008). Osteoprotegerin inhibits cartilage degradation through an effect on trabecular bone in murine experimental osteoarthritis. *Arthritis & Rheumatology*, 58: 2379-2386.
- Kammermann, J.; Kincaid, S.; Rumph, P.; Baird, D. and Visco, D. (1996). Tumor necrosis factor- α (TNF- α) in canine osteoarthritis: immunolocalization of TNF- α , stromelysin and TNF receptors in canine osteoarthritic cartilage. *Osteoarthritis and Cartilage*, 4: 23-34.
- Kellgren, J. and Lawrence, J. (1957). Radiological assessment of osteo-arthrosis. *Annals of the Rheumatic Diseases*, 16: 494.
- Lorenz, H. and Richter, W. (2006). Osteoarthritis: cellular and molecular changes in degenerating cartilage. *Progress in Histochemistry and Cytochemistry*, 40: 135-163.
- Lubar, D.; White, P.H.; Callahan, L.F.; Chang, R.W.; Helmick, C.G.C.; Lappin, D.R. et al. (2010). A national public health agenda for osteoarthritis 2010. paper presented at Seminars in Arthritis and Rheumatism, Elsevier, 39: 323-326.
- Nikahval, B.; Nazifi, S.; Aliabadi, F.; Mansourian, M. and Imani, H. (2013). Measurement of interleukin-1 β and interleukin-6 in synovial fluid of osteoarthritic dogs. *Bulgarian Journal of Veterinary Medicine*, 16: 282-288.
- Pelletier, J.P.; Boileau, C.; Brunet, J.; Boily, M.; Lajeunesse, D.; Reboul, P. et al. (2004). The inhibition of subchondral bone resorption in the early phase of experimental dog osteoarthritis by licofelone is associated with a reduction in the synthesis of MMP-13 and cathepsin K. *Bone*, 34: 527-538.
- Pelletier, J.P.; Martel-Pelletier, J. and Abramson, S.B. (2001). Osteoarthritis, an inflammatory disease: potential implication for the selection of new therapeutic targets. *Arthritis & Rheumatology*, 44: 1237-1247.
- Pilichou, A.; Papassotiropou, I.; Michalakakou, K.; Fessatou, S.; Fandridis, E.; Papachristou, G. and Terpos, E. (2008). High levels of synovial fluid osteoprotegerin (OPG) and increased serum ratio of receptor activator of nuclear factor- κ B ligand (RANKL) to OPG correlate with disease severity in patients with primary knee osteoarthritis. *Clinical Biochemistry*, 4: 746-749.

- Pond, M. and Nuki, G. (1973). Experimentally-induced osteoarthritis in the dog. *Annals of the Rheumatic Diseases*, 32: 387.
- Radin, E.L. and Rose, R.M. (1986). Role of subchondral bone in the initiation and progression of cartilage damage. *Clinical Orthopaedics and Related Research*, 213: 34-40.
- Riyazi, N.; Slagboom, E.; de Craen, A.J.; Meulenbelt, I.; Houwing-Duistermaat, J.J.; Kroon, H.M. et al. (2005). Association of the risk of osteoarthritis with high innate production of interleukin-1 β and low innate production of interleukin-10 ex vivo, upon lipopolysaccharide stimulation. *Arthritis & Rheumatology*, 52: 1443-1450.
- Shimizu, S.; Asou, Y.; Itoh, S.; Chung, U.I.; Kawaguchi, H.; Shinomiya, K. and Muneta, T. (2007). Prevention of cartilage destruction with intraarticular osteoclastogenesis inhibitory factor/osteoprotegerin in a murine model of osteoarthritis. *Arthritis & Rheumatology*, 56: 3358-3365.
- Spahni, A.I.; Schawalder, P.; Rothen, B.; Bosshardt, D.D.; Lang, N. and Stoffel, M.H. (2009). Immunohistochemical localization of RANK, RANKL and OPG in healthy and arthritic canine elbow joints. *Veterinary Surgery*, 38(6):780-786.
- Stannus, O.; Jones, G.; Cicuttini, F.; Parameswaran, V.; Quinn, S.; Burgess, J. and Ding, C. (2010). Circulating levels of IL-6 and TNF- α are associated with knee radiographic osteoarthritis and knee cartilage loss in older adults. *Osteoarthritis and Cartilage*, 18: 1441-1447.