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OSTEOARTHRITIS

Animal data show VEGF blocker inhibits post-traumatic OA

Early treatment with the anti-VEGF antibody bevacizumab retards the development of post-traumatic knee osteoarthritis (OA), according to new results published in *Arthritis Research & Therapy*.

Masato Sato and colleagues' study shows that systemic bevacizumab treatment reduces synovitis, osteophyte formation and articular cartilage degradation in a rabbit model of OA caused by anterior cruciate ligament (ACL) transection. Moreover, intra-articular administration of bevacizumab additionally reduced pain-related behaviours in these animals.

Intravenous bevacizumab was not associated with adverse effects in healthy control rabbits or animals with OA, and the researchers concluded that intravenous administration of bevacizumab could be a promising treatment option for polyarthritis, whereas intra-articular administration might be considered for patients with single-site arthritis.

> "...intra-articular administration might be considered for patients with single-site arthritis"

Gene expression profiling experiments showed that in rabbits receiving intravenous bevacizumab synovial expression of *MMP13* and *ADAMTS5* was considerably lower than in control animals with untreated OA (suggesting decreased inflammation, although synovial *IL1B* expression was unchanged). Moreover, expression of *LECT1* in articular cartilage was elevated (suggesting inhibition of angiogenesis and stabililization of chrondrocyte phenotype), in rabbits receiving intravenous bevacizumab versus controls with untreated OA.

Thus, VEGF blockade seems to prevent both synovial inflammation and angiogenesis (which is associated with innervation) in articular cartilage. The pain relief associated with intra-articular bevacizumab might be related to either or both these effects.

By contrast, bevacizumab treatment had no effect on *VEGF* gene expression or mRNA levels in the synovium—perhaps because these markers were measured just 4 weeks after ACL transection. Binding of bevacizumab to VEGF does not prevent expression of *VEGF*, which is needed for cartilage survival. VEGF is also essential for chondrocyte survival, and expression of *RUNX2*, which regulates subchondral bone formation, also significantly decreased with bevacizumab treatment. "Bevacizumab contributes to the inhibition of osteosclerosis in the subchondral bone and inhibits osteophyte formation," Sato *et al.*'s report concludes.

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Original article Nagai, T. *et al.* Bevacizumab, an anti-vascular endothelial growth factor antibody, inhibits osteoarthritis. *Arthritis Res. Ther.* doi:10.1186/s13075-014-0427-y