Treating Experimental Osteoarthritis And Rheumatoid Arthritis With Calcitonin – A Systematic Review And Meta-Analysis Of Preclinical Data

General Topics / Basic Sciences

Mara Meyer Günderoth¹, Alexandra Bannach-Brown², Alexander Hildebrandt¹, Florian Nima Fleckenstein³, Tobias Winkler¹, Carsten Perka¹, Ulrich Stöckle¹, Georg Duda⁴, Serafeim Tsitsilonis¹, Johannes Keller⁵, Robert Karl Zahn¹, Tazio Maleitzke¹

- 1. Charité Universitätsmedizin Berlin, Center for Musculoskeletal Surgery, Berlin, Germany
- 2. Charité Universitätsmedizin Berlin; QUEST Center for Transforming Biomedical Research, Berlin Institute of Health, Berlin, Germany
- 3. Charité Universitätsmedizin Berlin, Department of Diagnostic and Interventional Radiology, Berlin, Germany
- 4. Berlin Institute of Health at Charité Universitätsmedizin Berlin, Julius Wolff Institute, Berlin, Germany, Berlin, Germany
- 5. Department of Trauma and Orthopedic Surgery, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Keywords: Bone, Cartilage, Calca, Calcitonin, Joint

Background

Rheumatoid arthritis (RA) and osteoarthritis (OA) are the most common forms of arthritis and affect large parts of the global population. To date, pharmacological therapies have been ineffective in addressing bone erosions and cartilage degradation. Calcitonin (CT), a 32 amino acid peptide, has known anti-resorptive effects on cartilage and bone and was formally applied in osteoporosis treatment. An unfavorable safety profile and high costs led to an almost complete withdrawal of CT from the osteoporosis market, yet efficacy data for RA and OA treatment are still scarce.

Objectives

To investigate the efficacy of CT administration in animal models of experimental OA and RA.

Study Design & Methods

A systemic literature search was conducted in PubMed/MEDLINE and Embase databases to identify articles with original data on CT treatment of preclinical OA and RA. The SYRCLE's risk of bias tool for animal intervention studies was used to assess methodological quality. To provide summary estimates of efficacy, a meta-analysis was conducted for outcomes reported in four or more studies, using a random-effects model. Subgroup analyses were employed to correct for study specifics. The study followed PRISMA guidelines.

Results

Twenty-six studies were ultimately included in the systematic review. Data from 13 studies were used for the meta-analysis, which included the following outcomes: bone mineral density, bone volume, levels of cross-linked C-telopeptide of type I collagen, Mankin score and mechanical allodynia. For all considered outcome parameters, CT-treated groups were significantly superior to control groups (p=0.002; p=0.01; p<0.00001; p=0.0009; p=0.04). For most outcomes, effect sizes were significantly greater in OA than in RA (p<0.05) and when interventions lasted for longer than 56 days (p<0.05).

Conclusions

There is preclinical evidence for an antioxidant, anti-inflammatory, antinociceptive, cartilage- and bone-protective effect of CT in RA and OA. Given these effects, CT presents a promising agent for the treatment of both diseases, although the potential seems to be greater in OA. New CT formulations have recently been introduced, promising fewer side effects and greater efficacy, that may be further explored in the context of RA and OA.