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Intra-articular metallic **gold micro particles relieve pain** and enhance function in patients with **knee osteoarthritis**

A pilot study

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Aim of Investigations

Many patients suffering from osteoarthritis (OA) do not get adequate pain relieve. Current therapies relieve pain to some extent and up to 30 % having an arthroplasty do not achieve sufficient improvement.

Animal studies indicate gold ions have a long-acting effect on OA pain. The immuno-modulatory effect of gold ions have for more than 50 years a known anti-inflammatory effect in the treatment of rheumatic arthritis. Gold ions alter the function of macrophages by inhibiting lysosomal enzymes and lowering production of pro-inflammatory cytokines[1-2].

Dissolucytotic metallic gold (DMG) ions have an immune-suppressive effect in laboratory testing[3-5] (**Figure 1-3**). Animal studies prove the effect of gold implantation in arthritic joints[6-9]. Injection of DMG in animal models stimulate the immune system[10-11]. The carrier for injecting the DMG micro particles is hyaluronic acid [12-13].

No studies have investigated the effect of intraarticular gold micro particle implants for treatment of knee osteoarthritis in humans. The present open, pilot study aimed to investigate if gold ions have a role in treating knee osteoarthritis[14].

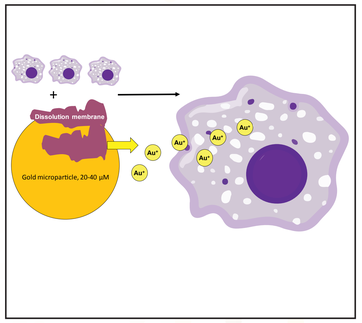

Figure 1: Macrophages controls the dissolution membrane which liberate the gold ions by oxidation of the surface. Once the ions are liberated, most likely as Dicyanogold [Au(CN)2]-, they are free to diffuse through the immediate microenvironment. The gold-loaded molecules are taken up into the cells, primarily macrophages, mastcells and histocytes.

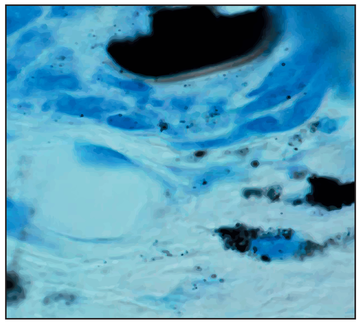

Figure 2: Close to the gold implant gold-loaded molecular clusters are located outside cells. The two loaded cells are believed to be macrophages loaded with gold ions. The gold ions accumulate primarily in the lysosymes. 3. Danscher G. Histochem Cell Biol 2002; 117:447–452

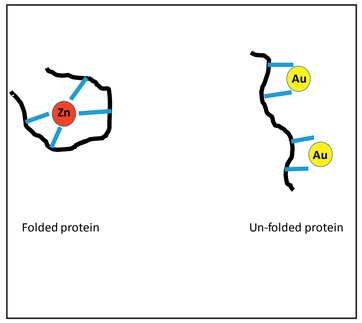

Figure 3: Once in the intercellular fluid and the intracellular compartments, i.e. lysosomes, the gold ions act in the same ways that have been demonstrated for systemically administered gold ions. Gold ions suppress inflammation locally probably partly by affecting certain signalling molecules and binding enzymes essential for the inflammatory process. The reduced production of pro-inflammatory cytokines might relate to the ability of the gold ions to unfold the protein structures.

Methods

A cohort of 30 patients referred for treatment of knee OA, aged ≥18years, pain ≥ 3 months, synovial effusion on MRI, and Kellgren-Lawrence OA grade 3-4 were included. Exclusion criteria were malignancy, active infection and antibiotic treatment, active treatment with steroids, biological or other anti-Rheumatic medication, inability to comply with the protocol, inadequacy in written and spoken national language. Of 38 eligible patients, 32 met the criteria, 1 did not attend and 1 refused. Age was 63 (46-75) year, BMI 28.8 (22.8-41.7), 18 were men 12 women. Metallic gold 20 mg, 72.000 pieces, 20-40 my-meter in diameter (Berlock-Micro-Implants, BMI, Goldtreat APS) [12-13] were injected into the knee joint using the patient's own synovial fluid as the carrier. Outcome measures were WOMAC pain, stiffness and function, PainDetect questionnaire, and Quantitative Sensory Testing (QST) (pressure pain threshold assessed over the knee joint) at inclusion and after 8 weeks.

Results

Pain and function improved in 25 of 30 patients. Womac pain decreased from 9 (6-16) to 3 (0-15), stiffness from 4 (1-8) to 2 (0-8), function from 29 (14-51) to 11 (0-41) (**Figure 4**), PainDetect decreased from 10 (1-26) to 3 (0-19) (**Figure 5**). Pain pressure thresholds increased (anti-hyperalgesia) from 598 kPa (276-1043) to 616 kPa (349-1089) (**Figure 6**). All differences, P < 0.05 (Wilcoxon sign test).

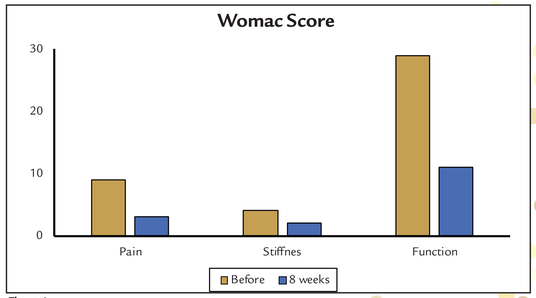

Figure 4

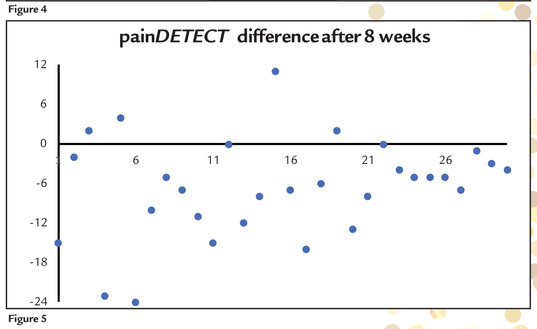

Figure 5

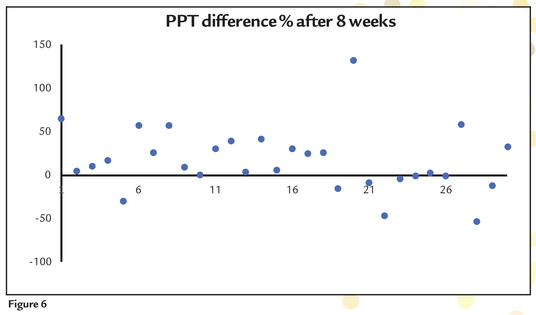

Figure 6

Conclusions

Intra-articular metallic gold improved joint pain, stiffness and function. The increased pressure pain threshold indicate less joint hyperalgesia. Intra articular gold particles may modify the synovial inflammation as a part of the sensitization in knee OA patients. In this cohort of patients with moderate to severe knee osteoarthritis and synovial effusion intra-articular metallic gold relieved pain and enhanced function in more than 80 % of the patients. This study suggests a basis for a future placebo controlled randomized trial in OA patients.

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