Letters to the Editor

Effects of intra-articular hyaluronic acid and corticosteroid therapies on articular cartilage in experimental severe osteoarthritis

Sirs,

Although both corticosteroid and hyaluronic acid (HA) injections are widely used to palliate the symptoms of knee osteoarthritis (OA), Intraarticular steroids are recommended in several guidelines for the treatment of OA. While it was reported in some previous studies that it resulted in the worsening of osteoarthritic lesions (1), it has been demonstrated in experimental models that steroid injections reduce progression in cartilage erosions (2). These contradictory publications about steroids, always leave suspicion in the physicians' mind regarding their usage. HA has been reported to exert a disease-modifying OA drug effect in some experimental models of OA (3). However, there are also opinions defending that HA is not superior to placebo and therefore it may not be involved in the routine treatment of OA (4).

The effect of hyaluronan was compared with that of a corticosteroid which is accepted to have beneficial effects in OA. However, there is no evident data regarding their efficacy in severe knee OA. The present study examined the effect of intraarticular HA and methylprednisolone injection on the articular cartilage and synovium that occured during the advanced stage of OA in the experimental model.

Twenty-two adult New Zealand rabbits were used in this study. The experimental OA was induced by papain (2 mg). Five weeks after the intraarticular injection of papain, the rabbits were randomly divided into two goups. Group 1: In 12 rabbits, 20 mg methylprednisolone was injected into the right knee once weekly for three weeks. Group 2: In 10 rabbits, HA was injected into the right knee once weekly for three weeks. The left knee joints were used as controls. Macroscopic evaluation of the lesions, including measurement of surface lesions on the condyles and plateaus was conducted along with histologic evaluations of the severity of the lesions.

There were no significant differences between the groups for macroscopic and histologic grades of cartilage lesions on condyles and plateaus and synovium at the end of the treatment ($p > 0.05$). Furthermore, no statistically significant difference was observed between the treated and control knees of the rabbits in each group ($p > 0.05$).

We observed that both treatment methods were not different for macroscopic and histologic evaluations and did not create any effect resulted in regeneration or progression for cartilage lesions.

Although there is some data which reveals that intraarticular HA application has the feature of modifying the disease (3), this effect may not be supported throughout by the present limited evidence. Furthermore, there is no exact evidence regarding its effects in such cases with further stages of OA. Contrary to studies revealing that minimal degrees of benefits were gained from intrarticular HA (4, 5), some clinical studies (6) have suggested that HA compared with placebo has chondroprotective effects (3, 7). Brandt (8) recently found that neither prophylactic nor therapeutic administration of HA an effect on the severity of OA pathology.

Studies in which steroid and HA applications are compared with each other are present in literature (9, 10). In these studies, HA and steroid have been found to be effective clinically but HA has a long-term beneficial effect (11).

It has been revealed that treatments applied in this way not only have useful effects, but they also do not have any harmful effects on the lesion and its surroundings.

No study has been seen in which these two treatments are compared in only severe knee OA. Whereas, all of these treatments are used distinctly in clinical practice. These treatments have been found to be ineffective histologically in severe knee OA, while their efficacy has been revealed clinically and histologically in early stages of knee OA.

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References

1. ROBION FC, DOIZE B, BOURE L *et al.*: Use of synovial fluid markers of cartilage synthesis and turnover to study effects of repeated intra-articular administration of methylprednisolone acetate on articular cartilage *in vivo*. *J Orthop Res* 2001; 19: 250-8.
2. PELLETIER JP, MINEAU F, RAYNAULD JP, WOESSNER JF, SMITH ZG, PELLETIER JM: Intraarticular injections with methylprednisolone acetate reduce osteoarthritic lesions in paralel with chondrocyte stromelysin synthesis in experimental osteoarthritis. *Arthritis Rheum* 1994; 37: 414-23.
3. TAKAHASHI K, GOOMER RS, HARWOOD F, KUBO T, HIRASAWA Y, AMIEL D: The effects of hyaluronan on matrix metalloproteinase-3, interleukin -1 beta and tissue inhibitor of metalloproteinase-1 gene expression during the development of osteoarthritis. *Osteoarthritis Cart* 1999; 7: 182-190.
4. TAMIR E, ROBINSON D, KOREN R, AGAR G, HALPERIN N: Intra-articular hyaluronan injections for the treatment of osteoarthritis of the knee: A randomized, double blind, placebo controlled study. *Clin Exp Rheumatol* 2001; 19: 265-70.
5. KAWANO T, MIURA H, MAWATARI T *et al.*: Mechanical effects of the intraarticular administration of high molecular weight hyaluronic acid plus phospholipid on synovial joint lubrication and prevention of articular cartilage degeneration in experimental osteoarthritis. *Arthritis Rheum* 2003; 48: 1923-9.
6. KARATOSUN V, UNVER B, GOCEN Z, SEN A: Comparison of two hyaluronan drugs in patients with advanced osteoarthritis of the knee. A prospective, randomized, double-blind study with long term follow-up. *Clin Exp Rheumatol* 2005; 23: 213-8.
7. TAKAHASHI K, HASHIMOTO S, KUBO T, HIRASAWA Y, LOTZ M, AMIEL D: Effect of hyaluronan on chondrocyte apoptosis and nitric oxide production in experimentally induced osteoarthritis. *J Rheumatol* 2000; 27: 1713-20.
8. BRANDT KD, SMITH GN, MYERS SL: Hyaluronan injection affects neither osteoarthritis progression nor loading of the OA knee in dogs. *Biorheology* 2004; 41: 493-502.
9. RONCHETTI P, GUERRA D, TAPARELLI F *et al.*: Morphological analysis of knee synovial membrane biopsies from a randomized controlled clinical study comparing the effects of sodium hyaluronate (Hyalgan) and methylprednisolone acetate (Depomedrol) in osteoarthritis. *Rheumatology* (*Oxford*) 2001; 40: 158-69.
10. CABORN D, RUSH J, LANZER W, PARENTI D, MURRAY C: Synvisc 901 study group. A randomized, single-blind comparison of the efficacy and tolerability of hylan G-F 20 and triamcinolone hexacetonide in patients with osteoarthritis of the knee. *J Rheumatol* 2004; 31: 333-43.
11. TASCIOGLU F, ÖNER C: Efficacy of intra-articular sodium hyaluronate in the treatment of knee osteoarthritis. *Clin Rheumatol* 2003; 22: 112-7.

Erratum corrige

In abstract no. **J6** entitled: **Musculoskeletal Manifestations in Adamantiades-Behçet's Disease,** published in Supplement no. 42 *Behçet's Disease and Other Autoinflammatory Conditions no. 6*, (2006; 24: (Suppl. 42) S-41) the authors have brought to our attention that only the name of one author was given. We apologise for this error. The co-authors of this abstract are the following: **P.P. Sphikakis, A. Elezoglou, G. Vaiopoulos, N. Markomichelakis, N. Myriokefalitakis, Ph. Kaklamnis.**