Letters to the Editor

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Re: Karlsson et al. Comparison of two hyaluronan drugs and placebo in patients with knee osteoarthritis. A controlled, randomized, double-blind, parallel-design multicentre study

Sirs, Karlsson et al. [1] are to be congratulated for their well-controlled trial in which the efficacy and safety of intra-articular injections of a hyaluronan (Artzal) and a cross-linked hylan (Synvisc) were compared with those in a phosphate-buffered saline placebo control group. They report statistically significant clinical improvement from baseline at 26 weeks after intra-articular injection in all three treatment groups. A longer duration of benefit of the active treatments compared with placebo was noted only when data for the hyaluronan and hylan groups were pooled.

These results would suggest minimal clinical benefit in knee osteoarthritis (OA) from either a hyaluronan or a hylan. However, 40, 39 and 42% of the patients randomized to the Artzal, Synvise and placebo groups, respectively, had complete loss of joint space, the criterion for Ahlback’s grade II classification [2]. These results differ from those of an earlier randomized controlled trial in knee OA reported by Lohmander et al. [3], in which superior clinical benefit from Artzal compared with placebo was found. In that trial, only 17% of the patients who received Artzal had grade II Ahlback changes. Moreover, the most severe knee for OA radiological grade entry criterion in the majority of published controlled, prospective studies on the safety and efficacy of Synvise was Kellgren and Lawrence grade 3 [4–7]. Although the Kellgren and Lawrence grading scale focuses primarily upon osteophytes [8], the grade 3 classification includes definite narrowing but not complete loss of joint space. Indeed, Petersson et al. [9] found agreement between Kellgren and Lawrence grades 2–3 and Ahlback grade I (0.76) as well as Kellgren and Lawrence grades 3–4 and the Ahlback grade I–II (0.78).

Hylans and hyaluronans appear to be most efficacious in patients with earlier OA who have maintained some radiographic evidence of joint space [10]. The inclusion of a high proportion of OA patients with more advanced disease that may have been refractory to intra-articular hyaluronan therapy would leave their study underpowered to show differences in efficacy between placebo and either Artzal or Synvisc.

The authors have declared no conflicts of interest.

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We thank Drs Magilavy, Polisson and Parenti for their interesting letter concerning our trial comparing different intra-articular treatments with hyaluronan. They have put forward an interesting hypothesis to explain the comparative lack of differences in outcome between the treatment groups in our trial.

The earlier study they referred to, by Lohmander et al. [1], did not find a difference between placebo (saline) and hyaluronan for the whole treatment population. However, subgroup analysis showed an advantage for the hyaluronan-treated group when this...
was limited to those older than 65 yr and with more severe symptoms. Radiological stage of osteoarthritis (OA) was found not to influence outcome in this trial. With this knowledge, the subsequent trial was planned to focus on this particular subgroup of knee OA patients, and found only a small difference between hyaluronan and placebo, and no difference between the two different hyaluronan preparations. A subgroup analysis was not performed in this trial due to power limitations.

Comparison of outcome in different trials of OA is complex because of differences in outcome measures, study populations and other causes. While the explanation suggested by Dr Magilavy and colleagues remains a possibility, there may be many other possible reasons for the different outcomes and conclusions of these trials.

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Reactivation of ancient trochanteric tuberculosis
60 years after surgical drainage

Sir, Tuberculous bursitis with associated osteitis of the greater trochanter is a rare cause of lateral hip pain and most cases were diagnosed in the early part of the twentieth century [1]. However, in those countries such as Spain where tuberculosis infection has had a higher incidence in the past, elderly people are susceptible to reactivate an ancient tuberculosis owing to the impairment of their immune system. With the re-emergence of tuberculosis more atypical osteoarticular cases have been reported [2–4]. Nowadays, the latest modalities in diagnosis and the specific antituberculous drug therapies allow us to make an earlier diagnosis and to find a definitive cure. However, it is necessary to keep in mind that tuberculosis is one of the causes of severe hip pain in elderly people.

We describe an 80-yr-old woman who had a surgical drainage of the trochanter area owing to tuberculous osteitis when she was 20. The patient was admitted to our hospital in 1995 complaining of lateral right hip pain, limping gait, tenderness over the greater trochanter and a skin fistula with a white supurative fluid. Radiographs of the hip showed a partial destruction of the margin of the greater trochanter, lytic foci in the underlying bone and a small focus of calcification in the adjacent soft tissues (Fig. 1). Magnetic resonance imaging showed fluid around the greater trochanter in the subgulteus medium and maximum bursae, revealing the extent of the inflammation within the adjacent marrow and delineating the extent of abscess formation in the gluteal region and subcutaneous tissues (Fig. 2). The bone scan with technetium-99m-labelled leucocytes showed an important uptake of the trochanteric area and tender tissues around it. Blood tests revealed an erythrocyte sedimentation rate of 35 mm/h, C-reactive protein of