Letters to the Editor

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The management of osteoarthritis. Landing on the ground of reality

Sir, The EULAR 2003 recommendations for knee osteoarthritis (OA) include a table with an ‘evidence based final set of 10 recommendations’ [1]. Recommendation number 8 states: ‘SYSADOA [symptomatic slow-acting drugs in osteoarthritis] (glucosamine sulphate, chondroitin sulphate, ASU [avocado and soya unsaponifiables], diacerein, and hyaluronic acid) have symptomatic effects and may modify structure’. Concerning the modifying effect of glucosamine sulphate (GS), the authors refer to just one study (supported by a pharmaceutical manufacturer), including 106 patients with mild to moderate knee OA who showed delayed progression of joint space loss and improvement in pain and function scores with GS compared with placebo over a 3-yr period [2]. The authors also presented these EULAR recommendations at the annual British Society for Rheumatology meeting in Edinburgh in April 2004 and the abstract is included in the April 2004 supplement issue of Rheumatology [3].

I wonder if ‘suggestions’ from studies (with questionable methodological considerations) offer a suitable evidence-based approach for the final EULAR recommendations. One basic comment is that the measure of the width of the medial tibio-femoral joint space in standing antero-posterior radiographs is a problematic approach and not a reliable index of structural modification [4]. It is also a common clinical observation that radiographic severity does not necessarily correlate with clinical symptoms.

We know that GS acts as a substrate for the biosynthesis of glycosaminoglycan chains (GAG) and subsequently for the production of proteoglycans (PG). Even if we accept that the absorption and metabolic fate of oral GS, until its distribution in the articular cartilage for the production of new PGs and cartilage repair, are all successful, we don’t know if the quality of new products is normal. Besides, PG synthesis by chondrocytes is already increased in the early stages of the disease, but new PGs are different from normal ones in the composition and distribution of their GAG, the size of the PG subunit and their ability to aggregate with hyaluronic acid, and this can result in faulty organization of the repair molecules and could even accelerate the breakdown of the cartilage [5].

The same scepticism concerns all the SYSADOA in these final EULAR recommendations. Interestingly, concerning diacerein (DC) the authors identify only one randomized controlled trial in patients with knee OA [6]. Actually this study (again supported by a manufacturer) does not conclude structural modification but it compares only the efficacy of three DC dosages on symptoms of the disease.

I am afraid that at the moment there is no clear evidence for any of the available drugs or dietary supplements in the market that may modify OA progress. Even a symptomatic effect of GA is uniformly positive? Rheum Dis Clin North Am 2003;29:789–801.

I believe there is only one possibility for modifying the progression of the disease: very early diagnosis. MRI is a good diagnostic tool for the study of articular cartilage but it is expensive. Biochemical markers of bone and cartilage metabolism (BMBCM) help but they are not specific (they originate from several tissues, we don’t know if their origin is catabolic or anabolic at a certain time, etc.) [8]. When there is accurate and cost-effective imaging technology for articular cartilage and more specific (and cost-effective) BMBCM become available, the population at high risk for knee OA (e.g. age over 50, female sex, obese) could be screened for early diagnosis. There is now extensive research being done on BMBCM [9]. At the moment the only real management for this disease is to control pain and physical function of the joint using several factors or techniques (non-pharmacological, pharmacological, intra-articular or surgical). Non-pharmacological management, particularly exercises/physiotherapy/education, is the keystone of OA treatment, but unfortunately is under-utilized. In case of pharmacological treatment, as an adjunct [10], paracetamol is the first analgesic of choice as most guidelines suggest [11]. Doctors wishing to use GS or DC could include them in pharmacological management if they really control the pain and physical function of the joint, and probably for safety reasons—but not as disease- or structure-modifying drugs. Medical doctors must be optimistic and convey their optimism to their patients, but in addition they have to be realistic and independent of the influence of pharmaceutical manufacturers.

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Uptake of influenza vaccination in rheumatology patients: reply

Sir, We read with interest the letter regarding uptake of influenza vaccination [1]. We undertook a similar survey in our department in 2003 [2].

Sixty patients on immunosuppressive therapy were identified using data collected from the department’s annual 4-week survey of out-patient activity. These patients were interviewed by telephone. A further 51 patients on immunosuppressive therapy who attended the day case unit or rheumatology ward during April 2003 were interviewed in person.

Data were collected on whether these 111 patients had received their influenza vaccine during the preceding winter and what sources of information about vaccination they were aware of and had utilized. In addition information regarding pneumovax injections was also collected.

As reported by the Grimsby group [1], the majority of patients (81%) had rheumatoid arthritis; just over a quarter were aged less than 50 yr (27%). Sixty-three per cent of patients were on conventional DMARD therapy and/or corticosteroids; the other 37% were on anti-TNF therapy in addition to DMARDs and/or corticosteroids.

Seventy per cent of patients had received their influenza vaccination. The Government’s target for uptake during this period was 70% [3]. Previous departmental surveys of influenza vaccination in 1997 and 2000 showed uptakes of 40% and 56% respectively. There was a clear difference in influenza vaccine uptake according to patient age with the highest uptake in patients over 50 yr of age (83%) compared with only 37% in patients under the age of 50.

The majority of patients (78%) had received information from their GPs; in addition 60% had been aware of information through the media and 64% had received information from the rheumatology department. Six patients sought their vaccinations purely as a result of information provided by the rheumatology department; all six were under the age of 50.

Of the 33 patients who had not received influenza vaccination, 14 would have declined vaccination even if offered and three of these were under the age of 50. All of the remaining 19 patients indicated that they would have accepted vaccination had this been offered; 16 of these were under the age of 50.

Uptake of pneumovax injection within the preceding 10 yr was poor in this patient group (33%). There is currently no Government target for the uptake of pneumovax vaccination and this may well be contributing to the low uptake of this vaccine.

Our results show that, for the local population as a whole, Government targets for influenza vaccination are being met but that there is significant underachievement of these targets in the younger age group. As a result of these findings our department has adopted a policy of more actively targeting influenza vaccine uptake according to patient age with the highest uptake in patients over 50 yr of age (83%) compared with only 37% in patients under the age of 50.

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Weekly alendronate-induced acute pseudogout

Sir, A 47-yr-old nursery nurse with a history of chronic asthma and bilateral knee osteoarthritis sustained three low-trauma fractures over a period of 3 yr. After investigation, she was diagnosed with osteoporosis and commenced on weekly alendronate 70 mg. A few hours after her first dose, she noticed pain and swelling of her right knee. This settled spontaneously over the subsequent 3 days. After the second dose of alendronate, her knee symptoms recurred. The pain was severe, she was unable to weight bear and she felt generally unwell. She was seen in the hospital admissions unit, where she was found to have a warm, swollen and tender right knee with restricted movement. She was systemically well, and blood tests including full blood count, bone biochemistry, urate, erythrocyte sedimentation rate and C-reactive protein were normal. The right knee joint was aspirated and fluid sent for culture. She was treated empirically for a septic monoarthritis and transferred to the rheumatology ward. Synovial fluid culture revealed no growth. Two days later, her left knee also began to swell. Both knees were then aspirated and a yellow, turbid fluid drawn from each knee. Polarizing light microscopy revealed intracellular, rhomboid-shaped crystals with weak positive birefringence; findings typical of calcium pyrophosphate dihydrate (CPPD) crystals. Radiographs of the right knee also revealed chondrocalcinosis. Each knee was injected with intra-articular steroid (Adcortyl) and both settled rapidly. Daily alendronate 10 mg was then commenced, as we hoped that this lower-dose preparation would be less likely to trigger pseudogout, but the patient discontinued the treatment after 2 days because of nausea. During the following 6 months, the patient has avoided bisphosphonates and has had no further attacks of pseudogout. We have attempted to treat her osteoporosis with raloxifene, but she had to stop this after developing a rash. She currently remains on calcium and vitamin D supplements and is awaiting funding approval for a trial of parathormone receptor agonist therapy.

The formation and deposition of inorganic pyrophosphate as CPPD crystals is not fully understood [1]. All bisphosphonates are structurally similar to pyrophosphate, and in vitro evidence suggests some effect of bisphosphonates on inorganic pyrophosphate metabolism [2]. However, the precise mechanisms by which

References