OARSI TREATMENT GUIDELINES FOR HIP AND KNEE OSTEOARTHRITIS

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To develop evidence-based international consensus recommendations for the management of hip and knee osteoarthritis (OA). Sixteen experts from 4 medical disciplines (primary care, rheumatology, orthopaedics and evidence based medicine), 2 continents and 6 countries (USA, UK, France, Netherlands, Sweden and Canada) formed the guidelines development team. A systematic review of existing guidelines for the management of hip and knee OA published between 1945 and January 2006 was undertaken using the validated AGREE instrument. The core management modalities were generated based on the agreement between guidelines. Evidence before 2002 was based on a systematic review conducted by EULAR and evidence after 2002 was updated using MEDLINE, EMBASE, CINAHL, AMED, the Cochrane Library and HTA reports. The quality of evidence was evaluated, and where possible, effect size (ES), number needed to treat (NNT), relative risk (RR) or odds ratio (OR) and cost per quality adjusted life years (QALY) gained were estimated. Consensus recommendations were produced following a Delphi exercise and the strength of recommendation for propositions relating to each modality was determined using a visual analogue scale (VAS).

Twenty-three treatment guidelines for the management of hip and knee OA were identified from the literature search, including 6 opinion-based (mean quality score 28%), 5 evidence-based (41%) and 12 based on both expert opinion and research evidence (51%) (p=0.001). Fifty-one different treatment modalities were addressed by these guidelines, but only 20 were universally recommended. Effect size (ES) for pain relief varied from treatment to treatment. Overall there was no statistically significant difference between non-pharmacological therapies (ES=0.25, 95%CI 0.16, 0.34) and pharmacological therapies (ES=0.39, 95%CI 0.31, 0.47). Following six Delphi rounds and feedback from OARSI members on the draft recommendations, twenty-five recommendations, spanning non-pharmacological, pharmacological and surgical therapies were agreed. Strengths of recommendation and 95% confidence intervals were provided.

Twenty-five recommendations were generated based on the critical appraisal of existing guidelines, systematic review of research evidence and expert consensus. The recommendations may be adapted for use in different countries or regions according to the availability of treatment modalities and strength of recommendation for each modality of therapy. These recommendations will be revised regularly following systematic review of new research evidence as this becomes available.

ANIMAL MODELS OF OSTEOARTHRITIS: NOT A ONE-SIZE-FITS-ALL SCENARIO

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Purpose: Numerous animal models of osteoarthritis (OA) are utilized by industry and academia for evaluating potential DMOADs as well as understanding the pathophysiology of the disease. The choice of species and mode of OA induction are dependent upon a number of factors.

Methods: The selection of the species to be used depends on the type of study to be performed: e.g. KO studies are restricted to mice and gene profiling studies may be better suited to larger animals (dogs, rabbits) in order to be able to collect sufficient quantities of cartilage with no contamination of underlying bone. For the evaluation of potential DMOADs, the method of administration and expertise in those techniques for that species needs to be taken into account, along with compound mechanism, species difference, compound availability, metabolism and pharmacokinetics. Most OA studies are long-term (weeks to months) and require substantial amounts of compound to be synthesized. This in itself can make rodent models vastly more attractive. Certain situations preclude the use of some species. For example, a compound developed for interaction with a human target may not be active in other species, particularly rodents. Under these conditions, an alternate model in a higher species such as dog or monkey, which better mimic the human, should be sought. Where all the candidate animals differ from the human, a transgenic animal may be created which has the human sequence, for drug-screening purposes.

Results: The choice of OA induction, whether spontaneous, surgical or enzymatic, depends upon the question being asked as well as on the historic experience of the investigators. While spontaneous OA resembles the slowly developing nature of human OA in some regards, the unknown etiology of OA in many spontaneous models makes it challenging to obtain robust efficacy. The different sourcing of a similar strain (e.g. STR/ort) following 10 generations of breeding results in a distinct line so that the results may be quite dissimilar. In general, the long duration of spontaneous models requires substantial quantities of compound. The surgical models can vary vastly in the severity and location of the OA lesions induced. In general, we observe that models that are more severe (e.g. ACLT in mice) result in maximal biomechanical damage to the joint that can be challenging to ameliorate with pharmacological treatment. Therefore, a model with more moderate progression of OA over time may be preferred. The enzymatic models (e.g. IA collagenase in mice) can also result in severe erosion to the cartilage, which resembles the ACLT model in the severe erosion of the posterior plateau to the growth plate in a significant proportion of animals.

Conclusions: Since there is no DMOAD in the clinic, no animal model has been validated to be predictive of human OA. Until this situation is rectified, the evaluation of multiple models tailored to the specifics of the study and target is recommended. In this session we will discuss various rodent and non-rodent OA models and highlight the advantages and disadvantages of various models with specific examples where available.

RANDOMIZED CONTROLLED SURGICAL TRIALS: CHALLENGES AND APPROACHES

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Purpose: To highlight the challenges of randomized controlled trials of surgical interventions and to suggest approaches for meeting these challenges.

Methods: This workshop will address key methodological ques-