



## Optimizing the management of osteoarthritis—Transitioning evidence-based guidelines into practical guidance for real-world clinical practice



Osteoarthritis (OA) of the knee and hip is a major cause of disability, ranking as the 11th highest contributor to global disability in the 2010 Global Burden of Disease study [1]. Knee OA affects around 4% of the global population (hip OA, 0.85%) and the years of life lived with disability (YLDs) for hip and knee OA was calculated at 17.1 million in 2010 [1]. With the increasing aging population and rise in obesity worldwide, OA is forecast to become the fourth leading cause of disability by 2020 [2], placing a huge demand on health services to treat hip and knee OA. What can be done to halt the progression of this disease, minimize the impact on patient's quality of life, and restrict the burden on healthcare resources?

The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) has set out to provide practitioners with the latest clinical and economic information, allowing them to optimize the management of OA in their daily practice. A first step in this process was the publication of a treatment algorithm for knee OA derived from analysis of the evidence base but with emphasis on providing a practical, step-wise approach to the management of OA patients [3].

In this issue, the ESCEO task force has revisited this guidance, with an emphasis on real-world evidence for the clinical and economic aspects of OA disease management. The consensus statement included herein provides an update on selected pharmacological interventions that are demonstrated to furnish control of pain and other symptoms [4], improvement in function, and, in some cases, long-term disease-modifying effects that impact on healthcare resource utilization, such as delay in total joint replacement (TJR) surgery. A significant reduction ( $p = 0.024$ ) of 57% in the risk of TJR over 5 years has been demonstrated only following treatment with patented crystalline glucosamine sulfate (pCGS) (Rottapharm) [5] for 3 years [6].

Bruyère et al. [7] examine the evidence for one of the symptomatic slow-acting drugs in osteoarthritis (SYSADOAs), glucosamine, which has received some variance in the level of recommendation attributed to it, due to the multiple formulations that differ substantially in their molecular formulation and dose regimens and hence efficacy afforded. Overall, there is consensus across the guidelines to consider that glucosamine hydrochloride (GH) is deprived of any benefit. Conversely, in guidelines and meta-analyses that separately assess the various formulations of glucosamine, pCGS is consistently rated as providing a greater benefit than placebo or active comparators such as paracetamol (acetaminophen).

Real-life pharmaco-economic studies demonstrate a long-term reduction in the need for pain analgesia and non-steroidal anti-

inflammatory drugs (NSAIDs) with pCGS therapy over 12 months, with significant reduction, of over 50%, in costs associated with medication, healthcare consultations and examinations ( $p = 0.024$ ) [6,8]. The results of the Pharmacology of GonArthroSis (PEGASus) study that sought to determine the impact of SYSADOAs on the use of NSAIDs are presented in this issue [8]. Over 6450 hip and knee OA patients consulting with a general practitioner (GP) or rheumatologist in France for a symptom flare were recruited into the PEGASus study and received a SYSADOA treatment, which included pCGS, GH, chondroitin sulfate, avocado-soybean unsaponifiable, or diacerein. Starting SYSADOA treatment, switching SYSADOAs, continuation or discontinuation was permitted during the 2-year follow-up. Among all SYSADOA treatments, only pCGS achieved a significant reduction in NSAID use of 36% (odds ratio [OR] = 0.64, 95% CI: 0.45–0.92).

Rannou et al. [9] consider the evidence for the efficacy of topical NSAIDs in hand and knee OA. In real-life studies, topical NSAIDs demonstrate a level of efficacy equivalent to that of oral NSAIDs for knee pain during 1 year of treatment. There is some heterogeneity between different topical NSAID formulations and the selection of agents that demonstrate good absorption and thus bioavailability, such as etofenamate and diclofenac, is important for good efficacy. Topical NSAIDs are not associated with the side effects attributed to oral NSAIDs due to their lower systemic absorption.

The safety of oral NSAIDs in chronic administration has been called into question in recent years due to the appearance of significant upper gastrointestinal (GI) complications and cardiovascular (CV) adverse events. However, NSAIDs are non-homogenous and there are vast differences in adverse event (AE) risk for GI and CV events. Pelletier et al. [10] examine the safety evidence for oral NSAIDs finding that NSAIDs can provide a safe and effective treatment for OA in real-life situations if prescribed appropriately. Among OA patients who fail to respond to NSAIDs, use of the sustained-release formulation of the weak opioid tramadol, provides good pain control while minimizing AEs and treatment discontinuations.

Maheu et al. [11] examine the evidence from real-life studies for repeated intra-articular hyaluronic acid (IA HA) injection, which demonstrates that IA HA can provide an improvement in pain and function lasting up to 40 months (12 months after the last injection). The clinical benefit of IA HA may be 2-fold, comprising mechanical viscosupplementation and the induction of endogenous HA production, so providing lasting effect. There is increasing evidence that the molecular weight of the HA

preparation may be important, and the magnitude of the clinical effect is different for different HA products. IA HA injections are generally safe, although a higher occurrence of local reactions and flares has been reported with high molecular weight cross-linked hylans.

Ultimately, a goal of OA management is to prevent or delay development of the disease. The results of the PRevention of knee Osteoarthritis in Overweight Females (PROOF) study presented in this issue [12], demonstrate, for the first time, that the daily administration of pCGS (1500 mg/day) is able to prevent the onset of knee OA in women at risk. The incidence of newly diagnosed OA (measured as  $\geq 1$  mm minimum joint space narrowing) among the cohort of 204 women aged 50–60 years (with BMI  $\geq 27$  kg/m<sup>2</sup>) was reduced by 59% over 2.5 years of follow-up (OR = 0.41; 95% CI: 0.20–0.85;  $p = 0.02$ ). Notably, the addition of a 6-month diet and exercise program gave no significant benefit above that obtained with pCGS prophylaxis.

We hope that this joint effort of numerous clinicians and scientists across Europe and North America has produced a comprehensive and useful supplement to facilitate the practical management of OA worldwide, and that readers will benefit as much from this supplement as we have enjoyed collaborating on it.

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