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Intra-Articular Treatments Horizons in Osteoarthritis

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Arthritis falls into two very broad categories, which are not mutually exclusive. The most common is Osteoarthritis (OA), in which a primary feature is degeneration of articular cartilage, often accompanied by evidence of soft tissue inflammation ranging from subtle to overt. The other broad category contains inflammatory arthropathies, of which rheumatoid arthritis and psoriatic arthritis are the most common examples [1].

Therapies focus on reducing symptoms such as pain and stiffness, and minimizing functional limitation and disability. Being the primary aim of treatment patients, pain control is a primary outcome measure in evaluating treatment response. Symptomatic pharmacology for OA primarily consisted of non-steroidal anti-inflammatory drugs (NSAIDs) and intra-articualar (IA) injections of corticosteroids [1,2]. Other agents, including strong opioids, are often needed when the pain is severe and chronic and literature review suggests that few patients needed doses higher than an oral morphine equivalent amount (MEA) of 40-60 mg [3]. However, the associated side-effects of these agents generated interest in developing alternative treatment modalities [4]. One such modality is viscosupplementation, in which IA injection of Hyaluronic Acid (HA) is used to restore the viscoelastic properties of synovial fluid with the potential for disease modification through improvement of synovial fluid quality and/or quantity [5]. The efficacy and tolerability of HA have been demonstrated in numerous clinical trials carried out over the past 15 years [4-6]. In 2011, Migliori et al published results of their trial in which studied for 18 month a cohort of 120 patients affected by hip OA treated with ultrasound guided intra-articular HA injections administered every 6 months reporting a reduction in all algofunctional indexes at 3 months demonstrating a beneficial effect and safety in the management of symptomatic hip OA [6]. In the same last year, Navarro-Sarabia et al. [7] at conclusion of the AMELIA project, a multicentre, randomised, patient and evaluator-blinded, controlled study of 306 patients fulfilling American College of Rheumatology criteria for knee OA, grades II-III, reported evidence the repeated cycle of intrarticular injections of HA non only improve knee OA symptoms during the in-between cycle period but also exert a marked carry-over effect for at least 1 year after the last cycle. Moreover, Foti et al. [4] reported that the HA injections are safe and well tolerated and have a relevant rehabilitation impact in OA patients. There are actually a number of products that try to mimic what should b in the joint. They vary in their molecular weight and their concentrations. Recently, Pavelka et al. [8] reported that similar effects were founded using different HA with non-inferiority between two different HA. The idea behind all of them is that, if you can mimic what the joint needs, you would be able to forestall the progression of arthritis to the irreversible bone and cartilage changes, but also you could enable patients to function in a more normal way.

With new research horizons that aim towards the study of HA actions, Yu et al. [9] recalled that mechanically or physically,/rather than chemically, trapped HA could function as an "adaptive" or "emergency" boundary lubricant to eliminate wear damage in shearing cartilage surface. They reported that coefficient of friction and wear resistance depend on how the lubricating molecules are attached to and organized at the surface concluding that to provide both the low coefficient of friction and good wear protection of joints under physiological conditions, some or all of the four major components of joints-HA, lubricin, lipids and the cartilage fibril-must act synergically in ways that are still to be determined. Bao, Chen and Wu [10] reviewed recent findings with regard to the possible role of lubricin, a glycoprotein synthesized by chondrocytes located at the surface of articular cartilage, in the progression of OA and further discussed it as a novel potential biotherapeutic approaches for the treatment of OA. Recent studies demonstrate that administration with recombinant lubricin in the joint cavity would be effective in the prevention of cartilage degeneration in animal OA models. Medical science is moving forward at an unprecedented rate on all fronts and recent trials provided evidences of effectiveness of other molecules beyond HA such as Botulinum toxin type A [11,12], Capsaicin [13], Sodium clodronate [14] and Opioid [1,2]. As reported by Uthman et al. [1] in their review, other substances such as orgotein, radiation synovectomy, dextrose prolotherapy, silicone, saline lavage, saline injection without lavage, analgesic agents (bupivicaine, morphine), NSAIDs (tenoxicam, indoprofen, phenylbutazone), glucosamine, somatostatin, sodium pentosan polysulfate , chloroquin,mucopolysaccharide polysulfuric acid ester,lactic acid solution, thiotepa, cytostatica have been investigated as potentially therapeutic in the treatment of arthritic joints [1].Within all, two recent lines of research deserve here a mention: Platelet-rich plasma (PRP) and stem cell (SM). PRP actions are beyond the scope of this article; Kon have recently reported a prospective comparative study level II of evidence in which compared PRP and viscosupplementation reporting that autologous PRP injections showed more and longer efficacy than HA injections in reducing pain and symptoms and recovering articular function [15]. Mesenchymal SM, too, could have a role in the healing process of osteoarthritis as studied in animal models [16] and a recent major experimental tissue engineering initiative of a British Group [17] aims to have the potential to revolutionise the treatment of osteoarthritis aiming within five years to treat osteoarthritis by introducing stem cells into damaged joints via keyhole surgery. Next April 2012 in Boston USA- will be held the 8th Stem Cell Research and regenerative Medicine Summit where distinguished speakers will discuss the overcoming challenges in clinical development, the novel advances and technology in SM research, the regulatory guidance, updates and the funding opportunities for the advances in regenerative medicine and tissue engineering. Finally, intra-articular Interleukin-1 inibhitor deserve here a citation after that intra-articular injection of IL-1 into the knee joints of rabbits showed to produce a synovitis associated with the

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loss of proteoglycan from the matrix of articular cartilage. Researchers believe that this experimental finding [18] suggests that antagonism of IL-1 could offer a relatively new intra-articular therapeutic approach to OA. As we have briefly seen, contrary to the perception of many, it is not only the molecular sciences which are leading the way. Molecular biology certainly has played a major role in our understanding diseases, but new imaging techniques, new hardwares, biochemistry of tissue regulatory factors and new techniques in immunology have given us the opportunity to ask basic questions about OA processes which would have been thought impossible to address just a few years ago. In order to improve intra-articular treatment effectiveness, the different aspects of the process of OA need to be related to symptoms letting clinicians to "grade" the disease, and the future for clinical research in OA is so postulated. Examples are provided within the contributions of Wang Y et al. [19] about the increased Follistatin-like protein 1 expression that could be a characteristic of osteoarthritis (OA) patients. They reported FP1 to be a potential serum biomarker that might reflect the severity of joint damage with a potential application for monitoring the course of the disease and the efficacy of therapies in OA patients. In conclusion, managing OA is an arduous task. As it has happened before in the history of scientific communication [20], often some people with great passion and love for their discipline decided to unit their strength to report research thoroughly a new journal. Our passion, easily deduced from the title of the journal, is about a pathology whose impact is still underestimated. A physician interest who care patient suffering from Arthritis must extend in these fields, from basic Science to Clinical and Surgical Biomedicine and Rehabilitation and we have to believe wholeheartedly in our work, enjoy the support of researchers who share our passion, avoid scepticism and raise doubts about the effectiveness of all new medical approaches and prevent the therapeutic enthusiasm that can be rampant after a new singular approach.

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