MULTICENTER PROSPECTIVE STUDY TO ASSESS EFFICACY AND SAFETY OF INTRA-ARTICULAR INJECTION OF A SOLUTION COMBINING HYALURONIC ACID AND CHONDROITIN SULPHATE IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Objectives: To assess efficacy and safety of a single intra-articular injection of a solution combining hyaluronic acid (HA) 60 mg and chondroitin sulphate (CS) 90 mg in 3 ml on patients with knee osteoarthritis (OA) in a multicenter prospective study.

Methods: 79 outpatients (predominantly females - 81.0%) from 5 RF constituent territories with primary tibiofemoral Kellgren-Lawrence score grade II or III knee OA, ≤40 mm pain intensity during walking on visual analogue scale (VAS), requiring NSAIDs intake (for at least 30 days during 3 months prior to enrollment) were included into the study after signing the informed consent form. Mean age was 60.3 ± 8.7 years, mean BMI = 29.2 ± 4.7 kg/m ², disease duration – 6 (3 - 10) years. Grade II OA was documented in 68.4% of patients, Grade III - in 31.6%. The study lasted for 6 months. Efficacy and safety evaluations were made based on VAS pain assessment, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) – (WOMAC pain (0-500), WOMAC function (0-1700), WOMAC stiffness (0-200)), VAS patients’ health status, EQ-5D-based assessment of patients’ quality of life, global physician’s and patient’s efficacy assessment, and daily NSAIDs requirements.

Results: Obtained results demonstrate statistically significant VAS pain reduction during walking already in 1 week after intra-articular injection of the combination (respectively, 62 (55-72) and 41 (32-51) mm, p<0,0001). Moreover, pain continued to subside during all 3 months of follow up (in 1 month – 28 (20-42), in 3 months – 22 (14-37) mm). A significant pain reduction achieved at Mo 3 persisted until Mo 6 - 20 (14-42) mm, without documented pain increase (Fig. 1). Similar trends were observed with total WOMAC score (1125 (899-1540) – at baseline, and 552 (309-837) mm – by the end of the study, p<0,0001), and all WOMAC sub-scores (296 (189-312) – baseline WOMAC pain, 91 (48-171) mm – by the end of the study p<0,0001; Fig. 2); stiffness – 101 (59-130) and 40 (20-61) mm, p<0,0001; function – 802 (647-1095) and 402 (191-638) mm, p<0,0001, respectively). Median time to the onset of therapeutic effect was 7 (5-18) days. Statistically significant improvement of patients’ quality of life by EQ-5D and general health status was observed during all follow up period (respectively, 0.52 (-0.02-0.59) and 0.69 (0.59-0.80), p<0.0001; 48 (30-60) and 72 (60-80) mm, p<0.0001). One injection of the drug resulted in dose reduction or discontinuation of NSAIDs therapy: at baseline 76 patients (96.2%) were taking NSAIDs, in 1 month 31 (39.2%) patients discontinued NSAIDs, in 1 month – 72.2%, in 3 months – 73.4%, and by the end of the study at Mo 6 – 54.4% were not taking NSAIDs. These data were consistent with physician’s and patient’s global assessment of the efficacy of treatment, who stated «significant improvement» and «improvement» in the majority of cases, with only few «no effect» or «worsening» cases documented in analyzed population. Adverse events, such as worsening of pain and/or swelling of the joint, were documented in 8 patients (10.1%); they resolved spontaneously or following NSAIDs intake.

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Conclusion: These results suggest that intra-articular injections of hyaluronic acid plus chondroitin sulfate in patients with knee OA are efficient and safe. A single injection of the drug resulted in statistically significant reduction of pain and stiffness, reduction in NSAIDs intake, as well as improvement in patients' quality of life and function.

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Background: Osteoarthritis (OA) is a pathology that includes several disorders that produce the same symptomatology: pain, functional impotence and inflammation. It lacks therapies that act over the physiopathology of the disease, rather than over the symptoms [1]. Patients’ phenotyping is essential to describe the disorders underlying the OA symptoms, and would allow applying treatments to the altered conditions, in a personalized medicine approach.

Objectives: The HOLOA project aims to design a multivariate model that allows classifying knee OA patients according their characteristics in 3 areas: pain, clinical/morphological characteristics and articular defects. The present work is a preliminary study with the aim to describe the clinical and gait dynamics differences between OA patients classified by treatment: conservative (CNS) vs arthroplasty surgery (ART).

Methods: Prospective study of OA patients graded 2-3 in KL scale and classified by treatment. Both groups are paired by genre, age, and BMI. The studied variables are: WOMAC index (Pain (Wp), Stiffness (Wst) and Function (Wf), Hospital Anxiety and Depression Scale (HADS), London Chest Activity of Daily Living scale, Modified Baecke Physical Activity Questionnaire, Pain Catastrophizing Score (PCS), pain threshold (according to the extended peripatelar map of Arent-Nielsen) pain sensitization at the tibia anterior surface, pain temporal summation (these 3 parameters are measured with the use of an algometer [2]), ultrasound measurement of synovial hypertrophy and effusion, and gait analysis (with Helen Hayes marker protocol). Inverse dynamic analysis was performed to compute the reaction forces and torques of the OA and control leg [3]). Multivariate analysis of variance was performed for the treatment, genre, age and BMI.

Results: Only treatment factor related differences are reported. ART group present significant higher values in Wst (p=0.012), Wf (p=0.018), and PCS (p=0.018), than CNS group (Figure 1). Differences in PCS values show interaction with BMI (p=0.007) (Figure 2). Regarding the joint, number of painful sites depend on treatment and BMI group (p=0.032)(Figure 3). Finally, gait study show no direct effect of the treatment, interactions are observed in the reaction forces and torques when comparing control vs OA leg, in ART and CNS group (p=0.004 and p=0.002, respectively) (Figure 4).