Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3910

AB0872

EFFICACY AND SAFETY OF THE COMBINATION OF APOCYNIN AND PAEONOL (APPA) IN PATIENTS WITH OSTEOARTHRITIS: AN UNCONTROLLED PATIENT CASE SERIES

N. Larkins¹. ¹AKL Research and Development Ltd, Stevenage, United Kingdom

Background: Apocynin and paeonol are secondary metabolites of plants used in traditional Asian medicine for centuries. The combination of synthetic versions of these two molecules (APPA) was developed initially for the treatment of osteoarthritis (OA) in animals where it has been found at least as effective as meloxicam. Human clinical trials are currently ongoing.

Objectives: To report the outcomes from a case series of patients treated with APPA.

Methods: Subjects with a diagnosis of OA, who had tried unsuccessfully a number of standard therapies, requested treatment with APPA from the author (NL), often following successful treatment of their animals with the combination or via networking. The usual daily dose was 1240 mg paeonol and 352 mg of apocynin taken as two 400 mg capsules twice daily.

Results: Twenty-three subjects with a diagnosis of OA of whom 7 were scheduled for surgery have been treated with APPA. There were 10 female and 13 males with an age range from 40 to 81 years. Nine patients had OA of the knees, 5 of whom had bilateral involvement, 7 had hip OA, 5 bilaterally and 2 with end stage bone on bone disease. Four patients had hand OA, one of whom also had disease of the hip, lower back and feet. In 3 patients the joints involved was not recorded. In 19 patients treatment was reported as effective. In 4 patients the treatment was ineffective, all of who were scheduled or had been recommended for surgery. In 2 of these cases this was bone on bone. The duration of treatment for OA at the last recorded follow-up was reported for 16 patients in whom treatment was deemed effective and ranged from 9 to 120 months (median 24 months). In a further 3 patients the treatment the duration was not reported. In the 4 patients where no benefit was reported APPA was discontinued within a few weeks. In no case was there a report of APPA being discontinued due to adverse events. In 13 patients it was specifically stated that there had been no adverse events whereas for the remaining 10 patients it was not documented whether adverse events had occurred or not.

Conclusion: Treatment with APPA was reported as effective by 82.6% of patients. In all patients in which the combination was ineffective the disease was severe with joint replacement recommended or scheduled; in two patients this was bone on bone. This would suggest that APPA is not a simple analgesic, a conclusion supported by effects seen in the rat meniscal tear model where possible disease modifying effects have been reported (1).

References:

- 1] Glasson, S., Bendele, A. and Larkins, N. (2012). APPA provides disease modification in preclinical osteoarthritis. *Osteoarthritis and Cartilage* **20**: S72-S73 Abstract 132.

Disclosure of Interests: Nicholas Larkins Shareholder of: AKL R and D Ltd, Employee of: AKL R and D Ltd

DOI: 10.1136/annrheumdis-2020-eular.1221

AB0873

ULTRASOUND GUIDED INTRA-ARTICULAR INJECTION WITH HYALURONIC ACID AGENTS IN MODERATE HIP OSTEOARTHRITIS

M. Micu¹, A. Micu², S. Bolboacă³. ¹Rehabilitation Clinical Hospital Cluj- Napoca, Rheumatology Division, Cluj- Napoca, Romania; ²"Iuliu Hațieganu" University of Medicine and Pharmacy Cluj-Napoca, Cluj- Napoca, Romania; ³"Iuliu Hațieganu" University of Medicine and Pharmacy Cluj-Napoca, Department of Medical Informatics and Biostatistics, Cluj- Napoca, Romania

Background: Current guidelines usually only include hyaluronic acid (HA) intra-articular injection as an alternative therapy option for knee osteoarthritis (OA). When compared to the blind approach, ultrasound guided intra-articular injections (USGIA) have shown a higher efficacy and reduced number of adverse events due to injection techniques [1]. This has allowed targeting deep joints like the hip. The objective of the study is to evaluate the short and long term efficacy and safety of HA-USGIA in moderate hip OA.

Methods: Patients with Kellgren-Lawrence II and III hip OA (refractory to NSAIDs, pain killers and chondroprotective agents) were prospectively recruited to receive 3 consecutive weekly doses of HA-USGIA using free hand technique [2]. Informed written consent was signed. VAS pain scale and WOMAC score was performed at baseline and at 3 and 6 months after the end of treatment. The first injection was performed after a 1-month wash out. X ray assessment was made at baseline and after 6 months. Ultrasound evaluation was made at baseline and at each visit.

Results: Fifteen patients (median age 67 years, IQR 63-69 years, 13/15 women) with hip OA were enrolled and 28 hip joints were injected (Fig 1a,b). None of the hips presented ultrasound detected capsular distension (suggesting inflammation) during the study. Table 1 presents the results on medication efficacy at 3 and 6 months. The pain evaluated by VAS score showed a significant and progressive decrease from baseline to 3 and 6 months respectively (Table 1). Indeed, a significant and sustained decrease of total WOMAC scores and its separate domains- pain, stiffness and function was recorded from baseline to 3 and 6 months (Fig 2a,b). No significant changes were observed regarding the WOMAC score stiffness and function domains when comparing results at 3 and 6ms. Moreover, WOMAC-pain score was significantly lower at 6ms as compared to 3ms (Table 1), highlighting the dramatic and sustained medication impact on the most relevant parameter for clinical practice, in patients with hip OA. Neither drug-related nor injection technique related adverse effects were recorded. No patient developed signs of hip osteonecrosis or inflammatory lesions during follow-up.

Table 1. The trends of the scores expressed as medians and comparisons between follow-ups

Score	Median (Q1 to Q3)			P-values			
	Baseline (b)	3 ms	6 ms	all*	b vs. 3ms^	b vs. 6ms^	3ms vs. 6ms^
VAS pain	8 (7 to 8)	3 (2 to 4)	2 (2 to 3)	<0.0001	<0.0001	<0.0001	0.2472
WOMAC total	57 (45.5 to 64.5)	9 (6.8 to 16.3)	7 (4.8 to 12.0)	<0.0001	<0.0001	<0.0001	0.1671
WOMAC pain	10.5 (8.0 to 13.5)	2 (1 to 2.3)	0.5 (0 to 2)	<0.0001	<0.0001	<0.0001	0.0123
WOMAC stiffness	3.5 (3 to 5)	0 (0 to 1)	0 (0 to 0)	<0.0001	<0.0001	<0.0001	0.1118
WOMAC function	42 (32 to 49)	7 (3.8 to 16)	6 (4 to 11.5)	<0.0001	<0.0001	<0.0001	0.4279

Q1 = first quartile; Q3 = third quartile;

* Friedman test; ^ Wilcoxon test; 3 ms-3 months, 6ms-6 months, b-baseline

Fig.1. Legend: a.) Longitudinal scanning at hip joint level. F- femoral head, arrows showing the hyperechoic needle penetrating the muscles and arriving inside the anterior joint recess. b.) Post-procedural longitudinal scanning at the hip joint level. Arrowheads- showing the hyperechoic intra-articular drug moving anti-gravitationally and distending the capsule.

Fig 2. ab Legend. a.) Evolution of VAS for pain over time; b.) Evolution of WOMAC total score and its components over time. The line in the box is the value of median, the box is the first and the third quartile, the whiskers are the minimum and maximum and the x is the value of mean. 3ms- 3 months, 6ms- 6 months, WOMAC T- WOMAC total.

Conclusion: The results suggest that HA – USGIA may be an effective and safe treatment for moderate hip OA, due to its short and long term benefits. This treatment should not be delayed until advanced OA is diagnosed. Longitudinal controlled studies on larger cohorts are warranted to confirm these preliminary results.

References:

- 1] Migliore A, Giovannangeli F, Granata M and Lagana B. Hyalgan G-F 20: Review of its Safety and Efficacy in the Management of Joint Pain in Osteoarthritis. *Clinical Medical Insights: Arthritis and Musculoskeletal Disorders* 2010;3: 55-68.

- [2] Micu MC, Fodor D. Musculoskeletal ultrasound guided interventional manoeuvres. Musculoskeletal Ultrasonography in Rheumatic Diseases. Ed. Springer 2015, ISBN 978-3-319-15723-8.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1619

AB0874

FUNCTIONALITY IN OSTEOARTHRITIC GAIT IS RELATED TO TREATMENT DECISION. A MULTIFACTORIAL ANALYSIS

S. Tassani¹, L. Tío^{2,3}, F. Castro^{2,3}, J. Monfort^{2,3}, J. C. Monllau^{2,4}, M. Á. González-Ballester^{1,5}, J. Noailly¹. ¹Universitat Pompeu Fabra, BCN MedTech, DTIC, Barcelona, Spain; ²Municipal Institute of Medical Research, Barcelona, Spain; ³Hospital del Mar, Rheumatology Department, Barcelona, Spain; ⁴Hospital del Mar, Traumatology Department, Barcelona, Spain; ⁵Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain

Background: Osteoarthritis (OA) is a degenerative disease with complex underlying mechanisms¹⁻³. The interactions among several factors make the study of the disease very complex and often lead to different treatment, i.e. surgical or conservative, decisions for subjects clinically and radiographically similar. Recent explorations performed at the body level pointed out that macro-factors, like overweight or gait, can influence the development of the disease⁴. The number of related factors is high, and they are very likely to interact with each other. However, the literature lacks randomized and balanced studies to verify such effects of multiple factors⁵.

Objectives: The aim of this work was to develop a multifactorial analysis to explore whether and how gait functionality and dynamics can be related to treatment decision.

Methods: A multifactorial analysis of gait dynamics in OA subjects was developed. 81 OA subjects, graded 2-3 in KL, were selected based on 4 clinical factors: Gender (male – female), Age (60-67 – 68-75), BMI (25–29.9 – 30+) and Treatment (total knee replacement (TKR) – conservative treatment). Gait analysis was performed using 8 cameras BTS Smart-DX 700, 1.5 Mpixels 250 fps and 2 force plates BTS P-6000 500 Hz sampling (BTS S.p.A., Milan, Italy). Helen Hayes marker protocol with medial markers was used for the study. Each volunteer was asked to perform a minimum of 5 valid gait sequences. Functionality and dynamics parameters were measured.

Functionality: Velocity of gait and the time needed to perform a gait cycle were computed.

Dynamics: The reaction forces and torques at the ankles, knees and hips were computed through inverse dynamic analyses.

Analysis of variance was performed for the four factors described among the functionality and dynamics parameters.

Results: The multifactorial analysis showed that functionality values are more subjective to the studied factors than the dynamics ones.

Functionality seems to be directly related to the clinical treatment. Patients who selected TKR needed more time to make a step, spent more time in double stand position and walked slower ($p < 0.002$). Older subject also walked slower but this dependency seemed to vary with age (interaction between clinical treatment and age – $p < 0.02$ – Figure 1).

Figure 1 Interaction between Clinical treatment and age.

Dynamics: Forces at the joints seemed to be affected by the gender and an interaction between age and BMI ($p < 0.005$, $p < 0.02$) but not by the kind of therapy. Differently, torques were statistically related to the clinical treatment ($p < 0.007$). Age was also significant as was the interaction between age and BMI (both $p < 0.007$).

Conclusion: Reduced functionality seems to be related to the selection of therapy. In contrast to current paradigm, forces at the joints may have no role in the definition of the best therapy for OA subjects. Subjects requiring TKR do not present higher loads at the joints. However, torques seems to be related to the therapy selected. Instead of forces, kinematics and posture assessments might support rational definitions of the therapy and future multifactorial analysis should take them into consideration.

References:

- [1] Ding M. et al. *J Bone Joint Surg Br.* 2003;85(6):906-912.
- [2] Kamibayashi L. et al. *Calcif Tissue Int.* 1995;57:69-73.
- [3] Li B, Aspden RM. *J Bone Miner Res.* 1997;12(4):641-651.
- [4] Berenbaum F et al. *Curr Opin Rheumatol.* 2013;25(1):114-118.
- [5] Ioannidis JPA. *Soc Sci Med.* 2018;210(April):53-56.

Acknowledgments: MICINN Funds are acknowledged (HOLOA-DPI2016-80283-C2-1/2-R, RYC-2015-18888)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1051

AB0875

HYBRID COOPERATIVE COMPLEXES OF SODIUM HYALURONATE + SODIUM CHONDROITIN NON-SULFATED (HA-SC) IN THE TREATMENT OF HIP OA: CLINICAL RESULTS

R. Papalia¹. ¹Campus Bio-Medico University of Rome, Head of Department of Orthopaedics and Traumatology, Rome, Italy

Background: Hip Osteoarthritis (OA) is a widespread disease characterized by pain and functional impairment, which, particularly in the elderly, may compromise overall health and quality of life. In the last decades, Intra-articular (I.a.) injections of hyaluronic acid (HA) gained more space among the conservative treatment of OA because of their beneficial effects and positive outcomes without relevant complications. (1,2). An innovative and patented formulation containing hybrid cooperative complexes of sodium hyaluronate 2.4% + sodium chondroitin non-sulfated 1.6% of biotechnological origin (HA-SC) has been recently developed for the I.a. treatment of hip OA and evaluated in a pilot study (3).

Objectives: 1) Primary aim: Evaluation of the safety of HA-SC in the treatment of symptomatic hip OA; 2) Secondary aim: Evaluation of the efficacy of HA-SC in terms of pain reduction (VAS) and function improvement (Lequesne) of the affected hip joint.

Methods: This is a pilot, multicentric, open, prospective study. The following inclusion criteria were established: Patients (both genders) aged ≥ 40 years suffering for primary hip OA confirmed by X-Ray; Grade I-II-III according to K&L grading scale; Basal VAS pain at the target hip > 40 mm; Failure of at least two lines of conservative treatments. All patients underwent a single I.a. hip injection of a 3mL vial of HA-SC and followed-up for six months.

Results: 48 patients have been enrolled and completed the study. The treatment was generally well-tolerated, with only ten patients out of 48 (20.8%) reporting local effects mainly consisting of injection site pain and arthralgia localized in the treated area. All these patients completed the study. The treatment with HA-SC was associated with a statistically significant decrease of VAS scale from a basal value of 67.5 (mean) to 22.8 (mean, $p < 0.0001$) at the end of the observation period at six months, with a statistically significant decrease at seven days of follow-up evaluation (29.3, mean, $p < 0.0001$). The mean Lequesne's Index total score after the single injection of HA-SC decreased from a baseline value of 10.4 (mean) to 5.1 (mean, $p < 0.0001$) at six months. The decrease was marked and significant also at any of the other evaluated time point ($p < 0.0001$).

Conclusion: A single I.a. injection of the innovative formulation containing hybrid cooperative complexes of sodium hyaluronate + sodium chondroitin non-sulfated (HA-SC) showed to be well tolerated and safe in the treatment of symptomatic hip OA. A rapid and significant decrease in hip pain (VAS) and Lequesne's Index was also observed starting immediately after the I.a. injection and lasting until the end of the follow-up period. However, conservative treatment of hip OA is still challenging. This new formulation could represent a promising, long-lasting, and effective I.a. treatment.

References:

- [1] Papalia R. et al. *J. Biol. Regul. Homeost. Agents* 2017; 31 (4 Suppl. 2): 103-109.
- [2] Abate M. et al. *Int. J. Immunopathol. Pharmacol.* 2017; 30 (1): 89-93.
- [3] IBSA Data on file.