AB0983

HYALURONAN DERIVATIVE HYMOVIS® INCREASES CARTILAGE VOLUME AND TYPE II COLLAGEN TURNOVER IN OSTEOARTHRITIC KNEE: DATA FROM MOKHA STUDY

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Background: Intra-articular injections of hyaluronan represent one of the well-accepted standard of care for treating symptomatic knee osteoarthritis (OA). Until now, not much is known about the structural-modifying effect of this treatment justifying this pilot study.

Objectives: This exploratory non-controlled study aims to study effects of HYMOVIS on imaging, biological and clinical variables.

Methods: Forty six patients with symptomatic knee OA (mean age 61.4 years [min.35-max.80; 67.4% female; Kellgren and Lawrence grade II and III (63% and 37%, respectively); mean BMI 30.6 kg/m²) were enrolled in this open-label, prospective, multicenter, pilot study. Patients received two treatment cycles of intra-articular injections (3 mL) of Hymovis (8 mg/mL of the 500–730 kDa hyaluronic acid hexadecylamide) at 6 months interval. Each treatment cycle corresponded to two intra-articular injections one week apart. All patients had MRI of the target knee at baseline and 1 year, and blood samples (D30, D90, D180, D210 and D360) to assess joint biomarkers. The primary outcome was the change in type II collagen-specific biomarkers (Coll2-1, Coll2-1NO2 and CTX-II) after Hymovis treatment versus baseline. Secondary endpoints included levels changes in AGG, COMP, PIINP, MMP-3, MPO and IL-6 serum biomarkers, the ratio Coll2-1/PIINP, CTX-II/PIINP, MRI cartilage volume and KOOS index.

Results: Coll2-1 serum levels significantly increased overtime (0.05<P<0.001) while Coll2-1NO2 levels was only increased at D360 (p<0.05). Serum PIINP levels also progressively and significantly enhanced with time (p<0.001). In contrast, other serum biomarker levels including CTX-II, AGG, COMP, MMP-3, MPO or IL-6 did not change significantly overtime. Interestingly, the ratios Coll2-1/PIINP and CTX-II/PIINP decreased (p<0.005), indicating a decrease of cartilage catabolism. Compared to baseline value, MRI cartilage volume increased in lateral femoral and lateral trochlea compartments (p<0.05) and not in medial compartment. Interestingly, WOMBS effusion score, an indicator of synovitis, significantly decreased (p<0.016). Finally, global KOOS score and subscales significantly increased overtime (p<0.001) while pain at rest, walking pain and patients or investigators global assessment of disease activity decreased (p<0.001). The safety profile was favourable with a low incidence of injection-site pain.

Conclusions: Hymovis, a well-tolerated intra-articular treatment, significantly enhanced type II collagen turnover as suggested by the increase in Coll2-1 and PIINP levels and cartilage volume observed by MRI in lateral knee compartment. Importantly, this study highlighted the potential symptomatic benefit of Hymovis on pain and function and provides critical information for the design of a larger phase III clinical trial.

Disclosure of Interest: None declared

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AB0984

CADMIUM TOXICITY AS A PROBABLE CAUSE OF SMOKING INDUCED BONE LOSS

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Background: Cigarette smoking supposed to be a risk factor for osteoporosis. There is an inverse relationship between smoking and both bone mass and fracture risk. Tobacco smoking is the most important single source of cadmium exposure in the general population. The absorption of cadmium from the lungs is much more effective than that from the gut.

Objectives: This study was designed to evaluate the effect of cigarette smoking on bone mineral density, due to cadmium toxicity.

Methods: this study was carried on 100 persons, selected from AL-Azhar university hospital and divided into three groups: group I: included 40 persons with active smokers; group II: included 40 persons with passive smokers and group III included 20 nonsmokers. All persons were subjected to full history taking,

thorough clinical examination, routine lab tests, serum and urinary cadmium and lead, and bone mineral density was measured by DEXA.

Results: Serum and urinary cadmium and lead were statistically significantly higher in group I in comparison to groups II or III and in group II in comparison to group III. Also, there was statistically significant decrease of BMD in group I in comparison to either group II or group III and in group II in comparison to group III. There was an inverse statistically significant correlation between serum and urinary cadmium and bone mineral density.

Abstract AB0984 – Table 1. Comparison between studied groups as regard serum and urinary cadmium levels

		Mean	S. D	Minimum	Maximum	F	P
Serum cadmium (µg/l)	Group I	0.449	0.287	0.18	1.80	27.92	<0.001(S)
	Group II	0.232*	0.040	0.16	0.32		
	Group III	0.094*	0.047	0.01	0.16		
Urinary cadmium (µg/l)	Group I	0.555	0.304	0.30	2.00	27.16	<0.001(S)
	Group II	0.335*	0.042	0.26	0.42		
	Group III	0.181*	0.052	0.11	0.26		

*=statistically significant decrease in comparison to group I or group II

#=statistically significant decrease in comparison to group I

Conclusions: Results of the present study revealed that: there are harmful effects of smoking on the bone mineral density and it may be occurred by direct (increased blood and urinary levels of both cadmium and lead) or indirect effects (effects of both renal and liver functions) of cadmium and lead.

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AB0985

PERSISTENCE AND ADVERSE EVENTS IN PATIENTS TREATED WITH DENOSUMAB

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Background: Denosumab (DNS) is a human monoclonal antibody directed against RANKL, which blocks the maturation of the osteoclast, inhibiting bone resorption. The binding of DNS to RANKL suppresses bone resorption mediated by osteoclasts and decreases bone turnover.

Objectives: To evaluate the survival rate of DNS, adverse events and reasons for the DNS discontinuation.

Methods: This was a prospective observation study in patients with OP which initiated treatment with DNS between January 2013 and December 2017. Patients included were followed up in the Rheumatology Nurse Clinic every six months. Demographics data, disease features, concomitant disease and treatments, adverse events and reasons for discontinuation were collected.

Results: We included 220 patients (80.5% women) with a mean age (range, SD) of 67.19 (30–89, 11.2) years. In average (range, SD), patients received 3.85 (1–11, 2.2) doses of DNS, with a mean duration of treatment (range, SD) of 23.03 (6–66, 13.3) months. 191 (86.8%) patients received also treatment with calcium and vitamin D supplements. Before the start of the treatment with DNS, 123 (55.9%) patients had received another specific treatment for OP with mean previous treatment duration of 51.6 months. Previous fragility fractures were reported in 150 (68.1%) patients, of whom 91 (41.3%) patients had two or more fractures before starting treatment with DNS.

Of all included the patients, 108 (49%) patients had an inflammatory autoimmune disease (IAD) diagnosed. In addition, 100 (45.4%) patients had concomitant biological and/or synthetic treatment and 77 (35%) patients received concomitant treatment with corticosteroids.

During the treatment with DNS, 30 (13.6%) patients had new fractures, 5 (2.3%) patients had 2 fractures. Eleven fractures were vertebral, 3 of femur, one of radius and 21 other locations. There were no differences between patients with or without glucocorticoid treatment (0.234).

The most frequent adverse events (AE) were infections in 88 (40%) patients, muscle pain in 15 (0.6%) patients, fatigue in 7 (0.31%) patients, itching, heat and fever in 2 (0.9%) patients and osteonecrosis of the jaw in 2 (0.9%) patients. The 2 patients with osteonecrosis of the jaw had previous treatment with bisphosphonates for more than 24 months.

At 60 months, 185 (84.1%) patients continued with DNS. In 37 (1.6%) patients, DNS was discontinued; in 4 patients DNS was restarted. The reasons for suspension were hypercalciuria 1 (0.04%), hypocalcemia 1 (0.04%), local hypersensitivity reactions 4 (0.18%), normalisation of BMD 5 (0.2%), dental problems 11 (0.4%) and others 17 (0.7%). The mean (SD, 95% CI) of DNS survival was 51.2 (1.9; 47.3–55.1) months. There are no differences in the survival rates of DNS between patients with and without concomitant biologic therapy ($p=0.995$).

Conclusions: The majority of patients who started treatment with DNS continue the treatment with good tolerance. The most frequent adverse effects were infections but they have not led to suspension of treatment.

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AB0986

MANAGEMENT OF OSTEOPOROSIS AFTER MAJOR FRACTURE IN A COHORT OF WOMEN AGED OVER 50 IN A REAL LIFE SETTING

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Background: Osteoporosis is the most common metabolic bone disease. Fractures constitute a major health concern because prior fractures are associated with an increased risk of subsequent fracture. Moreover, osteoporotic fractures have been associated with increased mortality risk.¹ Hence secondary fracture prevention is recommended. Anti-osteoporotic drugs are available, but in the last decade an alarming decrease of anti-osteoporotic therapy use was observed.²

Objectives: The objective of this study was to analyse the management of osteoporosis after major fracture (hip, vertebral and humerus fractures) in women aged over 50 in a real life setting.

Methods: We conducted an observational study on all women over 50 years of age who experienced a major fracture at Nîmes University Hospital in 2015 identified by informatic codes. Only fragility fractures were included. Data collected prospectively in the computerised medical files were extracted: prescription of a post-menopausal osteoporosis therapy; therapy initiation; prescription and completion of generalised bone mineral density testing; and prescription and completion of blood sample tests to look for secondary osteoporosis. We also recorded the department in which the hospitalizations occurred and the fracture localization.

Results: Of 375 women over 50 with a registered fracture in 2015, 264 were included. The exclusion criteria were women with traumatic fracture or minor

osteoporotic fracture. The median age was 84 years old. The most common major fractures were hip (52.3%), humerus (20.8%) and spine (18.9%).

Forty-five (17.0%) patients had experienced a fracture prior to the 2015 fracture. Only 12 patients (4.5%; IC95%[2.4–7.8]) had an anti-osteoporotic drug prescription at the end of the hospitalisation and only 45 women (17%) had anti-osteoporotic drug prescription planned later. The median period until anticipated prescription was 9 days and the median period until prescription in practice was 18 days.

Assessment of bone mineral density was planned later in only 23 patients (8.7%; IC95% [5.6–12.8]). Blood sample tests were realised in 49 women (18.6%; IC95% [14.1–23.8]).

In surgical department, anti-osteoporotic drug prescription was planned in only 3 women (1.5%) compared with 40 women (56.3%) in medical departments.

Conclusions: A large majority of women with osteoporotic major fracture are not receiving appropriate therapy and recommended management in 2015 in Nîmes University Hospital. The rate is dependent on the department in which patients are hospitalised.

The results of our study highlight the urgent need for optimisation of osteoporotic fracture management, especially in the surgical department.

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AB0987

FREQUENCY OF UTILISATION OF THE CENTRAL DXA BONE DENSITOMETRY IN PATIENTS WITH MULTIPLE SCLEROSIS

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Background: Multiple sclerosis patients can have a higher risk from occurrence of osteoporosis. Reduced bone mass density can be related to a cumulative effect of different factors, most common ones being physical inactivity, reduced intake of vitamin D and use of medications such as glucocorticoids.

Objectives: The aim of this research was to explore the level of awareness in patients and physicians on the significance of the utilisation of DXA bone densitometry in patients with multiple sclerosis.

Methods: The observational analytical cross-section study included 366 multiple sclerosis patients on stationary treatment at the Special rehabilitation hospital "Banja Kanjiža" in Kanjiža in the period between 2013 and 2017. The following parameters were observed in patients: sex, age, duration and form of basic disease, the level on the Kurtzke Expanded Disability Status Scale, utilisation of glucocorticoids, occurrence of pathological fractures and intake of vitamin D, i.e. of medication for the treatment of osteoporosis in order to determine their impact on the frequency of the low bone mineral density (BMD). Statistical data processing and analysis was conducted in the SPSS ver 20.0 program by IBM corporation.

Results: In the period in question, an average of 128 multiple sclerosis patients were treated, out of those 62.3% ($n=228$) with relapsing-remitting type of disease, and $n=366$ first time patients. Within the given period, 36% more women than men were rehabilitated ($f=249$ vs. $m=117$). During the five-year long period of observation of said patients, only 8.5% ($n=31$) of patients with different levels of bone metabolic disorders established underwent central DXA bone densitometry. Pathological fracture on a small trauma was suffered in 6.8% ($n=25$) patients. Of the abovementioned parameters, only the female sex ($X^2=84.492$; $p<0.001$) and age ($t=2.100$; $p=0.036$) statistically significantly influenced the occurrence of low bone mineral density.

Conclusions: It is necessary to increase the level of health education of multiple sclerosis patients on the consequences of low bone mineral density. The highest risk of osteoporotic fracture is in older women suffering from multiple sclerosis.

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