OSTEOARTHRITIS AND HYALURONIC ACID
DISCLOSURES

Abbvie
Fidia SpA
Grunenthal
Menarini
Pfizer
MSD
EPIDEMIOLOGY OF OSTEOARTHRITIS

- The most common form of chronic arthritis/joint disease
- Strongly related with age
  radiological evidence in: 85% of aged at least 75 yrs, 50% of those over 65 yrs
  radiographic OA of the knee joint: 70% of the population over 60 yrs of age
- 15% of the population affected by symptomatic disease
- Most common reason for total hip and knee replacement
- Leading cause of chronic mobility disability
- Attributed annual costs (medical care and lost wages) ~ 65 millions in US
Causes of disability in the United States

- Arthritis & Rheumatic Diseases: 27%
- High Blood Pressure: 3%
- Cancer: 3%
- Stroke: 5%
- Blindness/Vision Problems: 6%
- Deafness/Hearing Problems: 6%
- Diabetes: 6%
- Mental/Emotional Problems: 7%
- Back/Spine Problems: 24%
- Lung/Respiratory Problems: 9%
- Heart Problems: 7%

Contribution of chronic diseases to the mild and severe disability burden in Belgium

Renata T. C. Yokota1,2*, Johan Van der Heyden1,3, Stefaan Demarest1, Jean Tafforeau1, Willma J. Nusselder4, Patrick Deboosere2 and Herman Van Oyen1,3

Abstract

Background: Population aging accompanied by an increased longevity with disability has raised international concern, especially due to its costs to the health care systems. Chronic diseases are the main causes of physical disability and their simultaneous occurrence in the population can impact the disablement process, resulting in different severity levels. In this study, the contribution of chronic diseases to both mild and severe disability burden in Belgium was investigated.

Methods: Data on 21 chronic diseases and disability from 35,799 individuals aged 15 years or older who participated in the 1997, 2001, 2004, or 2008 Belgian Health Interview Surveys were analysed. Mild and severe disability were defined based on questions related to six activities of daily living and/or mobility limitations. To attribute disability by severity level to selected chronic diseases, multiple additive hazard models were fitted to each disability outcome, separately for men and women.

Results: A stable prevalence of mild (5%) and severe (2–3%) disability was observed for the Belgian population aged 15 years or older between 1997 and 2008. Arthritis was the most important contributor in women with mild and severe disability. In men, low back pain and chronic respiratory diseases contributed most to the mild and severe disability burden, respectively. The contribution also differed by age: for mild disability, depression and chronic respiratory diseases were important contributors among young individuals, while heart attack had a large contribution for older individuals. For severe disability, neurological diseases and stroke presented a large contribution in young and elderly individuals, respectively.

Conclusions: Our results indicate that the assessment of the contribution of chronic diseases on disability is more informative if different levels of disability are taken into consideration. The identification of diseases which are related to different levels of disability – mild and severe – can assist policymakers in the definition and prioritisation of strategies to tackle disability, involving prevention, rehabilitation programs, support services, and training for disabled individuals.

Keywords: Severe disability, Mild disability, Activity of daily living, Mobility limitations, Chronic diseases, Belgium
The cause-specific contribution across age group and gender sum to 100%. Arthritis: osteoarthritis and rheumatoid arthritis; chronic respiratory diseases: asthma, chronic bronchitis, chronic obstructive pulmonary disease, emphysema; neurological diseases: epilepsy and Parkinson’s disease.

Fig. 4 Relative contribution of diseases (proportion of total disability prevalence) to the prevalence of mild and severe disability. Health Interview Survey, Belgium, 1997, 2001, 2004, and 2008.
FIGURE 1.
Age and sex-specific incidence rates (/1000 person-years) of knee osteoarthritis (black), hip osteoarthritis (red), and hand osteoarthritis (green). Solid, all population; short dash line, women; long dash line, men. Reproduced from [26].
American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee

MARC C. HOCHBERG,¹ ROY D. ALTMAN,² KARINE TOUPIN APRIL,³ MARIA BENKHALTI,³ GORDON GUYATT,⁴ JESSIE McGOWAN,³ TANVEER TOWHEED,⁵ VIVIAN WELCH,³ GEORGE WELLS,³ AND PETER TUGWELL³
Table 3. Nonpharmacologic recommendations for the management of knee OA

We strongly recommend that patients with knee OA should do the following:
- Participate in cardiovascular (aerobic) and/or resistance land-based exercise
- Participate in aquatic exercise
- Lose weight (for persons who are overweight)

We conditionally recommend that patients with knee OA should do the following:
- Participate in self-management programs
- Receive manual therapy in combination with supervised exercise
- Receive psychosocial interventions
- Use medially directed patellar taping
- Wear medially wedged insoles if they have lateral compartment OA
- Wear laterally wedged subtalar strapped insoles if they have medial compartment OA
- Be instructed in the use of thermal agents
- Receive walking aids, as needed
- Participate in tai chi programs
- Be treated with traditional Chinese acupuncture*
- Be instructed in the use of transcutaneous electrical stimulation*

We have no recommendations regarding the following:
- Participation in balance exercises, either alone or in combination with strengthening exercises
- Wearing laterally wedged insoles
- Receiving manual therapy alone
- Wearing knee braces
- Using laterally directed patellar taping

Table 4. Pharmacologic recommendations for the initial management of knee OA*

We conditionally recommend that patients with knee OA should use one of the following:
- Acetaminophen
- Oral NSAIDs
- Topical NSAIDs
- Tramadol
- Intraarticular corticosteroid injections

We conditionally recommend that patients with knee OA should not use the following:
- Chondroitin sulfate
- Glucosamine
- Topical capsaicin

We have no recommendations regarding the use of intraarticular hyaluronates, duloxetine, and opioid analgesics

* No strong recommendations were made for the initial pharmacologic management of knee osteoarthritis (OA). For patients who have an inadequate response to initial pharmacologic management, please see the Results for alternative strategies. NSAIDs = nonsteroidal antiinflammatory drugs.

* These modalities are conditionally recommended only when the patient with knee osteoarthritis (OA) has chronic moderate to severe pain and is a candidate for total knee arthroplasty but either is unwilling to undergo the procedure, has comorbid medical conditions, or is taking concomitant medications that lead to a relative or absolute contraindication to surgery or a decision by the surgeon not to recommend the procedure.
If the patient does not have a satisfactory clinical response to full-dose acetaminophen, then the TEP strongly recommends the use of oral or topical NSAIDs or intra-articular corticosteroid injections (18,19). Health care providers should not use oral NSAIDs in patients with contraindications to these agents and should be aware of the warnings and precautions associated with the use of these agents. Furthermore, for persons age ≥75 years, the TEP strongly recommends the use of topical rather than oral NSAIDs (28). In this scenario, the TEP conditionally recommends the use of tramadol, duloxetine, or intraarticular hyaluronan injections. If the patient has a history of a
Figure 2  High-risk medications used by participants.

Al Ahabadi et al, SJGM 2016
# Guidelines for Elderly Patients with Osteoarthritis

## Factors Suggestive of OA (Refer to Appendix A: History)

- Gradual onset
- Absence of inflammation (morning stiffness < 30 minutes, minimal heat, minimal swelling, no redness)
- Absence of systemic symptoms or signs suggesting alternate diagnoses (Red Flags in Appendix C)
- Joint pain with activity
- Joints most likely affected: hip, knee, cervical and lumbar spine, thumb CMC (Carpo-Metacarpal), finger PIP (Proximal Interphalangeal), DIP (Distal Interphalangeal), and first MTP (Metatarsophalangeal) joint

## Risk Factors for Disease

- Older age
- Family history of generalized OA
- Heavy physical activity
- Obesity
- Previous trauma or deformity

## Comorbidities to Consider in Treatment

- GI (ulcers, bleeds and hepatic disease)
- Cardiovascular (hypertension, ischemic heart disease, stroke, CHF)
- Hepatic disease
- Renal impairment
- Asthma (ASA and NSAIDs require caution)
- Depression

## Other Factors to Consider in Treatment

- Cognitive status (ability to learn and to adhere to treatment)
- Substance abuse and/or prior dependency
- Drug interactions (alcohol, OTC medications, supplements and herbs)
- Language issues (understand treatment recommendations)

## How Condition Impacts Pain and Function

- Sleep (night pain)
- Activities of daily living (ADLs/IADLs)
- Walking distance
- Others: falls, social isolation, depression
- Recreation
- Pain features and level
- Work (household, paid employment, volunteer activities)

BC guidelines, 2009
KNEE OSTEOARTHRITIS IS A LOCAL DISEASE

…Needing (First) Local Treatments

- Topical NSAIDs
- Intra-articular corticosteroids
- Intra-articular hyaluronic acid
Hyaluronic acid (HA) is a natural biological substance, a high-molecular weight glycosaminoglycan.

It is a major component of ligament, tendon, and cartilage structure and of synovial fluid, responsible for the visco-elastic properties of the latter.

Since depolymerization of HA in the synovial fluid of OA was considered one of the main causes of the mechanical pain, Balazs in 1960 first proposed to use the intra-articular (IA) HA administration with the aim to restore the rheological properties of synovial fluid, called visco-supplementation.

However many other mechanisms have been proposed, including an anti-inflammatory effect.

Preclinical and clinical evidence support the hypothesis that this treatment modality can be useful, and indeed, IA injections of HA have been shown to reduce pain and improve joint function in OA in many studies.
The following products have received FDA approval:

- **Hylan G-F 20 (Synvisc®)**, given once weekly for a total of three weeks.
- **Hylan G-F 20 (Synvisc-One™)**, given once per six months and limited to osteoarthritis of the knee.
- **Sodium hyaluronate (Hyalgan®, Supartz®, Euflexxa™)**.
  - Hyalgan® and Supartz®, given once weekly for a total of five injections (Hyalgan) or five weeks (Supartz®).
  - Euflexxa™, device indicated for a three-injection treatment regimen.
- **High molecular weight Hyaluronan (Orthovisc®)**, administered weekly for three to four weeks.
- **Hyaluronic acid (Gel-One®)**, intra-articular injections of the knee.
U.S. Hyaluronic Acid Market By Product, 2014 - 2025 (USD Million)
INTRA-ARTICULAR HYALURONIC ACID IN THE INTERNATIONAL RECOMMENDATIONS

EXTENDED REPORT

EULAR Recommendations 2003: an evidence based approach of a Clinical Evidence (ESC) Task Force

EULAR evidence based recommendations for the management of hand osteoarthritis: Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT)


OARSI recommendations for the management of hip and knee osteoarthritis, Part I: Critical appraisal of existing treatment guidelines


University of Edinburgh, Osteoarticular Research Group, The Queen's Medical Research Institute, 47 Little France Crescent, Edinburgh EH16 4TJ, United Kingdom
OARSI recommended the usage of HA for knee and Hip OA

Part I: 2007
Part II: 2008
Part III: 2009

2014: uncertain recommendation for knee-only OA
OARSI guidelines for the non-surgical management of knee osteoarthritis


OARSI Guidelines for the Non-surgical Management of Knee OA

Core Treatments
Appropriate for all individuals
- Land-based exercise
- Weight management
- Strength training
- Water-based exercise
- Self-mgmt and education

Recommended treatments*
Appropriate for the following OA types:

Knee-only OA
- without co-morbidities
  - Biomechanical interventions
  - Intra-articular/Corticosteroids
  - Topical NSAIDs
  - Walking Cane
  - Oral COX-2 Inhibitors (selective NSAIDs)
  - Capsaicin
  - Oral Non-selective NSAIDs
  - Duloxetine
  - Acetaminophen (Paracetamol)

Knee-only OA
- with co-morbidities
  - Biomechanical interventions
  - Walking Cane
  - Intra-articular Corticosteroids
  - Topical NSAIDs

Multi-joint OA
- without co-morbidities
  - Oral COX-2 Inhibitors (selective NSAIDs)
  - Intra-articular Corticosteroids
  - Oral Non-selective NSAIDs
  - Duloxetine
  - Biomechanical interventions
  - Acetaminophen (Paracetamol)

Multi-joint OA
- with co-morbidities
  - Balneotherapy
  - Biomechanical interventions
  - Intra-articular Corticosteroids
  - Oral COX-2 Inhibitors (selective NSAIDs)
  - Duloxetine

*OARSI also recommends referral for consideration of open orthopedic surgery if more conservative treatment modalities are found ineffective.

Fig. 1. Appropriate treatments summary.
**Hyaluronic acid (intra-articular injection)**

**Recommendation:**
- **Uncertain:** knee-only OA
- **Not appropriate:** multiple-joint OA

**Level of evidence:** SR and meta-analysis of RCTs.
**Quality of evidence:** Good.

**Estimated Effect Size for**

**Pain (SMD):** Ranges from $0.37 \ (0.28-0.46) \ ^{56}$ to $0.46 \ (0.28-0.65) \ ^{55}$.

**Physical function:** $0.33 \ (0.22-0.43) \ ^{56}$ to $0.31 \ (0.11-0.51) \ ^{55}$.

---

**Effect size (ES):** 0.2=small, 0.5=moderate, > 0.8=large
Intra-articular Hyaluronic acid in second line
STEP 2: Advanced pharmacological management in the persistent symptomatic patient

if still or severely symptomatic

- Intermittent or continuous (longer cycles) oral NSAIDs
  
  **NORMAL GI RISK**
  - Non selective NSAID with PPI
  - Cox-2 selective NSAID (consider PPI)
  
  **INCREASED GI RISK**
  - Cox-2 selective NSAID with PPI
  - Avoid non-selective NSAIDs
  
  **INCREASED CV RISK**
  - Prefer naproxen
  - Avoid high-dose diclofenac and ibuprofen (if on low-dose aspirin)
  - Caution with other non-selective NSAIDs
  - Avoid Cox-2 selective NSAIDs
  
  **INCREASED RENAL RISK**
  - Avoid NSAIDs†

  *Including use of low dose aspirin
  †With glomerular filtration rate <30 cc/min; caution in other cases

if still symptomatic

- Intraarticular hyalurionate
- Intraarticular corticosteroids

STEP 3: Last pharmacological attempts

- Short-term weak opioids
  - Duloxetine

STEP 4: End-stage disease management and surgery

if severely symptomatic and poor quality of life

- Total joint replacement
  - (Unicompartmental knee replacement)

if contraindicated

- Opioid analgesics

*thritis treatment algorithm. COX-2, cyclooxygenase-2; CV, cardiovascular; GI, gastrointestinal; NSAIDs, non-steroidal anti-inflammatory; iYSADOA, Symptomatic Slow Acting Drugs in Osteoarthritis.*
Commentary on recent therapeutic guidelines for osteoarthritis

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Table 4
Recommendations of intra-articular (i.a.) hyaluronate for knee osteoarthritis (OA)

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>EULAR</td>
<td></td>
</tr>
<tr>
<td>Evidence to support efficacy. Limitations: logistic and cost issues.</td>
<td>[8]</td>
</tr>
<tr>
<td>ACR</td>
<td></td>
</tr>
<tr>
<td>No recommendation in the initial management. Conditionally recommended if no satisfactory response to prior treatments.</td>
<td>[7]</td>
</tr>
<tr>
<td>OARSI</td>
<td></td>
</tr>
<tr>
<td>Uncertain but possible for knee-only OA.</td>
<td>[9]</td>
</tr>
<tr>
<td>Not appropriate for multi-joint OA.</td>
<td></td>
</tr>
<tr>
<td>ESCEO</td>
<td></td>
</tr>
<tr>
<td>Recommended for advanced pharmacological management in persistent symptomatic patients if still symptomatic after intermittent or longer cycles of oral NSAIDs.</td>
<td>[5]</td>
</tr>
</tbody>
</table>

ACR, American College of Rheumatology; ESCEO, European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis; EULAR, European League Against Rheumatism; i.a., intra-articular; NSAID, non-steroidal anti-inflammatory drug; OA, osteoarthritis; OARSI, Osteoarthritis Research Society International.
• Longer-lasting pain control has been reported with IA HA compared with IA corticosteroids, possibly delaying the need for total joint replacement

• No significant differences have been reported in symptom efficacy between IA HA and oral NSAIDs, suggesting that IA HA might be a good alternative to oral NSAIDs in older patients with knee OA or in those at a higher risk for NSAID-induced side effects

• A combination of IA HA and a corticosteroid often administered in the clinical setting, based on the different mechanisms of action and trajectories of the two compounds: the rapid effect of corticosteroids and the long-term effect of HA

• However, no clinical data are yet available from RCTs supporting such combined treatment

• The safety profile of IA HA has recently been questioned by a meta-analysis that reported a risk of side effects (serious adverse events and local adverse events) in addition to therapeutic effects that barely reached significance when the analysis was limited to a selected fraction of trials

• It is appropriate to point out that the considered studies were of poor methodological and reporting quality, rendering questionable the final conclusion that IA HA is not safe

• Furthermore, this analysis is also in complete disagreement with the clinical setting, where only sporadic flares and no severe systemic side effects have been reported after IA HA treatment.

Waddell DD, Bricker DC. J Manag Care Pharm 2007;13:113–21
Comparative safety profile of hyaluronic acid products for knee osteoarthritis: a systematic review and network meta-analysis

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**SUMMARY**

**Purpose:** Intra-articular (IA) hyaluronic acid (HA) is considered a safer alternative to oral Non-Steroidal Antiinflammatory Drugs (NSAIDs) and opioids for knee osteoarthritis (OA). A recent review raised potential safety concerns about HA, warranting further review of safety outcomes. We examined the risks of HA compared with IA placebo and investigated whether the risks vary among individual HA preparations.

**Methods:** We searched all relevant databases from inception to October 2015 and sought unpublished data. We included all knee OA trials which compared any of the 18 HA products and reported on adverse events (AEs) and withdrawals. We calculated odds ratios for safety data reported at the longest follow-up. Network meta-analysis was performed using a Bayesian hierarchical random effects model for mixed multiple treatment comparisons.

**Results:** We identified 74 studies involving 13,032 participants aged between 45 and 75 years. The proportion of women ranged from 28% to 100%. The overall incidence of local reactions reported across all products was 8.5%. Commonly reported AEs were transient local reactions, such as pain, swelling and arthralgia, which subsided rapidly. None of the HA products were statistically significantly different from IA placebo or from each other with regard to incidence of AEs. Three treatment-related serious adverse events (SAEs) were reported among 9214 participants.

**Conclusions:** Given the very low incidence of any particular AEs, we conclude that HA products are relatively well tolerated. These products have a similar safety profile compared to each other. This information along with the comparative effectiveness profile and relative cost would be helpful for clinicians in delivering individualized patient care.

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Fig. 2. Network of treatment comparisons for AEs. Circle size reflects total N participants for each product. Line size is indicative of the number of direct comparisons.
There are some problems...

- The lack of comprehensive comparative effectiveness studies that look at all modalities is making informed treatment decisions difficult.

- Previous meta-analyses mostly looked at the efficacy of treatments vs. placebo only:
  - Oral NSAIDs vs. oral Placebo: 0.44 (0.34 to 0.55)
  - IAHA vs. IA Placebo: 0.34 (0.22 to 0.46)

- In most treatment guidelines for knee OA, NSAIDs are recommended ahead of IA HA.

- Not all IA HA are the same, in term of efficacy and safety.
Effectiveness and Implications of Alternative Placebo Treatments
A Systematic Review and Network Meta-analysis of Osteoarthritis Trials

Raveendhara R. Bannuru, MD, PhD; Timothy E. McAlindon, MD; Matthew C. Sullivan, BA; John B. Wong, MD; David M. Kent, MD; and Christopher H. Schmid, PhD

**Background:** Placebo controls are essential in evaluating the effectiveness of medical treatments. Although it is unclear whether different placebo interventions for osteoarthritis vary in efficacy, systematic differences would substantially affect interpretation of the results of placebo-controlled trials.

**Objective:** To evaluate the effects of alternative placebo types on pain outcomes in knee osteoarthritis.

**Data Sources:** MEDLINE, EMBASE, Web of Science, Google Scholar, and Cochrane Database from inception through 1 June 2015 and unpublished data.

**Study Selection:** 149 randomized trials of adults with knee osteoarthritis that reported pain outcomes and compared widely used pharmaceuticals against oral, intra-articular, topical, and oral plus topical placebos.

**Data Extraction:** Study data were independently double-extracted; study quality was assessed by using the Cochrane risk of bias tool.

**Data Synthesis:** Placebo effects that were evaluated by using a network meta-analysis with 4 separate placebo nodes (differential model) showed that intra-articular placebo (effect size, 0.29 [95% credible interval, 0.09 to 0.49]) and topical placebo (effect size, 0.20 [credible interval, 0.02 to 0.38]) had significantly greater effect sizes than did oral placebo. This differential model showed marked differences in the relative efficacies and hierarchy of the active treatments compared with a network model that considered all placebos equivalent. In the model accounting for differential effects, intra-articular and topical therapies were superior to oral treatments in reducing pain. When these differential effects were ignored, oral nonsteroidal anti-inflammatory drugs were superior.

**Limitations:** Few studies compared different placebos directly. The study could not decisively conclude whether disease severity and co-interventions systematically differed between trials evaluating different placebos.

**Conclusion:** All placebos are not equal, and some can trigger clinically relevant responses. Differential placebo effects can substantially alter estimates of the relative efficacies of active treatments, an important consideration for the design of clinical trials and interpretation of their results.

**Primary Funding Source:** Agency for Healthcare Research and Quality.

For author affiliations, see end of text.
This article was published online first at www.annals.org on 28 July 2015.
Forest plot of absolute treatment effects

- Acetaminophen: 19.55 (16.48, 22.85)
- IA Placebo: 21.97 (16.48, 27.46)
- Celecoxib: 22.85 (21.09, 24.83)
- Naproxen: 23.95 (21.53, 26.36)
- Ibuprofen: 25.27 (21.09, 29.44)
- Diclofenac: 27.02 (23.07, 30.76)
- IA Corticosteroids: 29.00 (22.63, 35.15)
- IA Hyaluronic acid: 29.44 (24.17, 34.93)

Red line at 20.00 represents the line of clinical significance.
**Appendix Table 4.** Sensitivity Analyses Exploring for Changes in Relative Efficacies of Active Treatments Based on Different Reference Placebos*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Oral Placebo</th>
<th>Oral + Topical Placebo</th>
<th>Topical Placebo</th>
<th>Intra-articular Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-articular hyaluronic acid</td>
<td>0.60 (0.40, 0.80)†</td>
<td>0.47 (0.20, 0.75)†</td>
<td>0.40 (0.14, 0.66)†</td>
<td>0.31 (0.24, 0.38)†</td>
</tr>
<tr>
<td>Intra-articular corticosteroids</td>
<td>0.58 (0.34, 0.82)†</td>
<td>0.46 (0.16, 0.76)†</td>
<td>0.38 (0.09, 0.67)†</td>
<td>0.29 (0.15, 0.44)†</td>
</tr>
<tr>
<td>Non-selective NSAIDs</td>
<td>0.43 (0.35, 0.51)†</td>
<td>0.31 (0.10, 0.51)†</td>
<td>0.23 (0.05, 0.42)†</td>
<td>0.14 (−0.04, 0.32)</td>
</tr>
<tr>
<td>Topical NSAIDs</td>
<td>0.34 (0.19, 0.50)†</td>
<td>0.22 (0.02, 0.42)†</td>
<td>0.14 (0.01, 0.28)†</td>
<td>0.05 (−0.19, 0.29)</td>
</tr>
<tr>
<td>COX-2 - selective NSAIDs</td>
<td>0.34 (0.27, 0.42)†</td>
<td>0.22 (0.01, 0.43)†</td>
<td>0.14 (−0.04, 0.32)</td>
<td>0.05 (−0.15, 0.26)</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>0.18 (0.05, 0.30)†</td>
<td>0.05 (−0.18, 0.29)</td>
<td>−0.02 (−0.24, 0.19)</td>
<td>−0.11 (−0.34, 0.12)</td>
</tr>
</tbody>
</table>

COX = cyclooxygenase; NSAID = nonsteroidal anti-inflammatory drug.
*Reported as standardized mean differences (adjusted for small samples) with 95% credible intervals. Positive effect sizes favor the left-hand (row label) intervention in each comparison, and negative effect sizes favor the above (column heading) reference intervention.
†Statistically significant effect sizes.

**Effect size (ES): 0.2=small, 0.5=moderate, > 0.8=large**
HyalOne® in the treatment of symptomatic hip OA – data from the ANTIAGE register: seven years of observation

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Abstract. - OBJECTIVE: Several studies on knee osteoarthritis suggest that the intra-articular administration of hyaluronic acid products may be a relevant option in the management of patients with persistent pain. The aim of this study is to report the data of efficacy of US-guided HyalOne®/Hyalubrix® 60 injections in a large population of patients with hip osteoarthritis, repeated at least 2 times per year for up to seven years.

METHODS: This is a prospective, post-marketing, cohort study. Data were collected from the ANTIAGE registry. Values of Lequesne index, pain VAS, NSAIDs intake, global medical and patients assessments were evaluated every six months from the baseline to the end of the follow-up, seven years later. The inclusion criteria were: age ≥18 years, symptomatic hip osteoarthritis of at least 1-year duration, and up to 84 months of follow-up. All the patients received hyaluronic acid injections at least six months, using ultrasound guidance to ensure accurate placement.

RESULTS: 1022 patients were included in the study. The patients were categorized by age, sex, and body mass index (BMI). All the groups show a statistically significant reduction at all time points compared to baseline values of Lequesne index, pain VAS, NSAIDs intake, global medical and patients assessments. There are slight differences in the subgroups: overweight, obese and over 70 years patients.

CONCLUSIONS: Our study supports the clinical efficacy and safety of HyalOne®/Hyalubrix® 60 in patients affected by osteoarthritis. This is the first study, reporting on a large cohort of patients in different categories with a long follow-up on seven years. The data confirm the proper use of ultrasound-guided viscosupplementation (VS) as background therapy in the management of hip osteoarthritis.

Key Words: Hip osteoarthritis, Viscosupplementation, HyalOne®

Introduction

OA is the most common cause of joint pain in adults, particularly among the elderly. It is the cause of morbidity and progressively leads to disability and social isolation, especially when the hip and knee are involved. The prevalence of hip OA is about 17% in the white male over the age of 60 years and 9% in the white women of the same age. The aim of the treatment is the relief of pain and the preservation or restoration of joint mobility.

Several studies on knee OA suggest that the intra-articular administration of hyaluronic acid (HA) products may be a relevant option in the management of patients with persistent pain. However, some discrepancies can be noted between some guidelines and clinical practice. More recently, two expert consensuses have confirmed a positive effect of viscosupplementation (VS) in OA joints. HyalOne® (Hyalubrix® 60 Italian brand) is a sterile, non-pyrogenic, viscoselastic solution manufactured with hyaluronic acid sodium salt, obtained by bacterial fermentation from a fraction of high molecular weight with a range of 1.500-2.000 kDa and is marketed in several European countries. Its residence time in the knee is 120 hours. It is indicated for the treatment of all joints and has been used widely in the treatment of knee OA. A post-marketing study on 1.523 patients suffering from knee OA, supported the clinical efficacy and safety of Hyalubrix in
HyalOne® in the treatment of symptomatic hip OA – data from the ANTIAGE register

Figure 1. Results of five parameters categorized by classes of age.