

Effect of a Monoshot Injection of a High-Density Hyaluronic Acid Gel in Patients with Primary Knee Osteoarthritis. Preliminary Results of the “No-Dolor” Study

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Abstract

Objective: Pronolis® HD Mono 2.5% (4.8 mL) is a sterile viscoelastic solution of Hyaluronic Acid (HA) that has been recently commercialized (medical device class III). It contains the highest concentration of HA (2.5%: 120 mg HA in 4.8 mL) and is currently available in Spain for intraarticular injection in the knee.

The main objective of the study is to evaluate the evolution of pain in patients diagnosed with primary knee osteoarthritis treated with Pronolis® HD Mono 2.5% (4.8 mL).

Methods: An observational, real-life, multicentric (60 specialized care centers), prospective, open study planned to include 300 patients diagnosed with primary knee osteoarthritis (according to ACR criteria, pain at inclusion equal or superior to 4 out of 10) in order to evaluate the pain evolution, measured by the Visual Analogue Scale (VAS).

After a single dose of Pronolis® HD Mono 2.5% (4.8 mL), patients are followed for 6 months. Preliminary results are presented to observe the first trends of change, 3 months vs. basal:

- In the pain domain score of the WOMAC-A questionnaire (main criteria).
- In the score of the domain of joint stiffness, functional capacity and pain in movement (WOMAC-B and C and 1st question of WOMAC-A) (secondary criteria).
- In the evolution of the quality of life measured by the international standardized health questionnaire EQ-5D-5L.

The study is approved by the Ethics Committee for Clinical Research of the Hospital del Mar in Barcelona (CEIC-Parc de Salut Mar).

Results: Currently, 3 months data of 14 patients is available out of the 24 patients included to date.

The degree of pain assessed by the Western Ontario and McMaster Universities Arthritis Index (WOMAC-A) shows an average improvement in pain of 7.71 points (54.5%). In 11 (78.6%) of the 14 patients, the average degree of pain improvement is equal to or greater than 30%.

The degree of stiffness in the joint, the functional capacity of the patient and the degree of pain in movement show an average improvement of 3.71 points (62.87%), of 30.64 points (58.08%) and of 1, 71 points (55.95%), respectively.

Quality of life improves in the 5 dimensions of the EQ-5D-5L improvement of quality of life has measured 34.52% in mobility, 41.67% in personal care, 39.88% in daily activities, 45.83% in pain/discomfort and 61.90% in anxiety/depression.

No patient has presented adverse reactions to the investigational product.

Conclusion: After 3 months of the intra-articular injection of a mono-shot, high-density HA gel (Pronolis® HD Mono-Shot 2.5%) patients with primary knee osteoarthritis show an important tendency to improve pain, joint stiffness, functional capacity and quality of life. These preliminary results need to be confirmed upon study completion.

Keywords: High-density Hyaluronic Acid; high concentration viscosupplementation; mono-shot HA; Primary knee Osteoarthritis; Pain; WOMAC

Introduction

Osteoarthritis (OA) is the most common form of joint disease, and its impact is set to grow as the prevalence of obesity rises and our elderly population increases. Many clinicians regard OA as simply a disease of ‘wear and tear’, and by implication one in which disease modification is not possible.

In addition, OA is associated with the breakdown of a joint’s cartilage. Cartilage is a firm, rubbery material that covers and cushions the ends of bones in normal joints. Its main function is to reduce friction in the joints and serve as a “shock absorber” (Figure 1).

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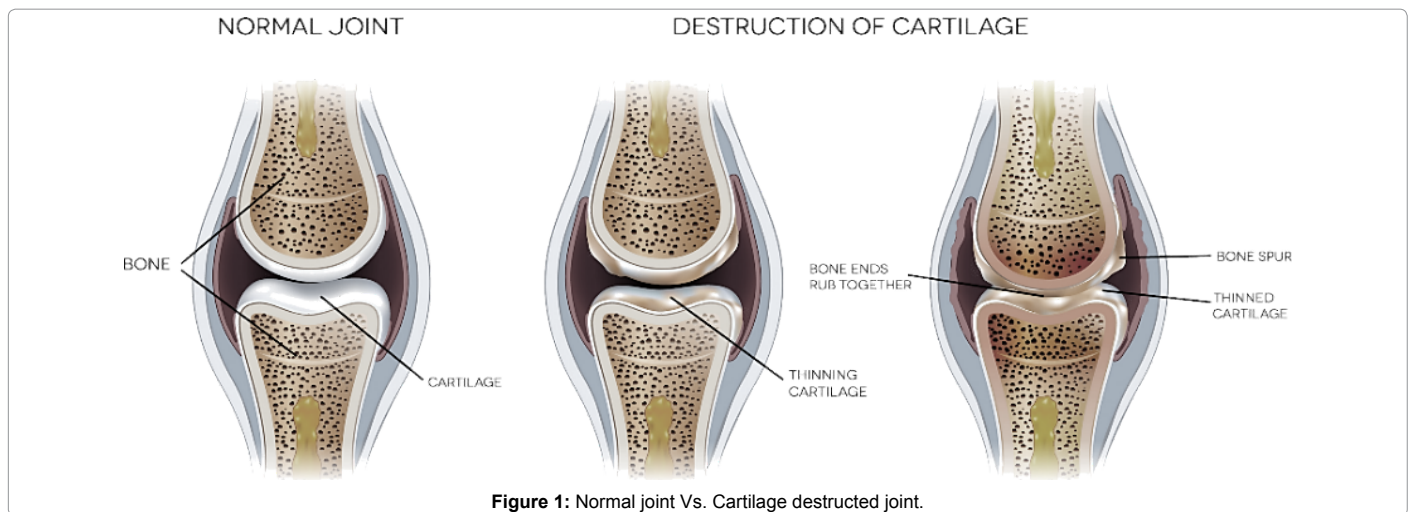


Figure 1: Normal joint Vs. Cartilage destroyed joint.

Osteoarthritis causes the cartilage in a joint to become stiff and lose its elasticity, making it more susceptible to damage. Over time, the cartilage may wear away in some areas, greatly decreasing its ability to act as a shock absorber. As the cartilage wears away, tendons and ligaments stretch, causing pain. If the condition worsens, the bones could rub against each other, causing even more pain and loss of movement.

In OA of the knee, both synovial fluid elastoviscosity and hyaluronan concentration are reduced. For compensation, intraarticular injection of a hyaluronic acid (HA) viscoelastic gel is applied to the affected joint, also referred to as viscosupplementation (VS). Current evidence indicates that HA injections are beneficial and safe for patients with OA of the knee. Intraarticular injections of HA treat the symptoms of knee OA and may also have disease-modifying properties, potentially delaying progression of OA [1,2].

Recently a study has shown that the lubrication of the joint depends on the synergism between different molecules. Two of the most involved molecules in this process are HA and Proteoglycan 4 (PRG4). The study confirms that the capacity of synergy between both molecules increases when the HA concentration increases [1,3].

Pronolis^{HD} is a class III medical device. It is a sterile viscoelastic solution of HA. The HA contained in Pronolis^{HD} is obtained by bacterial fermentation. It has a physiological molecular weight (between 1.2- 3 MDa according to the concentration) and is available in a wide range of concentrations (1%, 1.6%, 2.2% and 2.5%), which allows a stepped and individualized treatment of the patient. In fact, Pronolis^{HD} is the viscosupplement with the highest concentration of HA currently available in the market [1].

Methods

An observational, real-life, multicentric (60 specialized care centers), prospective, open study planned to include 300 patients diagnosed with primary knee osteoarthritis (according to ACR criteria, pain at inclusion equal or superior to 4 out of 10) in order to evaluate the pain evolution, measured by the Visual Analogue Scale (VAS)- an unidimensional measure of pain intensity- which has been widely used in diverse adult populations.

The Western Ontario and McMaster Universities Arthritis Index (WOMAC) is widely used in the evaluation of Hip and Knee

Osteoarthritis. It is a self-administered questionnaire consisting of 24 items divided into 3 subscales: [4]

- Pain (5 items): during walking, using stairs, in bed, sitting or lying, and standing upright
- Stiffness (2 items): after first waking and later in the day
- Physical Function (17 items): using stairs, rising from sitting, standing, bending, walking, getting in / out of a car, shopping, putting on / taking off socks, rising from bed, lying in bed, getting in / out of bath, sitting, getting on / off toilet, heavy domestic duties, light domestic duties.

WOMAC Index was developed in 1982 at Western Ontario and McMaster Universities. WOMAC is available in over 65 languages and has been linguistically validated [5].

After a single dose of Pronolis^{HD} Mono 2.5% (4.8 mL), patients are followed for 6 months. Preliminary results are presented to observe the first trends of change, 3 months vs. basal:

- In the pain domain score of the WOMAC-A questionnaire (main criteria).
- In the score of the domain of joint stiffness, functional capacity and pain in movement (WOMAC-B and C and first question of WOMAC-A) (secondary criteria).
- In the evolution of the quality of life measured by the international standardized health questionnaire EQ-5D-5L (EQ-5D is a standardized measure of health status developed by the EuroQol Group in order to provide a simple, generic measure of health for clinical and economic appraisal) [6,7].

The study is approved by the Ethics Committee for Clinical Research of the Hospital del Mar in Barcelona (CEIC-Parc de Salut Mar).

Results

Currently, 3 months data of 14 patients is available out of the 24 patients included to date.

Evolution of the degree of pain of the joint (visit 3 months on baseline) measured by domain A of the WOMAC questionnaire.

For the 14 patients with data in V3, the mean score of the WOMAC-A questionnaire in V0 was 12.71 points and in V3 it was

5.00 points. After 3 months from the injection with PRONOLIS *HD, the degree of pain evaluated according to domain A of the WOMAC questionnaire shows an improvement in pain of 7.71 points (54.5%).

Only 1 of the 14 patients has worsened in terms of the degree of joint pain (PAC=100104). In 11 (78.6%) of the 14 patients, the degree of pain improvement at 3 months with respect to the baseline situation is equal to or greater than 30%.

The degree of pain assessed by the Western Ontario and McMaster Universities Arthritis Index (WOMAC-A) shows an average improvement in pain of 7.71 points (54.5%). In 11 (78.6%) of the 14 patients, the average degree of pain improvement is equal to or greater than 30%.

The degree of stiffness in the joint, the functional capacity of the patient and the degree of pain in movement show an average improvement of 3.71 points (62.87%), of 30.64 points (58.08%) and of 1, 71 points (55.95%), respectively.

Quality of life improves in the 5 dimensions of the EQ-5D-5L improvement of quality of life has measured 34.52% in mobility, 41.67% in personal care, 39.88% in daily activities, 45.83% in pain/discomfort and 61, 90% in anxiety/depression.

After 3 months from the injection with PRONOLIS *HD, the degree of pain in movement evaluated according to the first question of the WOMAC-A questionnaire shows a pain improvement of 1.71 points (55.95%).

No patient has presented adverse reactions to the investigational product.

Conclusion

After 3 months of the intra-articular injection of a mono-shot, high-density HA gel (Pronolis® HD Mono-Shot 2.5%) patients with primary knee osteoarthritis show an important tendency to improve pain, joint stiffness, functional capacity and quality of life. These preliminary results need to be confirmed upon study completion.

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