

Ultrasound Study in Patients with Gonarthrosis, Previous and Post-treatment with Stem Cell Implantation

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ABSTRACT Through sonographic study, joint and peri-articular structures can be visualized quickly. This advantage has allowed its use as a guide in infiltration with stem cells in patients with gonarthrosis. However, it is necessary to evaluate over time, the subjects who have received this treatment, for this the researchers set themselves the objective: Identify the sonographic modifications that present subjects with gonarthrosis, before and after applying therapy with stem cells. A longitudinal, quantitative and non-experimental study was carried out on 30 subjects with gonarthrosis, who were evaluated sonographically before and after one year of having received treatment with stem cells. As results were found prior to treatment, high incidence of intra-articular effusion, echographic changes of articular cartilage, osteophytes and popliteal communicating cysts, after one year, there was a significant decrease in intra-articular effusion, popliteal cysts, and clinical improvement, not evidencing changes in bone structures.

INTRODUCTION

In recent years there have been numerous studies related to the treatment with regenerative medicine and its use in different pathologies among which degenerative injuries of knee, tendon, hip, muscle, among others (Rodríguez et al. 2016).

This therapy is characterized by the stimulation and regeneration of cells, tissues or organs to restore or establish a normal function. Among the procedures included, an emphasis is placed on the application of stem cells, and platelet concentrates (Roque et al. 2018).

Chahla et al. (2016) point out that the treatment with stem and progenitor cells holds a promising future for osteoarthritis and chondral lesions. Furthermore, highlighting that the stem cell is the one that has the power to self-generate and in this process the cell is divided asymmetrically, producing two daughter cells, a cell identical to the initial one that is available for a new division, and a second daughter cell called

progenitor, which does not divide or differentiate. These two cells are used for treatment, requiring rigorous techniques that allow an adequate identification of the concentration and therapeutic potential of the stem and progenitor cells.

On the other hand, Tusell and Jiménez in 2018 stated that although the application of regenerative medicine, particularly concentrated platelets in the treatment of osteoarthritis of the knee, seems to be satisfactory; more research is needed, which supports it, before its daily clinical application.

Imaging has played a prominent role in the diagnosis of degenerative knee conditions. Standing out among these diagnostic means are nuclear magnetic resonance and skeletal muscle ultrasound.

The latter allows to assess bone erosions and articular cartilage changes with great precision, from the early stages of osteoarthritis, in the same way, agrees to evaluate synovial bladder, estimate the amount of fluid, intra-articular alterations and peri-joints, as well as the presence of osteophytes (León et al. 2018).

It is well known that the advantages of ultrasound for the diagnosis of osteoarthritis, however, do not require sufficient evidence to show

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the echographic evolution of subjects treated with regenerative medicine and stem cells. Therefore, it is necessary to identify the changes in the echographic pattern presented by the knee joint before and after applying treatment with stem cells; for them, the following objectives have been proposed.

Objectives

General Purpose

To identify the sonographic changes that subjects with gonarthrosis present before and after applying treatment with stem cells.

Specific Purpose

- ♦ To determine the modifications of the echographic pattern in the articular and peri-articular structures of subjects with gonarthrosis, before and after one year of treatment with stem cells.
- ♦ Recognize the advantages and limitations of ultrasound in the diagnosis and monitoring of subjects with gonarthrosis, who have been treated with stem cells.

METHODOLOGY

A non-experimental, quantitative, longitudinal, prospective study was conducted over a period of one year. Thirty subjects, 17 women, and 13 men, aged between 60 and 70 years old, with grade III/IV osteoarthritis, with the presence of accompanying symptomatology, were evaluated, considering one knee in each patient subject to treatment. The selection of the sample was made intentionally, based on inclusion and exclusion criteria, in the same way, it was taken into account, the approval of the bioethics committee of the institution and compliance of the researched participation.

The selected subjects underwent treatment with regenerative medicine (stem cells) in the affected knee, evaluating the articular and peri-articular structures sonographically, before treatment with stem cells and after one year of evolution. The source of the stem cells was the peripheral venous blood.

Patients with gonarthrosis with refractory symptoms and who met the inclusion criteria for the implantation of “stem cells”, were referred to

the clinic, where they were extracted peripheral blood, which was processed in a specialized laboratory, subsequently, was administered by injection percutaneously inserted into the articular cavity of the injured knee in an amount of 500 ml/per knees.

Prior to the treatment with stem cells, an echographic study of the knee was performed in 30 patients, being considered as normal patterns of the intra and peri-articular knee structures established by the Images Laboratory of the Institute of Sports Medicine (Anillo et al. 2009).

For the development of this research, the researchers used a high-resolution ultrasound equipment brand Aloka, multi frequential transducers of 6.5 MHz to 10 MHz. The subjects were evaluated by specialists in musculoskeletal ultrasound with more than 10 years of experience.

Procedure

Description of the Ultrasound Evaluation of the Knee

The knee ultrasound technique used began with the study in the anterior plane, with the transducer in longitudinal section (SL), extending the study along the midline of the knee, from the supra-patellar region to the anterior tuberosity of the tibia. In this section, the tendon of the quadriceps femoris was observed in its entirety; in this section, the suprapatellar bursa (BSP) was seen. Under normal conditions, a thin layer of liquid separating the bursa walls can be observed.

With the transducer placed in longitudinal section (SL) in the infrapatellar region, the researchers can trace the entire cortical surface of the patella, which produces acoustic shadow and whose lower pole originates the patellar tendon (TP) that has a uniform thickness in all its length, with an approximate thickness of 3 to 5 mm. Below the patellar tendon, there is a mass of heterogeneous echogenicity, located in front of the joint, which corresponds to Hoffa's fat.

With the transducer in medial longitudinal section (MSL), the medial collateral ligament can be visualized, forming part of a set of structures that adopt a trilaminar appearance, called the medial capsule-ligament complex; while the lateral collateral ligament is observed from its origin in the lateral femoral epicondyle, until its insertion in the fibula, completely independent.

Articular cartilage can be observed as a homogeneous hypoechoic image. Ultrasound shows some limitations in the exploration of cartilage on the articular surface of the patella (retropatellar cartilage) and the tibial plateau.

The exploration of the posterior region of the knee was performed with the subject in the prone position, to evaluate the popliteal fossa, discarding in it the presence of communicating synovial cysts and changes in the meniscus echo structure.

Statistical Analysis

The variables evaluated were collected in previously designed spreadsheets. For later analysis, an Excel database was made with the information gathered, which was processed automatically using the statistical package SPSS-PC in its version 21 for Windows. Means and percentages summarized the data, and measures of cen-

tral tendency and dispersion were used for the continuous quantitative variables. The ninety-five percent confidence intervals were estimated to complete the point estimate of the measures mentioned.

RESULTS

The advantages provided by ultrasound, allowed to evaluate 30 patients with gonarthrosis prior to treatment with stem cells, being found in 28 subjects (93.3%), with a sign of joint effusion, which manifested in different degrees (large, moderate and small), being its location in the suprapatellar bursa and sometimes took both ramps (lateral and medial) (Fig. 1).

At the level of the medial and lateral joint spaces, osteoarthritic changes were evident, showing osteophytes, which sometimes produced closure of the joint space. In the same way, changes in the sonographic pattern of the

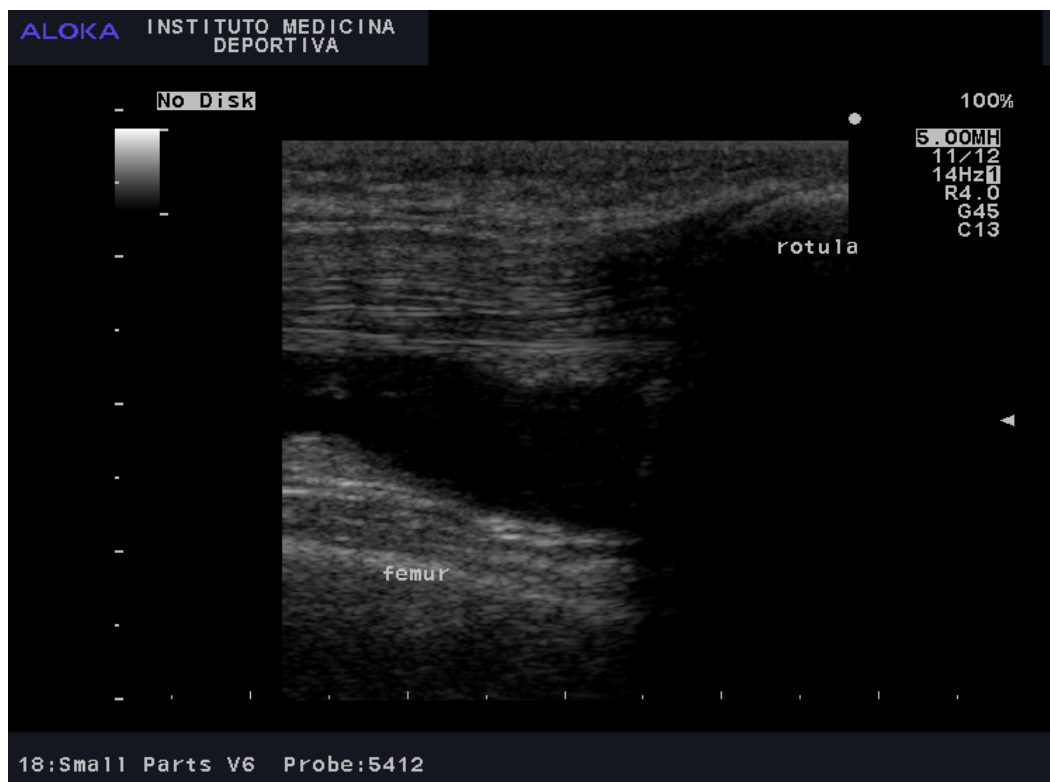


Fig. 1. Patient 65-year-old male with signs of osteoarthritis joint effusion level of suprapatellar region prior to treatment with stem cells

meniscus could be visualized in 20 subjects, suggesting degenerative alterations in these structures. Figure 2 shows a 65-year-old patient with osteophytes that close the joint space.

The integrity and thickness of the articular cartilage at the level of the knees could be evaluated employing the echographic study. Observing as characteristics of normality, a band or fringe that is ecocuid, regular and homogeneous, well defined, measuring in adults' 2 mm. However, in 15 studied subjects, it was possible to check echographic signs of cartilage injury, manifesting as thickening and low echogenicity image with well-defined borders (exudative chondropathy), on the other hand, it was observed in 28 subjects, thinning of the cartilage articular (erosive chondropathy). Figure 3 illustrates a 68-year-old patient who presents with decreased joint space (erosive chondropathy).

When performing the sonographic examination of the popliteal fossa, before the treatment with stem cells, changes in the meniscus sonographic pattern were evidenced in 7 subjects, as well as the presence of communicating popliteal cysts in 25 subjects (Fig. 4).

One year after having received treatment with stem cells, an echographic study was carried

out again, not observing significant changes in the echographic pattern of the bone structures, however, in 26 of the 30 subjects studied, there was a significant decrease in the intra-articular effusion.

Figure 5 as well shows a decrease in the incidence of popliteal cysts, which were observed in three subjects. Concerning the changes in the echographic pattern of the articular cartilage, a slight decrease in exudative chondropathy could be observed, as shown in Table 1.

Table 1: Sonographic findings prior and post treatment with stem cells in patients with gonarthrosis

| <i>Sonographic findings</i> | <i>Before treatment with stem cells</i> | <i>After treatment with stem cells</i> |
|-----------------------------|---|--|
| Intra-articular effusion | 28 | 4 |
| Presence of osteophytes | 29 | 29 |
| Meniscus degeneration | 27 | 27 |
| Chondropathy exudative | 15 | 10 |
| Erosive chondropathy | 28 | 28 |
| Presence of popliteal cysts | 25 | 3 |
| Total patients | 30 | 30 |

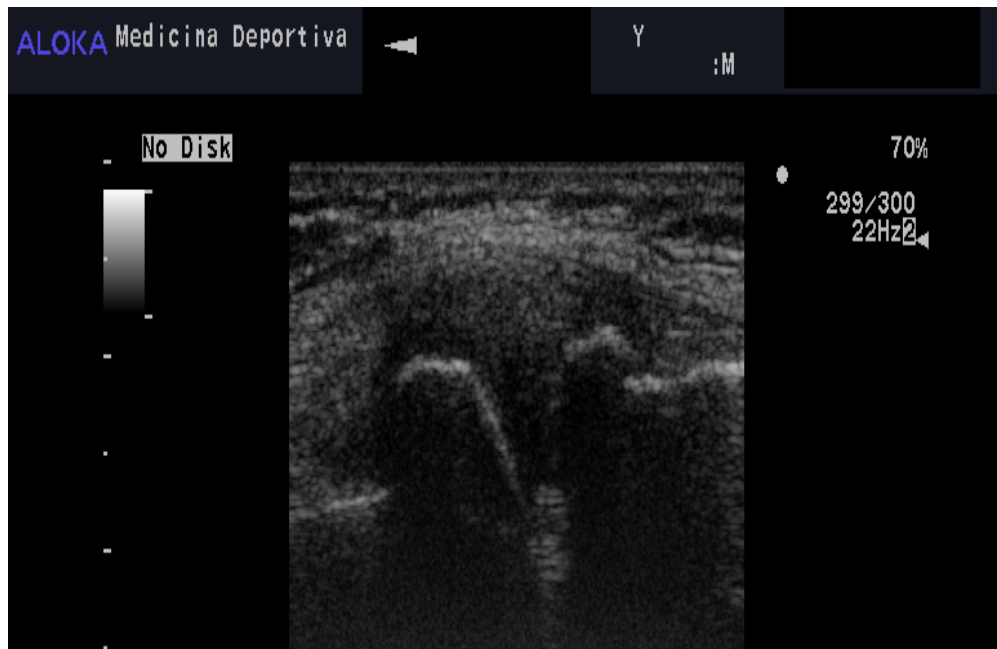


Fig. 2. Patient female 65 years with osteophytes causing closure marked joint space prior to treatment with stem cells



Fig. 3. Female patient 68 years old with thinning of joint space (erosive chondropathy), prior to treatment with stem cells



Fig. 4. Patient male 68 years old popliteal cyst presence of posterior communicating, prior to treatment with stem cells



Fig. 5. Patient 65 years old, male, osteoarthritis with decreased intraarticular suprapatellar effusion after three months of receiving stem cell treatment

DISCUSSION

The structural complexity of the knee makes it difficult to study, imposing the need to access different diagnostic techniques, notably ultrasound, which has significantly changed the way to evaluate specific joints, especially the knee. In the present study, through the use of ultrasound, it has been possible to observe a high incidence of intra-articular effusion in subjects with gonarthrosis, which coincides with the research carried out by Álvarez et al. (2013), who pointed out the presence of joint effusion in subjects with degenerative changes of the knee.

Similarly, Valverde et al. (2009), evaluated the effectiveness of Vimang in patients with osteoarthritis of the knee, highlighting the importance of ultrasound monitoring, which allowed to determine the presence and synovial inhibition in the subjects before and after having received treatment.

Changes in articular cartilage can be observed through an ultrasound study, which was demonstrated by Cisneros et al. in the year 2015. This research was carried out on subjects with osteoarthritis of the knee; they showed the pres-

ence of thinning of the articular cartilage (less than 3 mm) and marginal osteophytes in eighty-six and twenty-nine percent, respectively.

The evolution of a subject with gonarthrosis, after having received treatment with stem cells, is necessary, to evaluate the effect of the treatment on the articular and peri-articular structures. At this point, Jo et al. (2012), applied treatment with regenerative medicine to 18 patients with gonarthrosis, by intra-articular infusion, evidencing in their results improvement in function and pain reduction, at the same time, they could check benefits at the cartilage level, achieving a regenerative effect.

In the present study, it was possible to demonstrate that the subjects submitted to treatments with stem cells presented improvement from the clinical point of view, which coincides with the studies carried out by Johnson et al. (2012), Wong et al. (2013) and Vangsnæs et al. (2014).

Russo et al. (2017), carried out an evolutionary follow-up for one year in 30 patients affected by diffuse degenerative chondral lesions who received a single treatment with an intra-articular injection of autologous and micro-fragment-

ed adipose tissue. Highlighting in their results, the safety, and viability of this treatment, noting further, that these techniques are safe, minimally invasive, simple, one-step and with a low percentage of complications.

On the other hand, Bansal et al. (2017), applied treatment with regenerative medicine, applying injection with stromal cells derived from adipose tissue (stromal vascular fraction) at the knees in subjects with osteoarthritis, concluding that the patients evaluated were satisfied with the results of the treatment. They also reported a reduction in pain, mainly after 3 months of treatment. In the same way, they emphasize that the procedure proved to be safe, without severity or complications.

Hamada et al. (2018) compared the efficacy of platelet-rich plasma (PRP) and Hyaluronic acid (HA) intra-articular injections as monotherapeutic options for primary knee osteoarthritis, and to determine whether the clinical outcomes are associated with changes in the ultrasonography structural appearance. Concluding that, while both PRP and HA injections resulted in the improvement of all outcome measures at 3- and 6-months follow up, they were significantly better in the platelet-rich plasma group than in the Hyaluronic acid group.

For its part, Di et al. (2018), analyzed seven articles reporting 908 patients and 908 knees, including forty-four percent men and fifty-six percent women with a mean age of 59.8 years. All studies showed statistically significant improvements in clinical outcomes, including pain, physical function, and stiffness, with PRP treatment. All except two studies showed significant differences between platelet-rich plasma and Hyaluronic acid regarding clinical outcomes of pain and function.

Cruz et al. (2017) carried out a study with a duration of two years to 123 adult patients with osteoarthritis of knees, who underwent intra-articular implantation of autologous peripheral blood mononuclear cells (CMN-SP). Mobilized by the stimulating factor of granulocytic colonies; concluding that the implantation of CMN-SP is a feasible, simple, safe and inexpensive method for the treatment of knee osteoarthritis, which coincides with the criteria issued by the authors of the present study.

Through the echographic study, it was possible to evolve the subjects that were operated on with stem cell implants. In the present study,

in spite of not showing changes in bone structures, changes could be verified in relation to articular cartilage, the presence of joint effusion and popliteal cysts, which was also observed by Battaglia et al. (2013), who highlighted the effectiveness of ultrasound to be used as a guide for joint intervention with stem cells.

CONCLUSION

The ultrasound allowed to show images of the articular and peri-articular structures of the knee in patients with osteoarthritis, highlighting in the pre-treatment study, the presence of intra-articular effusion, changes in the echographic pattern of the articular cartilage such as exudative chondropathy and erosive chondropathy, communicating popliteal cysts, and osteophytes at the level of the medial and lateral joint space. Once one year after having received treatment with stem cells, the patients showed clinical improvement, with a marked decrease in pain, in the same way, it was possible to confirm by means of ultrasound study, decrease in intra-articular effusion, popliteal and light cysts improvement at the articular cartilage level, however, no significant changes were observed in the bone structures.

RECOMMENDATIONS

The researchers recommend carrying out studies with a larger sample and perform a comparative analysis with the intra-articular application of stem cells from the adipose tissue.

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