EVALUATION OF COMBINED INTRAVESICAL TREATMENT OF HYALURONIC ACID WITH CHONDROITIN SULFATE IN BLADDER PAIN SYNDROME.

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Abstract

Glycosaminoglycans (GAGs) of the external surface of the urothelium form a sealing and neutralizing barrier against toxic and irritating substances that can be found in urine. Changes in this barrier play a major role in the conditions that determine the appearance of Bladder Pain Syndrome (BPS). Among GAGs, chondroitin sulfate (CS) and hyaluronic acid (HA) are essential "players" in this protective function.

We evaluated 30 patients diagnosed with BPS treated with intravesical instillation protocol of HA/CS (Ialuril ®). We were evaluated the at the end of the complete cycle, 6 months after finishing it, and a year later. For this, the Visual Algesic Scale (VAS) and the Voiding Diary (VD) were used, in addition to the subjective assessment of the result.6 feet away.

Instillation protocol of HA/CS decrease pain and urinary symptoms with a very low rate of adverse events.

Introduction

The surface of the urothelium is covered by a layer of polyanionic molecules, the main component of which are amino sugars called glycosaminoglycans (GAGs). These form a sealing and neutralizing barrier, essentially protective, against toxic and irritating substances that can be found in urine. Thus, qualitative and quantitative changes in this layer would deactivate the barrier effect, leading to a series of conditions that can determine the appearance of inflammatory phenomena or cystitis, which are largely responsible for these chronic painful bladder conditions. Among the GAGs that form this barrier, chondroitin sulfate (CS) and hyaluronic acid (HA) play a major role in this function.

Bladder pain syndrome (BPS) is a condition that is included in Chronic Pelvic Pain Syndrome (CPPS), within which it is characterized by an essentially urothelial phenotype. Its etiology is diverse and only partially known, which results in a local inflammatory reaction. There is no unified definition for BPS, although we have used the most widely used today: that of the Chronic Pelvic Pain Working Group (CPPWG) of the International Continence Society (ICS): "persistent or recurrent chronic pelvic pain, pressure or discomfort , related to the bladder, accompanied by at least one urinary symptom such as urgency or increased micturition frequency", in the absence of infection or other pathology that may cause it . It is a condition with a clear predominance in women and a prevalence in Europe, between 5 and 300 cases per 100,000 women.

Intravesical treatment is considered by the different Clinical Practice Guidelines (EAU and AUA) as a second line of treatment, after conservative pharmacological and non-pharmacological treatment (hygienic-dietary measures, rehabilitation and psychological support). Neither HA nor CS treatment is mentioned in the AUA guidelines, on the contrary, in the EAU guidelines, in which they have a level of evidence 2b and a weak degree of recommendation, despite which it is widely used due to the scarcity of adverse effects and because it is compatible with oral pharmacological treatment.

The commercial preparation Ialuril ® Prefill has been used: Sterile solution of sodium hyaluronate (1.6% - 800 mg/50 ml) and sodium chondroitin sulfate (2% - 1 g /50 ml).

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Methods and Materials

Design: Retrospective observational study.

Method : we treated 30 patients diagnosed with chronic BPS according to the aforementioned definition of the CPPWG of the ICS with a duration of at least 6 months, and having ruled out the presence of other pathologies by means of blood tests, urine sediment, urine culture, ultrasonography and cystoscopy.

HA/CS (Ialuril ®) instillation protocol: intravesical instillation of an ampoule (800/1000mg in 50ml) weekly for 8 weeks, biweekly for 4 months and monthly for up to a year.

A first evaluation of the patients was carried out at the end of the two-month period of weekly instillations, at which time the absence of subjective and objective response conditioned the cessation of treatment. The improvement of symptoms after two months implied completing of the full course of instillations.
Likewise, symptoms were evaluated at the end of the complete cycle, 6 months after finishing it, and a year later. For this, the Visual Algesic Scale (VAS) and the Voiding Diary (VD) were used, in addition to the subjective assessment of the result.

Results

Thirty patients diagnosed with BPS in whom first-line oral treatment had failed were recruited. All were women, with a mean age of 59.4 years (40-78). At the end of the weekly phase, 15 patients (50%) abandoned the treatment due to lack of efficacy. There were only two minor adverse effects, which were resolved by stopping the instillations.

The VAS score at the start of treatment was 7.2 (5-10). In those who completed the treatment, the mean initial score was 7.1 (5-10) and at the end of the treatment it was 2.5 (1-5), a decrease of 4.6 points.

The mean daytime urinary frequency (DUF) was 13.5 (6-20). In those who completed the treatment it was 13.9 (10-20) and at the end of the treatment it was 8.6, which means a decrease of 5.3.

The mean Nocturnal Urinary Frequency (NUF) was 3.9 (1-10) both in those who completed it and overall. In those who completed, the final NUF was 1.5 (1-3), which represents a decrease of 2.4.

The subjective evaluation at the end of the treatment in the group of patients who completed the protocol was Good/Very Good in 12 patients (80% of those who completed, 40% of the total), and indifferent in 3. At 6 months the patients of the group that assessed their situation as Good/Very Good was 9 (60% of those who finished it), 4 patients were indifferent and 2 were worse. At 12 months there were 7, 5 and 3 respectively.

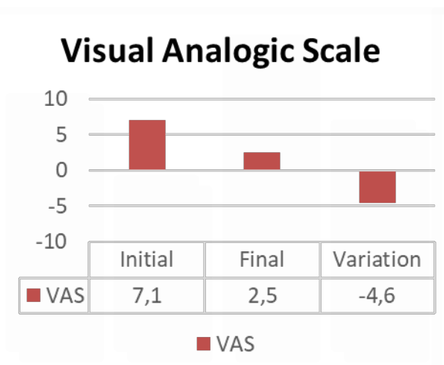

Figure 1. Visual Analogic Scale (VAS).

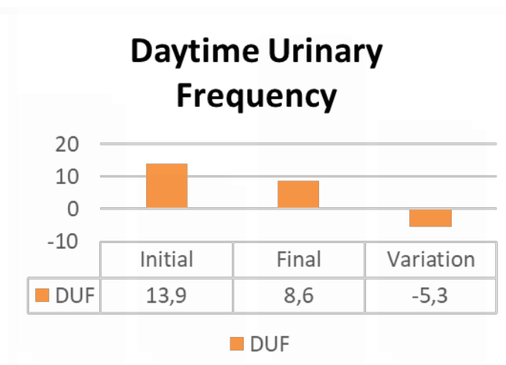

Figure 2. Daytime Urinary Frequency (DUF)

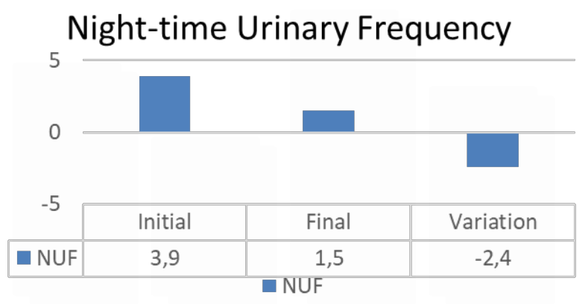

Figure 3. Night-time Urinary Frequency (NUF)

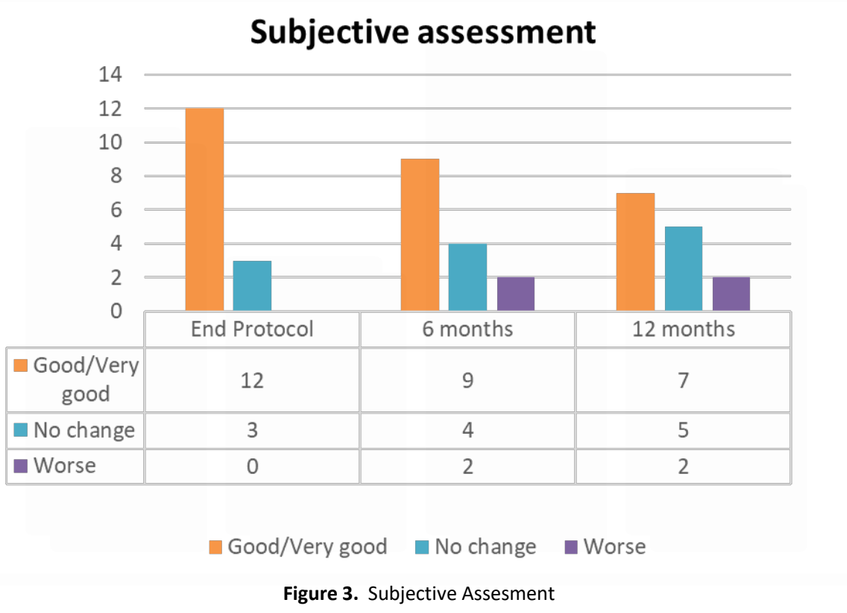

Figure 3. Subjective Assesment

Discussion

Glycosaminoglycan (GAGs) layer is an essential component of the impermeable, protective and neutralizing barrier of the urothelium against toxic and irritating substances and agents that may be present in urine. Its alteration in inflammatory processes seems to play a key role in the symptoms of BPS, which is why its replacement is an important approach for its treatment.

Although the degree of alteration in this barrier is not uniform in this process of heterogeneous nature, the instillation of HA with CS, given the clinical results in our population, can be considered a valid therapeutic option in the group of patients with BPS who do not respond to the first line treatment.

The rate of adverse effects observed in our series is below that published in the literature.

Conclusions

Intravesical instillation of HA with CS of HA/Cs has an acceptable clinical response rate in the treatment of BPS, which, together with its low rate of adverse effects, means that it can be considered a valid therapeutic option in the group of patients with BPS who do not respond to the first line treatment.

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