



Trabajo Original

Clinical study of hyaluronic acid gel in dyspareunia caused by vaginal dryness

Estudio clínico con un gel de ácido hialurónico en la dispareunia por sequedad vaginal

Juan Antonio Mieza Arana¹, Rafael Cortés Ceballos², Pilar Blasco Zapater³, José Luis Neyro Bilbao¹, Cristian Albert Casali⁴, Carmen Chacón Aguilar², Inmaculada Santamaría Ortiz⁵, Elena Ruiz Domingo⁶, Marina Arenas García⁷, Elena Flores Aznar², María Antonia Sánchez Oliver², Germán Francisco Torralva Piñero⁸, Eva María Soto Sánchez⁹, Pablo Juaristi Oria¹⁰, Ricard Rubio Salazar¹¹, David Beltrán Vaquero¹² y Esteban Rodríguez Bueno¹³

¹Servicio de Ginecología y Obstetricia. Hospital Universitario Cruces. Barakaldo. ²Hospital Virgen del Rocío. Sevilla. ³ASSIR Santa Coloma de Gramenet. Santa Coloma de Gramenet. Barcelona. ⁴ASSIR Badalona. Badalona. ⁵Centro de Salud de Leioa. Vizcaya. ⁶Centro de Atención Primaria "Antoni Creus". Terrassa. Barcelona. ⁷Hospital Quirón Sagrado Corazón. Sevilla. ⁸Clínica Santa Isabel. Sevilla. ⁹Hospital Universitario Infanta Leonor. Madrid. ¹⁰Centro de Salud Doctor Areilza. Bilbao. ¹¹Hospital del Mar (IMAS). Barcelona. ¹²Centro Municipal de Salud Vicálvaro. Madrid. ¹³ASSIR Sant Andreu. Barcelona

Abstract

Objective: Hyaluronic acid plays a key role in the hydration, elasticity, and lubrication of the vagina. We evaluated the efficacy of a hyaluronic acid gel (Hyaluron mucus®) in the treatment of dyspareunia due to vaginal dryness.

Material and methods: A total of 150 women applied the gel using their fingers before intercourse. The gel could also be applied simultaneously by the partner. We assessed the intensity of pain, discomfort during intercourse, and degree of vaginal dryness; we also recorded overall opinion (physician and/or patient) on the efficacy and tolerability of the gel and on its cosmetic and medical properties. Adverse effects and their causality were also recorded.

Results: An improvement in pain, discomfort during intercourse, and vaginal dryness was reported by 91%, 84%, and 92% of patients, respectively. Medical opinion was favorable in 81% of cases and moderate in the remaining 19%. Patient opinion was favorable in 82%, moderate in 15%, and poor in 3%. Tolerability was good (2 cases of pruritus, 3 of stinging, and 1 of burning sensation). Compared with the previous treatment, the new gel was considered better by 64% of the women, equal or similar by 33%, and worse by 4%.

Conclusions: The hyaluronic acid gel studied (Hyaluron mucus®) significantly improved vaginal dryness and dyspareunia with good tolerability and favorable cosmetic-medical properties in around 90% of cases.

Key words:

Hyaluronic acid.
Vaginal disorders.
Lubrication.
Dyspareunia.
Medical device.
Menopause.

Resumen

Objetivo: el ácido hialurónico es clave en la hidratación, elasticidad y lubricación vaginal. Hemos valorado la eficacia de un gel de ácido hialurónico (Hyaluron mucus®) en el tratamiento de la dispareunia asociada a sequedad vaginal.

Material y métodos: 150 mujeres se aplicaron el gel en la vagina digitalmente antes de cada relación sexual, y se dejó abierta la posibilidad de que se aplicara simultáneamente por la pareja. Se valoraron la intensidad del dolor, la dificultad en la relación y el grado de sequedad vaginal; se registró la opinión global (del médico y/o del paciente) sobre la eficacia, la tolerabilidad y las características cosmético-galénicas del gel. También se recogieron los efectos adversos y su imputabilidad.

Resultados: el dolor, la dificultad en la relación y la sequedad vaginal mejoraron en el 91%, el 84% y el 92%, respectivamente. El juicio médico global fue bueno para el 81% de los casos y moderado en el 19% restante, para las pacientes fue bueno en el 82%, moderado en el 15% y malo en un 3%. La tolerabilidad ha sido buena (2 casos de prurito, 3 de escozor y 1 de quemazón). El gel en estudio fue considerado mejor por el 64% de las mujeres, igual o semejante por el 33% y peor por el 4%, respecto al tratamiento previo.

Conclusiones: el gel de ácido hialurónico estudiado mejora de forma relevante en torno al 90% de los casos la sequedad vaginal y la dispareunia con una buena tolerabilidad y aceptabilidad cosmético-galénica.

Palabras clave:

Ácido hialurónico.
Trastornos vaginales.
Lubricación.
Dispareunia.
Producto sanitario.
Menopausia.

Recibido: 17/02/2018
Aceptado: 12/06/2018

Mieza Arana JA, Cortés Ceballos R, Blasco Zapater P, Neyro Bilbao JL, Albert Casali C, Chacón Aguilar C, et al. Clinical study of hyaluronic acid gel in dyspareunia caused by vaginal dryness. Prog Obstet Ginecol 2018;61(4):341-344. DOI: 10.20960/j.pog.00111

Correspondencia:

Juan Antonio Mieza Arana
Servicio de Ginecología y Obstetricia
Hospital Universitario Cruces
Plaza de Cruces, s/n
48903 Barakaldo
e-mail: jonmieza@yahoo.es

INTRODUCTION

Vaginal dryness is particularly common during and after the menopause and, together with dyspareunia, it is one of the main symptoms of the genitourinary syndrome that affects approximately 50% of postmenopausal women (1). Although it may have several causes, the most common is the reduction in estrogen levels leading to a negative effect in urogenital integrity and epithelial barrier function (2). A decrease in the production of vaginal lubricant can lead to vaginal dryness and irritation. These modifications imply the appearance of vulvovaginal discomfort, which may take the form of local itching, irritation, burning sensation, and even pain during intercourse (dyspareunia). Dyspareunia may seriously inhibit sexual desire and lead to vaginismus and anorgasmia.

Hyaluronic acid is a key mucopolysaccharide in the extracellular matrix. It is present in the skin and in many other tissues, including the vaginal mucosa. Its extraordinary hydrophilic capacity and its viscoelastic nature make it a key molecule in tissue hydration and elasticity by stimulating collagen synthesis in the skin and mucosa (3). Given that hyaluronic acid can retain large amounts of water molecules and help to form an extracellular aqueous film to maintain the water balance, it counters the symptoms associated with vaginal dryness (4). Hyaluronic acid also participates in healing of wounds and ulcers, thus highlighting its regenerative ability.

The present study evaluates the efficacy and safety profile of a hyaluronic acid gel—Hyaluron mucus®—in patients of various ages who presented with dyspareunia associated with vaginal dryness.

MATERIAL AND METHODS

We performed a multicenter, open-label, prospective clinical trial, for which we selected 150 women aged <75 years with dyspareunia associated with vaginal dryness. Informed consent was obtained from all patients before inclusion in the study. The study procedures complied with the ethical stipulations of the Declaration of Helsinki of 1975 (1983 Revision).

The exclusion criteria were pregnancy, breastfeeding, and any type of vaginal disorder (infections, lesions, tumors) or severe associated systemic disease requiring specific treatment other than that proposed for the study. We also excluded any participant who received another vaginal treatment during the trial.

The preparation used for the study (Hyaluron mucus®) consists of a hydrogel with hyaluronic acid 0.025% and a physiological pH equivalent to that of the vaginal mucosa. It does not contain acrylamides and is compatible with condoms. The product is applied to the vagina with the fingers before intercourse. It can also be used

simultaneously by the partner. The minimum number of sexual relations for evaluation of efficacy was 2 during the 6-month study period.

We evaluated various effectiveness parameters: pain intensity, discomfort during intercourse, and vaginal dryness before and after treatment with the gel. Measurements were on a scale of 0 to 3, where 0 is absent, 1 mild, 2 moderate, and 3 severe.

In addition, when treatment was complete, overall opinion—both doctor and patient—on the effectiveness and tolerability of the gel was recorded.

Similarly, we recorded adverse events occurring outside the treatment. Imputability was classed as "possible", "probable", "improbable", or "not related".

Finally, we evaluated medical and cosmetic parameters of the gel, which included applicability, texture, and smell. These were classed by the patient as "good", "normal", or "poor". Similarly, the questionnaire collected the subjective impression of the patient on the duration of the lubricant effect as "sufficient", "limited", or "insufficient".

The results were expressed as a percentage of the patients for each response according to the abovementioned scales.

RESULTS

Demographic data

A total of 150 patients completed the study. No dropouts were recorded in any of the 13 centers. Mean age was 54 ± 9 years (range, 20-72 years) (Table I). Eighty-one patients (54%) were within the 51-60 year age group, and 55% of the sample (83 patients) had previously received treatment for dyspareunia, with modest results (34% good, 56% normal, 10% poor).

The number of sexual relations and the method of application of the gel (only by the patient or by the patient and partner) are shown in table II. The gel was applied in a mean of 7 sexual relations. A single application was sufficient in 84% of the sample. The remainder (16%) required another application at initiation of intercourse.

Table I.

Distribution of the 150 patients by age at the start of the study

Age range (y)	No. (%)
20-40	16 (11)
41-50	20 (13)
51-60	81 (54)
61-72	33 (22)

Table II.
Frequency and form of application (woman or woman/partner) of hyaluronic acid gel

Frequency of application	No. (%)
On 2-5 occasions	89 (61)
On 6-10 occasions	35 (24)
On more than 10 occasions	23 (16)
Simultaneous use by partner	No. (%)
Yes	63 (44)
No	53 (36)
Sometimes	29 (20)

Decrease in the sensation of pain

The perception of pain during sexual intercourse improved in 91% of the women, remained unchanged in 8%, and increased from mild to moderate in 1 case (Fig. 1). In the cases of improvement, pain disappeared in 44% and decreased from moderate to mild in 38%, severe to mild in 10%, and severe to moderate in 8%. Discomfort during intercourse was also evaluated. This improved in 84% of participants and remained unchanged in 16% (Fig. 1). Of the patients who improved, 51% experienced no discomfort. Discomfort decreased from moderate to mild in 28%, from severe to mild in 10%, and from severe to moderate in 11%.

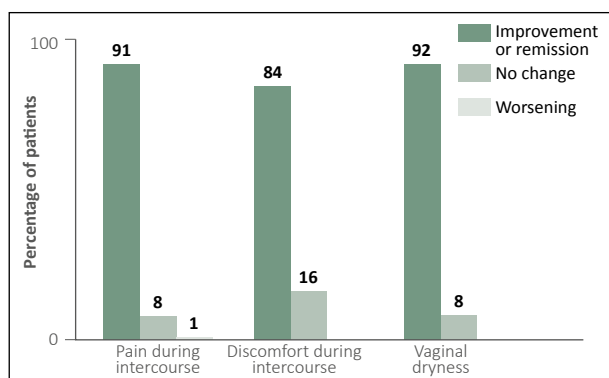


Figure 1. Clinical course after treatment with hyaluronic acid gel.

Improvement in vaginal dryness

Vaginal dryness improved in 92% of cases and remained unchanged in the remaining 8% (Fig. 1). In patients whose condition improved, dryness resolved in 35% and decreased from moderate to mild in 39%, from severe to mild in 17%, and from severe to moderate in 9%. The doctor’s opinion was favorable for 81% of cases and moderate

for the remaining 19%; the patient’s opinion was favorable in 82%, moderate in 15%, and poor in 3% (Fig. 2).

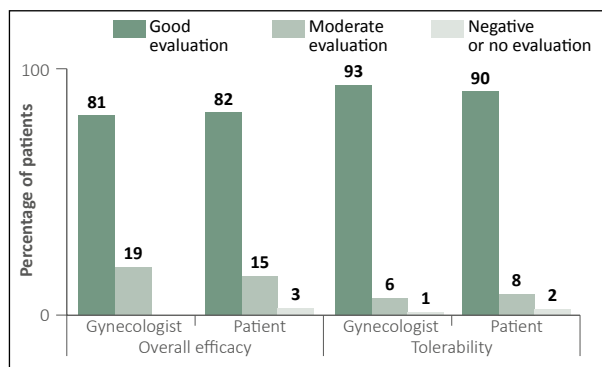


Figure 2. Overall opinion on the efficacy and tolerability of hyaluronic acid gel.

Tolerability and cosmetic acceptance

The product was generally well tolerated. No adverse reactions were recorded in 96%. Six patients reported itching, stinging, or burning sensation. The association with the gel was considered improbable in 2 cases, probable in 2 cases, and possible in 1 case. No causality was established in 1 patient. With respect to adverse events after treatment, urinary tract infection was reported in 1 case, itching in 1 case, mild itching in the partner in 1 case, stinging with swelling and heat sensation in 1 case, and continued dryness in 4 cases.

The evaluation of cosmetic acceptability (applicability, texture, smell) is summarized in figure 3. This was generally very good. The duration of the lubricant effect was considered sufficient in 75% of cases, limited in 21%, and insufficient in 4%.

In the case of patients who had previously received treatment, the study gel was considered better in 64% of cases, the same or similar in 33%, and worse in 4%.

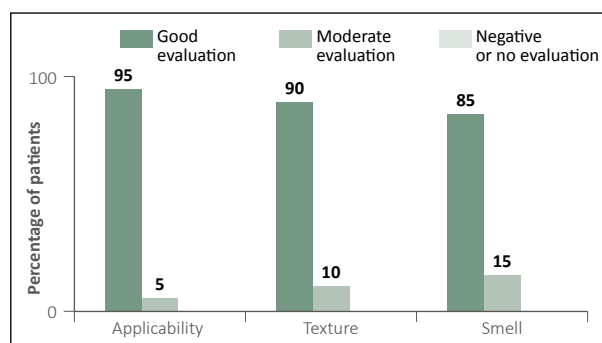


Figure 3. Patients’ overall opinion on the cosmetic and medical applicability of hyaluronic acid gel.

DISCUSSION

Hyaluronic acid plays a key role in vaginal hydration, elasticity, and lubrication. We evaluated the efficacy of a hyaluronic acid gel in the treatment of dyspareunia associated with vaginal dryness. Our prospective study shows that hyaluronic acid gel improved symptoms in around 90% of women in terms of perception of pain and discomfort during intercourse. We also observed an improvement in baseline vaginal dryness. Similarly, the study formulation had good tolerability and excellent medical-cosmetic properties. These results are comparable to those reported by other authors who studied the use of hyaluronic acid gels for vaginal dryness and atrophy (5-8). Of particular interest are the results of a recently published study, which showed a decrease in de novo dyspareunia associated with hormonal contraception. The authors found that patients treated both with estriol vaginal gel and with hyaluronic acid reported improved sexual relations (9).

CONCLUSIONS

The organoleptic properties of hyaluronic acid gel used in the present study are very similar to those of cervical mucus, particularly in terms of its texture and its oily and elastic nature, which make it a lubricant that is capable of easing the contact between surfaces. Its formulation enables it to be used with a condom. The partner also used the gel in 44% of cases. In 20% of cases, the partner used the gel only sometimes, and in the remaining 36%, only the woman used the gel. The evaluations of efficacy and tolerability are similar in all cases.

The ability of hyaluronic acid gel to retain water and to adhere to the mucosa enables prolonged hydration and

regeneration (3). These properties of hyaluronic acid gel also make it possible to counteract the symptoms of vaginal dryness and atrophy, as well as dyspareunia, which is a cause of considerable discomfort (1). Our study shows that application of hyaluronic acid gel before intercourse considerably improves vaginal dryness and dyspareunia in around 90% of cases. It is well tolerated and accepted because of its medical and cosmetic properties.

REFERENCES

1. Portman DJ, Gass ML. Vulvovaginal atrophy terminology consensus conference panel. Genitourinary syndrome of menopause: New terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. *Maturitas* 2014;79:349-54.
2. Ghumman S. Atrophic vaginitis: Diagnosis and treatment. *J South Asian Feder Menopause Soc* 2013;1:4-12.
3. Anderson I. The properties of hyaluronan and its role in wound healing. *Prof Nurse* 2001;17:232-5.
4. Brown MB, Jones SA. Hyaluronic acid: A unique topical vehicle for the localized delivery of drugs to the skin. *J Eur Acad Dermatol Venerol* 2005;19:308-18.
5. Chen J, Geng L, Song X, Li H, Giordan N, Liao Q. Evaluation of the efficacy and safety of hyaluronic acid vaginal gel to ease vaginal dryness: A multicenter, randomized, controlled, open-label, parallel-group, clinical trial. *J Sex Med* 2013;10:1575-84.
6. Grimaldi EF, Restaino S, Inglese S, Foltran L, Sorz A, Di Lorenzo G, et al. Role of high molecular weight hyaluronic acid in postmenopausal vaginal discomfort. *Minerva Ginecol* 2012;64:321-9.
7. Karaosmanoglu O, Cogendez E, Sozen H, Asoglu MR, Akdemir Y, Eren S. Hyaluronic acid in the treatment of postmenopausal women with atrophic vaginitis. *Int J Gynaecol Obstet* 2011;113:156-7.
8. Morali G, Polatti F, Metelitsa EN, Mascarucci P, Marre GB. Open, non-controlled clinical studies to assess the efficacy and safety of a medical device in form of gel topically and intravaginally used in postmenopausal women with genital atrophy. *Arzneimittelforschung* 2006;56:230-8.
9. Serati M, Bogani G, Di Dedda MC, Braghiroli A, Uccella S, Cromi A, et al. A comparison between vaginal estrogen and vaginal hyaluronic for the treatment of dyspareunia in women using hormonal contraceptive. *Eur J Obstet Gynecol Reprod Biol* 2015;191:48-50.