Clinical study on the anti wrinkle effectiveness of hyaluronic acid after repeated applications in normal conditions of use

1. ABSTRACT

The clinical study has been conducted to evaluate the effectiveness of hyaluronic acid in the treatment of wrinkles that accompany aging skin. The data presented in this report examined 29 patients or volunteers randomized to treatment. Method: All volunteers met the criteria for inclusion and exclusion according to the protocol of the study, vol unteers were enrolled under full informed consent in accordance with the Declaration of Helsinki, and were monitorized by medical researchers during the study, for a period of 6 months in the research laboratory of Don Benito (Badajoz Spain). Data were col lected in different categories, and where appropriate, analyzed comparatively between baseline or day 0 (T0, pretreatment), intermediate period (T1, at 3 months after the treatment starting) and the final period (T2, after treatment, at 6 months after star ting treatment). All data were evaluated for statistical significance and clinical relevance. P values (with a confidence interval of 95%) of ≤0.05, were considered significant. P values <0.01 considered highly significant. P values <0.001 were considered very highly significant. The main objectives of the study were as follows: Not only a comprehensive safety and side effects analysis, but also a control data on sociodemographic, anthropometric variables and measurements of elasticity (firmness, gross elas ticity, net elasticity, total elasticity and fatigue) were performed by the extensibility and elasticity of skin with a MPA with Dual Cutometer 580 in the right eye houndstooth. The results assess the skin resistance to suction (firmness) and the ir ability to return to its original position (elasticity).

2. MATERIALS

2.1. Inclusion criteria

• Consent to participate in the study.

2.2. Exclusion criteria

• To have intolerance or hypersensitivity to hyaluronic acid or any other part of the product.

• Pregnant women.

• Morbid obesity.

• Patients who have concomitant diseases or are receiving treatments that could interfere with the assessment of the effectiveness study.

3. METHODS

The study was designed, organized and implemented as a prospective clinical study of 6 months follow up. The study protocol was designed to capture data from monitoring at 3 and 6 months. The 29 female volunteers between 55-79 years old were assigned to the group treated with hyaluronic acid was administered as follows: for 6 months were given 1 capsule once a day at breakfast. No other drugs that could interfere with the results were allowed during the study. This assures the impact of hyaluronic acid without any confounder. All volunteers were given instructions on the form of administration and conservation of the product.

3.1. Variables

Primary variables

The clinical study collects and analyzes comparatively data related to objective changes: Measurements of elasticity (firmness, gross elasticity, net elasticity, total elasticity and fatigue) were performed using the extensibility and elasticity of the skin with Cutometer Dual MPA 580 in the houndstooth of the right eye. The results assess the skin resistance to suction (firmness) and its ability to return to its original position (elasticity).

Secondary Variables

• Report side effects and adverse reactions observed during treatment with hyaluronic acid and analyze the number, severity and nature of the same.

3.2. Measurements

Measurements of elasticity (firmness, elasticity gross, net elasticity, total elasticity and fatigue) were performed using the extensibility and elasticity of the skin with MPA Dual Cutometer 580 in the houndstooth of the right eye. The results assess the skin resistance to suction (firmness) and their ability to return to its original position (elasticity).

A. Baseline control (T0):

• Medical Record

• Information to volunteers about the medical device and completion of informed consent.

• Instructions on administration and conservation of the product and how to complete the registration booklet.

• Study measurements will be made for determination of:

- Measurements of elasticity (firmness, elasticity gross, net elasticity, total elasticity and fatigue) were performed using the extensibility and elasticity of the skin with MPA Dual Cutometer 58. The results assess the skin resistance to suction (firmness) and their ability to return to its original position (elasticity) were measured in the houndstooth of the right eye.

B. Intermediate Control (T1): At 3 months of starting treatment the same measurements were carried out as in the baseline control (T0).

C. Final control (T2): At 6 months of starting treatment the same measurements were carried out as in intermediate control (T1).

These data were specifically selected to build a comprehensive analytical framework designed to elucidate the potential safety, efficacy and clinical utility of hyaluronic acid in the treatment of wrinkles that accompany aging skin in a selected population that met both inclusion and exclusion criteria for clinical study.

4. RESULTS

4.1. Changes in skin firmness between T0 and T2

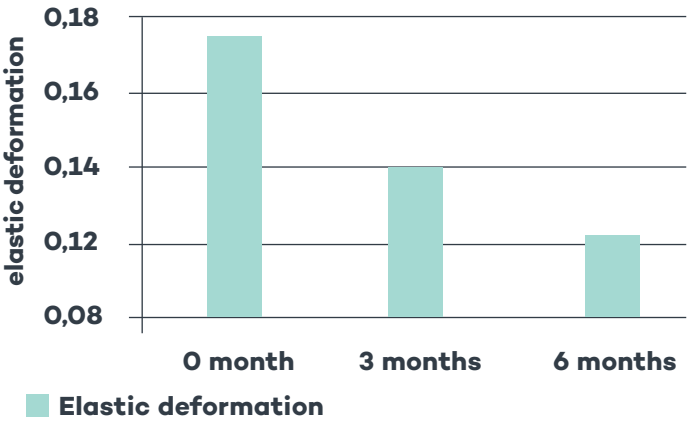

Figure 1 Changes in elastic deformation

Figure 1 refers to the reduction in elastic deformation of the skin in millimeters between baseline or Visit 1 (T0 pretreatment) and the final period or visit 3 (T2 post treatment) after performing the Wilcoxon signed-rank test. A reduction in this deformation led to an increase in firmness. Changes related to the treatment are observed (Figure 1). Voluntary decreased the mean elastic deformation by an average of 0.05 unit (29%) from baseline-T0-T2 period and final period, which was both statistically significant ($p < 0.0001$, with 95%) and clinically relevant (76% of volunteers improve firmness).

4.2. Changes in skin elasticity between T0 and T2

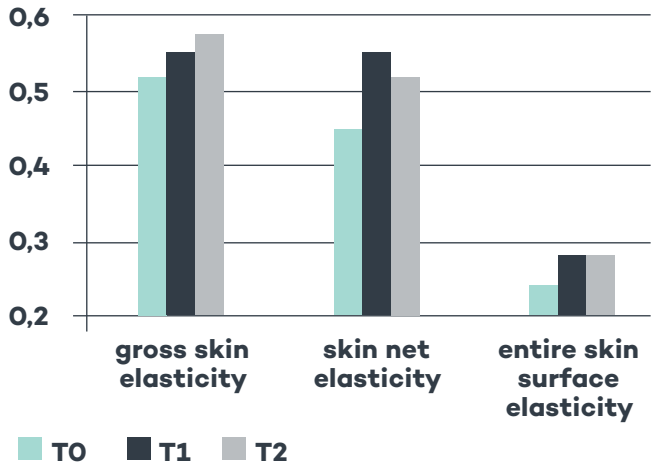

Figure 2 Changes in skin elasticity

In gross skin elasticity Variable between T0 and T2 after performing the Wilcoxon test, we observed the changes in skin gross elasticity related to treatment (Figure 2). Figure 2 shows the change in average gross skin elasticity. The volunteers increased the average gross elasticity of the skin by an average of 0.04 unit (7%) between baseline and period-end period T0-T2, being statistically significant (p = 0.033, with 95%) and clinically relevant (72% of volunteers improve its elasticity). After performing the Wilcoxon test in the variable skin net elasticity between baseline or visit 1 (T0 pretreatment) and the final period or visit 3 (T2 post treatment), we observed changes in net elasticity of the skin related to treatment (Figure 2). The chart shows the change in analysis the average skin net elasticity. Volunteers increased average net elasticity of the skin by an average of 0.08 unit (15%) between baseline and end period T0-T2, being statistically significant (p = 0.013 with 95%) and clinically relevant (76% of volunteers improve its elasticity).

Figure 2 shows the mean change in the elasticity of the entire surface of the skin between baseline or Visit 1 (T0 pretreatment) and the final period or visit 3 (T2 post treatment) after performing the Wilcoxon test. We observe the changes related to treatment (Figure 2). The graphic analysis shows the change in mean elasticity in the entire surface of the skin. Volunteers increased mean elasticity in the entire surface of the skin by an average of 0.03 unit (11%) from baseline period -T0 and final period -T2, being statistically significant (p = 0.006, with 95%) and clinically relevant (72% of volunteers improve its elasticity).

4.3. Safety assessment

The hyaluronic acid is indicated for the treatment of wrinkles that skin aging in a selected population of women. Reports of side effects and results: The study reflects the clinical follow-up visit of the females volunteers treated in improving wrinkles generated by skin aging. The objective and subjective measurements were collected along with information from daily entries in the study booklets made by all volunteers included in the study. Volunteers daily data reported side effects during the 6 months of treatment. No side effects associated with treatment among the volunteers who participated in the study were recorded.

5. CONCLUSIONS

Oral hyaluronic acid is a treatment that offers promising results in anti-wrinkles. Treatment with hyaluronic acid has proved to be effective, with statistically significant results on the parameters of elasticity (firmness, gross and net elasticity and elasticity of the entire surface of the skin), delaying or enhancing the vitality of the skin. During the study, no adverse or complications directly related to the treatment effect was observed.