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MONOPOLAR RADIOFREQUENCY CAPACITIVE RESISTIVE AT 448 kHz (INDIBA® SYSTEM) FOR THE TREATMENT OF CHRONIC PELVIC PAIN OF INFLAMMATORY ORIGIN

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INTRODUCTION

Pelvic floor is a complex anatomical structure formed by muscles, fasciae and ligaments. Its main function includes: supporting the abdominal floor, hold the vesical anatomical structure of the pelvis (urethra, vagina, bladder, rectum and uterus), urinary and fecal containment and maintain the vaginal tone, so the feminine sexuality as well (1, 2). Age, childbirth and lifestyle can affect the appearance of disorders such as pelvic pain, urinary and fecal incontinence, dyspareunia or vaginismus (3). As a whole, pelvic floor disorders have a high prevalence, being estimated that a third of the female population is affected by them (4, 5).
The treatment of the main part of pelvic floor pathologies needs a multidisciplinary approach that includes, among others, radiofrequency (RF) (1, 5, 6).
The present work is the clinical investigation to assess the efficacy and safety of INDIBA® 448 kHz RF device to treat chronic pelvic pain of inflammatory origin through intracavitary treatmens.

Objectives

The primary objective was to evaluate the effectiveness (at short and midterm) of manual therapy in combination with an intracavitary application of INDIBA® 448 kHz RF device (vagina/rectum) to treat chronic pelvic pain of inflammatory origin. To assess this objective the following variables were taken into account:

- Change of pain intensity using the visual analogue scale (VAS), and considering the change from the basal visit to the 10-S visit.
- Change in the chronic pelvic pain questioner of Mohedo (CPPQ-Mohedo).
- Change in the Depression and Anxiety Scale of Goldberg.
- Change in the National Institute of Health Chronic Prostatitis Symptoms Index (NIH-CPSI), only for male patients.
- Inflammatory clinical variables evaluated the professional staff.
- Global final evaluation by the patients and by the professional staff.

The second objective was to evaluate its safety and tolerability.

MATERIAL AND METHODS

Study type

This was a clinical study, single centre, prospective, interventional, randomised, with two parallel groups (active group: manual therapy plus INDIBA®; control group: manual therapy with sham INDIBA®), and double blinded.

Patients

All 49 patients included were adults, with a mean age of 40.3 years (control group) and 42.7 years (active group), of both sexes (56.0% women in the control group and 43.5% women in the active group), presenting chronic pelvic pain (from at least three months) of inflammatory origin.

Device

The signal generator was an INDIBA® 448 kHz RF device (INDIBA SA, Barcelona, Spain).

Treatment regimen and evaluations

For this study, the active group received RF by the resistive mode. The electrode was introduced in the vagina or in the rectum and with it manual therapy was applied. In the control group, the active and neutral electrodes were applied in the same positions, simulating the active treatment with the manual therapy, but without administering any current. Due to the fact that the output power applied in the active group was in the range of the subthermal power, patients were not expected to feel any thermal change, thus no further placebo strategies were implemented in the control group regading the sham exposure.

Ten sessions of RF or sham RF (45 minutes per session at 1-5% of the power range, subthermal level), administered along a two-week period (five daily sessions per week) was applied. All patients (active and control) also received manual therapy (specific to patient gender).

The study was scheduled in the following visits:

- Visit zero or basal (before treatment: B).
- Visit 1 (first day of treatment). Visit Basal and visit 1 could be in the same day.
- Visit 2 or 5-S (after five sessions of treatment).
- Visit 3 or 10-S (after 10 sessions of treatment).
- Visit 4 or 2-M (after two months from the first session of treatment). Follow-up period without treatment administration.
- Visit 5 or 4-M (after four months from the first session of treatment). Follow-up period without treatment administration.

This study was approved by the Ethics Committee of Clinical Research (CEIC: Comité Ético de Investigación Clínica) of the University Rey Juan Carlos, Madrid, Spain, as well as by the Agencia Española de Medicamentos y Productos Sanitarios (AEMPS).

Sample size and protocol compliance

A total of 49 patients took part in the study. The inclusion criteria were:

1. Older than 18 years of age.
2. Women hormonally active.
3. Chronic pelvic pain of inflammatory origin.
4. Duration of symptoms ≥3 months.
5. Score of pain intensity with:
   - VAS >2.
   - CPPQ-Mohedo* ≥10.5.
   - Score of anxiety in the Scale of Goldberg > 4.
   - Score of depression in the Scale of Goldberg > 3.
   - Score of NIH.CPSI (men) ≥ 22.

Exclusions criteria:

1. Pregnancy.
2. Use of intrauterine devices (IUD) for birth control or contraceptive vaginal ring.
3. Implanted pacemaker.
4. Severe neurological deficit in clinical exploration.
5. Total hysterectomy.
6. Dermal or epidermal lesions in the area to treat, except those that are not contraindicated for the treatment.
7. Concomitant medication.

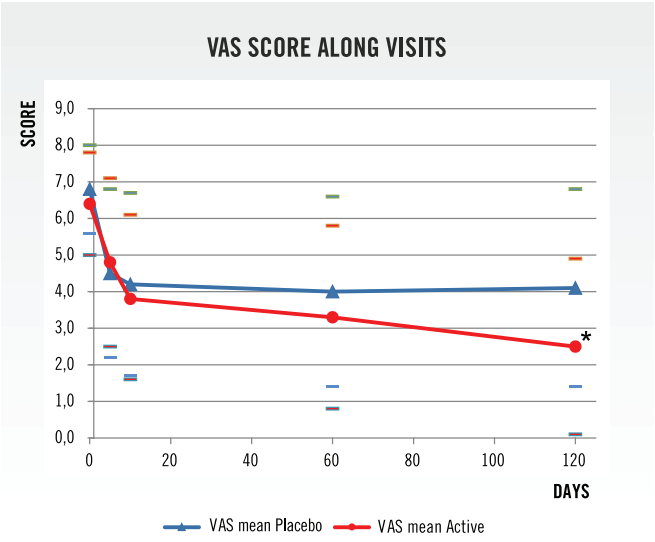
Results evaluation

The statistical analyses were performed with the SPSS Statistics software package. The significant differences were considered with $p<0.05$.

RESULTS

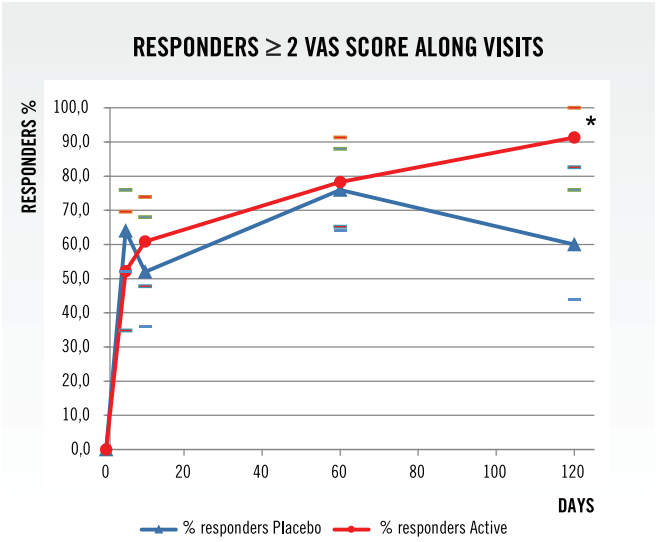
All patients, except one, completed the study accomplishing all the treatment sessions and visits established in the protocol. The only patient that ended the study prematurely had received one treatment session (active group) and for this reason his data was included in the safety analysis population. The reason for the withdrawal was personal (moving to another city).

VAS score showed a reduction of pain on both groups (38% control *vs* 40% active) but without statistical differences when comparing both treatments immediately after 10 sessions treatment (Graphic 1).



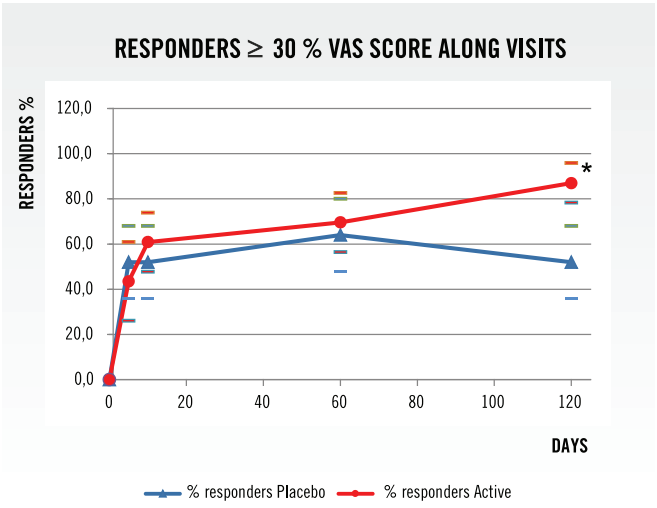
Graphic 1. Graphic representation of mean pain intensity (mean ± standard deviation) by VAS score along the visits of the study. Intention to treat population (n=48). The asterisk shows where the statistically significant difference (p=0.071) is with respect to the control.

The percentage of responders with ≥ 2 VAS score change from baseline at four months follow-up showed a significant difference (p=0.012) when compared with the control group (Graphic 2).



Graphic 2. Graphic representation of percentage of responders for a ≥ 2 change in VAS score (from basal to the different study visits) along the study. Intention to treat population (n=48; responders, 95% CI lower / upper limit). The asterisk shows where the statistically significant difference (p=0.012) is with respect to the control.

The percentage of responders with ≥ 30% VAS score change from baseline at four months follow-up showed a significant difference (p=0.009) when compared with the control group (Graphic 3).



Graphic 3. Graphic representation of responders for a ≥ 30% change in VAS score (from basal to the different study visits) along the study. Intention to treat population (n=48; responders, 95% confidence interval lower / upper limit). The asterisk shows where the statistically significant difference (p=0.009) is with respect to the control.

The rest of analysed variables did not show significant differences.

Safety analyses

INDIBA® 448 kHz device showed to be very safe. All the adverse events that occurred in this study were mild and none of them were likely to be related to the radiofrequency currents.

Treatment compliance was excellent; there were no missing treatment sessions.

* The Chronic Pelvic Pain Questionnaire - Mohedo (CPPQ-Mohedo) is a symptomatic rating of chronic pelvic pain.

DISCUSSION

In our study, the percentage improvements in VAS was close to 40% in both groups (active and control), after 10 treatments sessions (second week). These improvements persisted around the same percentage in patients receiving manual therapy at both 2 and 4 months post-treatment, while patients receiving active treatment improved their VAS by about 50% at 2 months and slightly over 60% at 4 months follow-up.

Differences in favour of the active group were maintained in the sub-analysis between responders of ≥ 2 degrees VAS at the end of the follow-up period (4 months) (91% patients treated with active *vs* 60% placebo) and non-responders (9% *vs* 40% respectively).

Not finding statistical differences immediately after the end of treatment among both groups can be attributed to different factors:

- Manual therapy being a standard active treatment in itself for pelvic floor pain.
- Too small sample to show statistical differences.
- Output power applied, optimizing thermal levels could increase the short term differences.

CONCLUSIONS

Both treatments reduced chronic pelvic pain of inflammatory origin.

INDIBA® 448 kHz radiofrequency device together with manual therapy, for the treatment of chronic pelvic pain of inflammatory origin has shown that manual therapy, a standard procedure in pelvic floor pain control, has the same effectiveness as its combination with RF immediately after the end of the 10 sessions treatment. Whereas at four months follow-up manual therapy combined with RF has shown a significant statistical difference, compared to the control, by improving the results.

The primary objective: effectiveness for the treatment of pain intensity was fulfilled at 4 months after 10 sessions administered in daily sessions within two weeks, together with manual therapy.

No clear efficacy response was appreciated in the rest of evaluated variables.

The second objective: intracavitary (vagina/rectum) treatment showed to be safe and well tolerated, and Proionic® Activ cream has also showed to be suitable to be used in this route.

Due to the experience coming from this study, and the long term effects provided by the active therapy, the treatment protocol could be improved by adding some hyperthermia component on the single subthermia provided in this protocol and by increasing the interval between sessions could also improve the comfort of the manual component intervention.

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