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Original Article

Influence of Low-Level Laser Irradiation of the Red and Infrared Spectral Range for Treating Chronic Testicular Pain: A Randomized Clinical Trial

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Abstract

Introduction: The treatment of chronic testicular pain is a complex condition that will be encountered by most practicing clinicians. In this study, the influence of low-level laser irradiation of the red and infrared spectral range for treating chronic testicular pain was evaluated and compared.

Methods: In this double-blind, placebo-controlled randomized clinical trial study, 60 patients were randomly divided into three groups of 20: (1) low-level laser group with red (650 nm, 50 mW), (2) low-level laser group with infrared (820 nm, 100 mW) and (3) laser placebo group. The treatment protocol consisted of 15 minutes, three times a week, for only 12 sessions. Then the patients were evaluated for pain and sexual satisfaction during the follow-up.

Results: There was a significant reduction in the pain score in the two groups of the low-level laser group with red (650 nm, 50 mW) and the low-level laser group with Infrared (820 nm, 100 mW) spectra compared with the control, at 6 and 12 weeks after the treatment ($P<0.05$). Also, the level of sexual satisfaction in the two groups of low-power laser with red and infrared spectra showed a significant improvement ($P<0.05$).

Conclusion: Low-level laser therapy is a safe, noninvasive, and useful method for treating patients with chronic testicular pain. Therefore, red (650 nm, 50 mW) and Infrared (820 nm, 100 mW) spectra low-level laser therapies improve testicular pain and sexual satisfaction.

Keywords: Chronic testicular pain; Infrared spectra; Low-level laser therapy; Red light spectra; Sexual satisfaction.

Introduction

Chronic testicular pain is associated with lower urinary tract symptoms or impaired sexual function.[1] This pain is persistent/intermittent and unilateral/bilateral that lasts for three months or more and is significantly annoying to the patient. Other causes such as infection, testicular mass, varicocele, hydrocele, abscess, or recurrent pain have also been ruled out.[2-4] This pain may represent itself with sexual intercourse, physical activity, or ejaculation.[5] This type of pain accounts for 2.5% to 5% of urological consultations.[6] History of vasectomy surgery, inguinal hernia surgery, abdominal surgery, diabetic neuropathy, imipramine use, and hyperemia are the most common causes of chronic testicular pain.[7-12] Unfortunately, the exact cause of chronic testicular pain has not yet been determined. However, it is hypothesized that the following factors may be the causes of chronic testicular pain: pain in sensory fibers passing along the spermatic cord and very low arousal threshold due to vasectomy, hernia surgery, renal resection, scrotal or pelvic trauma, recurrent testicular /epididymal infection, and local stimulation or inflammation parallel to nerve fibers. Therefore, conservative treatment in some patients caused the pain to resolve spontaneously from a few months to several years. In patients with significant pain and disruption of daily activity, invasive surgical interventions with dysfunction of nerve fibers lead to severe pain in these patients.[13-15] Understanding anatomy shows that adjacent to the testis by the scrotal and spermatic branches of the genitofemoral and ileo-inguinal nerves are sympathetic fibers along with the testicular artery. Based on this anatomy, it is assumed that the complete resection of nerve fibers by microsurgery is one of the surgical methods for treating chronic testicular pain.[7,11,16]

Despite the different types of treatment methods, choosing the proper type of treatment for these patients is very difficult and important. In the treatment of these patients, multidisciplinary strategies, medical consultations, medicinal treatments, ileo-inguinal nerve block, surgery, ablation, nerve block and other neurointervention are used according to the disease

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condition of the testis.[17]

Some studies have used a variety of successful therapeutic interventions to reduce lower urinary tract pain, including antibiotics, alpha-blockers, acupuncture, genitofemoral, ileo-inguinal, and spermatic nerve blocks, as well as laser therapy.[18,19]

Some studies have reported significant reductions in chronic musculoskeletal, joint, and neck pain, acute inflammatory pain, and pain after dental surgery using a low-level laser in the treatment of acute and chronic pain.[9,10,12,20,21]

A low-level laser is the treatment of choice for chronic pain and an alternative to medical treatments, which, despite its widespread use, is still a controversial medical issue. Low and medium-energy lasers such as GaAs or HeNe with a wavelength of 600-980 nm are used in various physiotherapy methods. A low-level laser is also effective in cellular and subcellular processes. Low-level laser with the mechanism of vasodilation, increased lymphatic drainage, and better tissue circulation reduces tissue edema, removes pressure from the nerve ending, and reduces its stimulation [22-24]. Although the low-level laser has many applications in the clinic, its exact mechanism for relieving pain has not yet been determined. To date, no pathological skeletal and musculoskeletal effects have been reported related to laser therapy.[22-24] Currently, chronic testicular pain treatment is one of the most important and controversial issues among urologists and pain specialists.

This study is the second clinical study to explore the curative effect of low-level laser irradiation of the red and infrared spectral range for treating chronic testicular pain in the Iranian population.

Materials and Methods

Sampling Method

Sixty patients were selected sequentially using the simple non-random sampling method, and they were randomly divided into three groups of 20 by the random number table method.

According to the study by Esmaeeli Djavid et al,[25] the sample size for each group was estimated to be 20 people considering $\alpha = 0.05$, $Z_{1-\alpha/2} = 1.96$, $Z_{1-\beta} = 1.28$, $p1 = 0.9$, and $p2 = 0.2$.

$$n = \frac{2(Z_{1-\alpha/2} + Z_{1-\beta})^2}{d^2}$$

$$d = \frac{P_1 - P_2}{\sqrt{P(1-P)}}$$

$$P = \frac{P_1 + P_2}{2}$$

Methods

The present study was conducted after the approval of the Ethics Committee of Shahid Beheshti University of Medical Sciences. This study was carried out as a double-blind, placebo-controlled randomized clinical trial (Parallel Design) on patients with chronic testicular pain who had been referred to the pain clinic of Imam Hossein, Shohada-e-Tajrish and Sajjad hospitals during 2015-2016. The patients with consent to participate in the study, age of 18 years and older, Patients with pain for at least 12 weeks were included, and patients with no consent to participate in the study and patients with malignant disease, epididymitis, epididymal cyst, flank pain, hydrocele, a history of varicocele surgery, varicocele disease, neurological defects, abnormal laboratory findings, systemic or psychiatric disease were excluded.

The patients were randomly divided into three groups of 20 using a random number table: (1) Red Low-level laser spectra (wavelength of 650 nm, 50 mW) group, (2) Infrared (IR) Low-level laser spectra (wavelength of 820 nm, 100 mW) group, and (3) low-level laser control group. The patients received laser therapy and placebo laser for 15 minutes, three times a week, for only 12 sessions. It should be noted that the treatment was done bilaterally. The therapist and the patient were not aware of laser therapy and placebo. The outcome of the treatment was assessed before the treatment, six weeks after the treatment (after the last intervention session), and 12 weeks after the start of the treatment (the last six weeks without intervention) by a physician who was not informed about the groups.

Intervention

The intervention groups were as follows: (1) Red Low-level laser spectra (wavelength of 650 nm, 50 mW) group, (2) Infrared (IR) Low-level laser spectra (wavelength of 820 nm, 100 mW) group. The power output was calibrated with a thermopile power meter. In each session, 3 points in the area of the upper scrotal nerve, which is the branch of the ilioinguinal nerve in T10-L1 segments, were irradiated by contact with a laser probe (L.H.H Medical Science Development CO., Ltd Beijing, China).

In the laser treatment groups, the patients were exposed to 6-25 J/cm²/d, while a passive probe was used in the placebo laser group (Figure 1).

Assessment of the Outcomes

The outcomes of the testicular pain and sexual satisfaction were measured by using the visual analogue scale (VAS) (0-10), based on which the patients were required to determine their testicular pain and sexual satisfaction levels by rating the VAS before the initiation of the treatment and 6 and 12 weeks after the initiation of the treatment.

If a complication was observed, it was recorded in the information form.

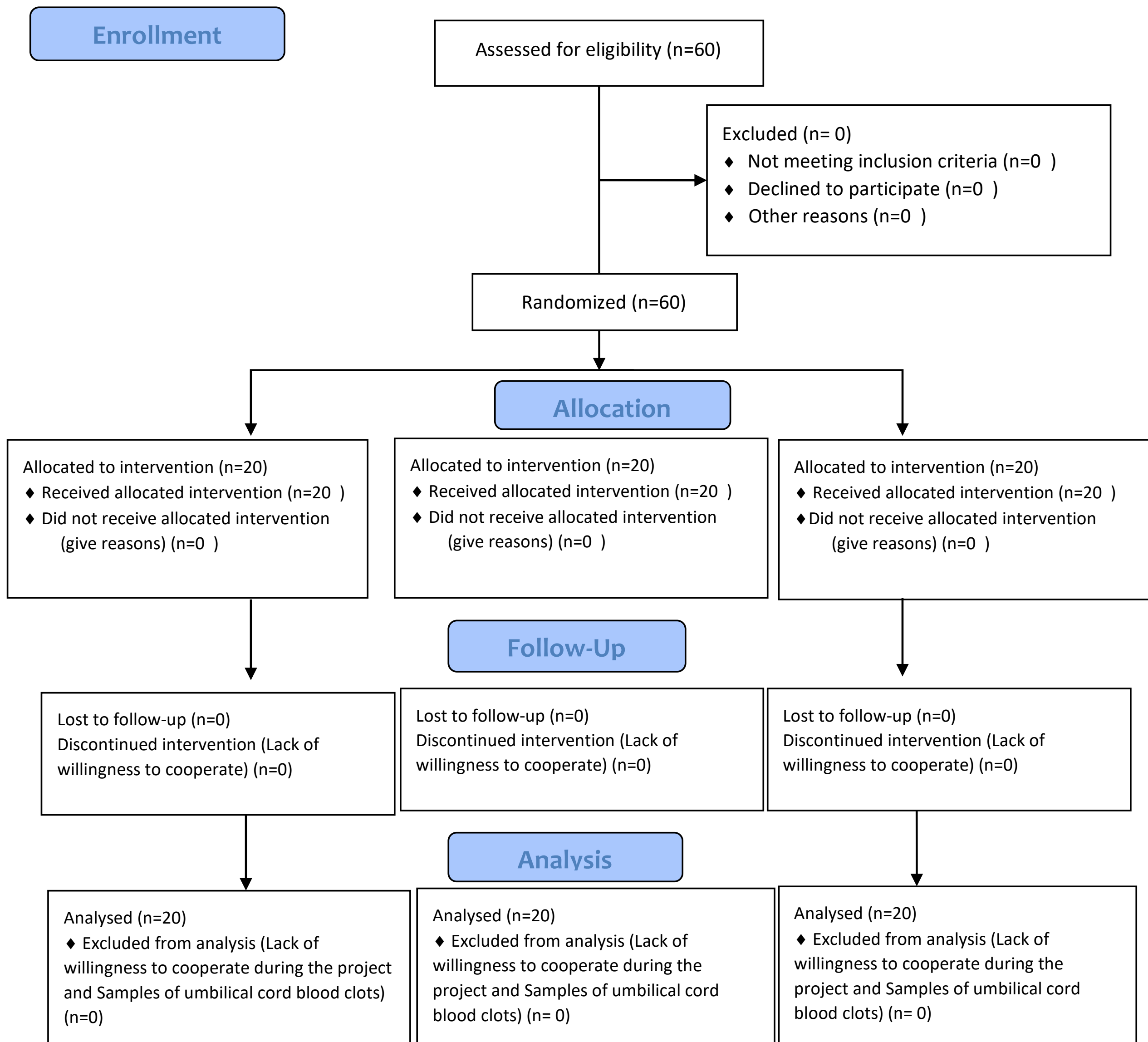

Figure 1. Consort Diagram of the Study

Statistical Analysis

The required information was recorded in a pre-prepared form, and then it was entered into statistical software SPSS version 19. After testing the normality of quantitative data scattering by the Kolmogorov-Smirnov test, we compared the mean of quantitative variables between the groups by paired t-tests, and the mean of quantitative variables was compared between the three groups by one-way ANOVA post hoc tests. Also, $P<0.05$ was considered statistically significant.

Results

A comparison of patients' demographic information between the three groups did not indicate statistically significant differences between the three groups ($P>0.05$) (Table 1).

The comparison of changes in the pain score based on the VAS at different times in the three groups is shown in Table 2 and Figure 2. The results showed a statistically significant decrease at different times after low-level laser therapy (LLLT) in comparison with the placebo group ($P<0.05$). A comparison between IR LLLT and Red LLT groups implicated no significant difference in the pain score at 6 and 12 weeks after the treatment (Table 2 and Figure 2).

Using the post hoc test, we found that six weeks after the treatment there was a statistically significant difference ($P=0.0001$) in the pain score between the placebo group and the IR LLLT group, and there was not a statistically significant difference ($P=0.781$) between the IR LLLT group and the Red LLLT group in that regard. Twelve weeks after the treatment, we observed a statistically significant difference ($P=0.0001$) between the placebo and IR LLLT groups, but the results did not indicate a statistically significant difference ($P=0.832$) between the IR LLLT and Red LLLT groups.

The comparison of changes in sexual satisfaction at different times in the three groups is shown in Table 3 and Figure 3. The results showed a statistically significant improvement at different times after LLLT compared to the placebo group ($P<0.05$). A comparison between the IR LLLT and Red LLT groups implicated no significant difference in the sexual satisfaction level at 12 weeks after the treatment (Table 3 and Figure 3). Using Post Hoc test, we found that there was a statistically significant difference in sexual satisfaction between the placebo group and the IR LLLT group six weeks after the treatment ($P=0.003$), but there was not a statistically significant difference between the IR LLLT group and the Red LLLT group ($P=0.730$). Twelve weeks after the treatment, a statistically significant difference was observed between the placebo and IR LLLT groups ($P=0.0001$), but the results did not show a statistically significant difference between the IR LLLT and Red LLLT groups ($P=0.839$).

None of the patients reported any complications related to the LLLT.

Discussion

Now, the treatment of chronic testicular pain is mainly traditional due to the lack of standardized protocols and is the main concern for most urologists. In chronic testicular pain treatment, the first line is usually the use of analgesics and non-steroidal anti-inflammatory drugs, which respond poorly to treatment. Also, low doses of tricyclic anxiolytics or antidepressants (such as amitriptyline, dapoxetine, and nortriptyline) can be used in appropriate doses to reduce pain.[23] The neuromodulating medications such as gabapentin, which significantly reduces pain in 80% of patients, may also be used.[24]

As a double-blind, placebo-controlled randomized clinical trial, this study is the second clinical study to evaluate the therapeutic effect of Red LLLT and IR LLLT on chronic testicular pain treatment.

In this study, we compared the therapeutic effect of three groups of Red LLLT with a wavelength of 650 nm, 50 mW, IR LLLT with a wavelength of 820 nm, 100 mW, and placebo laser on the patients.

The results of the study were reported after 12 sessions for four consecutive weeks with a follow-up period of three months.

In the present study, 6 and 12 weeks after the initiation of the treatment, the pain level in the two groups of Red LLLT and IR LLLT showed a significant improvement. Furthermore, the level of sexual satisfaction in the Red LLLT and IR LLLT groups showed a significant improvement. It seems that in patients with chronic testicular pain, LLLT with red and infrared spectra reduces pain and increases sexual satisfaction, and laser therapy with one of the low-level laser types with red and infrared spectra has an effective role in improving the quality of sexual life of these patients.

Considering the fact that so far no clinical study has

Table 1. The Comparison of the Demographic Data Between the Three Groups

	IR LLLT	Red LLLT	Placebo LLLT	*P* Value
Age (y)	25.4 ± 1.1	22.8 ± 4.6	27.0 ± 5.2	0.120
BMI (kg/m²)	27.0 ± 1.5	26.5 ± 3.2	28.0 ± 1.4	0.178

Table 2. The Comparison of the Pain VAS Between the Three Groups

	IR LLLT	Red LLLT	Placebo LLLT	*P* Value	*P* Value IR-Red	*P* Value IR-Placebo	*P* Value Red -Placebo
Before	9.1 ± 1.7	9.8 ± 1.4	8.9 ± 1.4	0.545	0.649	0.555	0.493
6 weeks after	3.2 ± 0.3	3.1 ± 0.9	4.5 ± 0.6	0.005	0.781	0.0001	0.0001
12 weeks after	2.0 ± 1.0	1.9 ± 0.4	3.6 ± 1.4	0.029	0.832	0.0001	0.0001

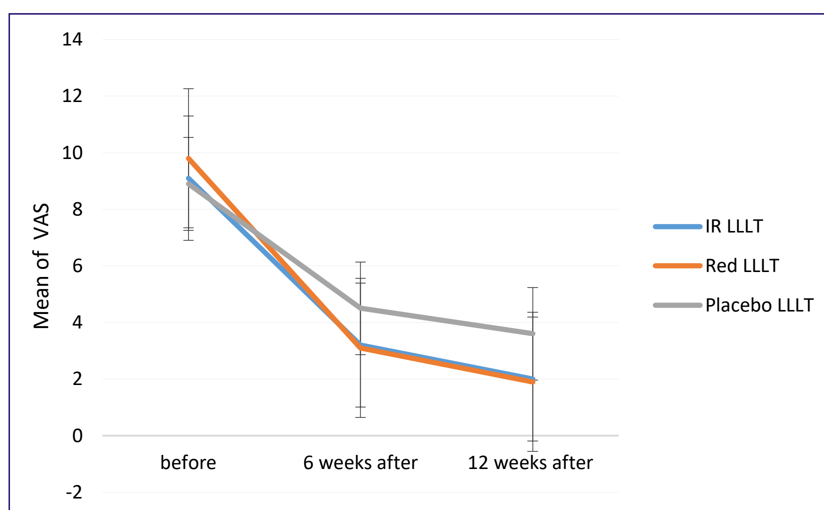

Figure 2. The Comparison of the Changes in Pain Score at Different Times Between the Groups ($P<0.05$). The data are shown as ANOVA

Table 3. The Comparison of the Sexual Satisfaction Levels Between the Three Groups

	IR LLLT	Red LLLT	Placebo LLLT	*P* Value	*P* Value IR-Red	*P* Value IR-Placebo	*P* Value Red -Placebo
Before	8.1 ± 0.4	8.0 ± 0.7	8.8 ± 1.4	0.548	0.898	0.759	0.591
6 weeks after	3.9 ± 0.5	3.8 ± 0.7	5.7 ± 0.9	0.013	0.730	0.003	0.001
12 weeks after	1.1 ± 0.2	1.9 ± 0.1	3.8 ± 1.8	0.046	0.839	0.0001	0.0001

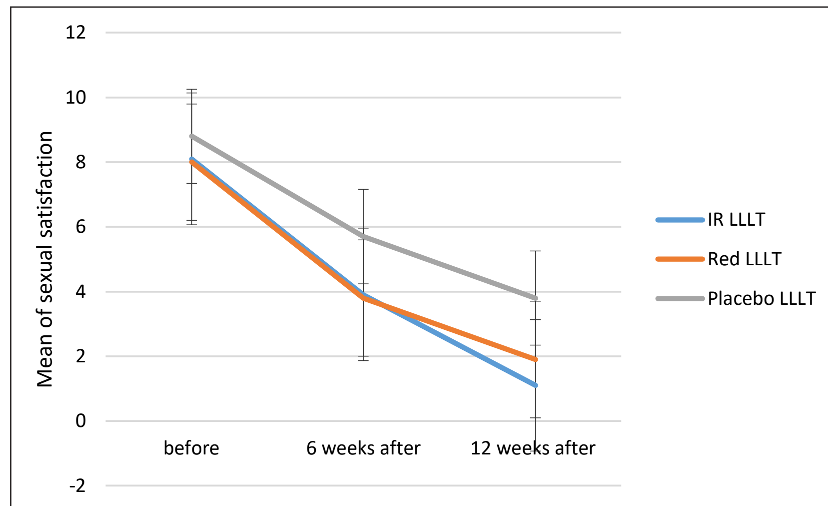

Figure 3. The Comparison of the Changes in Sexual Satisfaction Level at Different Times Between the Groups ($P < 0.05$). The data are shown as ANOVA

been performed with this method in chronic testicular pain treatment, the findings of this study cannot be compared with other studies. However, in a systematic study, the effect of low-level lasers on male infertility treatment was examined, and it was reported that low-level lasers significantly improved reproductive function and sexual activity in these patients. The local irradiation of red (635 nm) and infrared (904 nm) spectra range should have been used in combination with intravenous laser light with red (635 nm) and ultraviolet (UV) (365 nm) in the treatment of these patients.[11,20]

In some clinical studies, localized low-level laser radiation with red and violet light has been considered effective in male infertility treatment.[26-30]

In an animal study, the effect of low-level laser radiation on the rat testis in altering serum luteinizing hormone (LH) and testosterone levels was studied. The researchers of the study divided the mice into three groups: (1) laser radiation 4 J/cm²/d (50 mW × 10 s), (2) with a probe 12 J/cm²/d (50 mW × 30 s) with a wavelength of 660 nm for 5 days, and (3) control group. On the sixth day, they measured the serum levels of LH and testosterone and indicated that serum LH levels in group two showed a significant decrease but serum testosterone levels in three groups did not show a significant increase.[31]

It was previously thought that laser therapy was only auxiliary in nature and should be given with medication, or after completement of traditional treatment, laser therapy can be used as an adjunct to treatment.[32] However, further studies have completely rejected this view. Analytical studies have shown that laser therapy should be used as much as possible in the complex treatment of men with infertility because in these patients the effectiveness of this method is high and it often has no alternative.[32]

Therefore, most clinical researchers recommend the use of available low-level lasers with a wide range of methods in different organs determined by appropriate regulatory documentation and clinical recommendations by adjusting all laser parameters (such as wavelength, operating mode, frequency of pulsed lasers, power, power density set on by the exposure method, and focus on specific points).[33]

Our study is the second randomized clinical trial study that investigated the effect of two types of low-power lasers on reducing the intensity of chronic testicular pain. Our results are consistent with the findings of the first randomized clinical trial study in chronic groin and scrotal pain following varicocelectomy.[34]

The mechanism of LLLT is likely to be through reduction of prostaglandin-2 levels and mimicking cyclooxygenase 2 inhibitions.[35,36] While the mechanisms of action of LLLT have not been fully explained so far, it is clear that LLLT is associated with an analgesic effect.

We concluded that the use of a red low-level laser (wavelength of 650 nm, 50 mW) and an infrared low-level laser (wavelength of 820 nm, 100 mW) is a helpful, secure, noninvasive, and beneficial method for treating chronic testicular pain and increasing sexual satisfaction, with no specific side effects. The low-level laser with red/infrared spectra as mentioned by the protocol of this study can relieve chronic testicular pain and improve sexual satisfaction and quality of life. Chronic testicular pain is

a debilitating and difficult disease to treat and remains a challenge for urologists.

A thorough understanding of the pathology and its various causes, a multidisciplinary team approach to its treatment, and considering the patients' benefit from the various available treatment options are essential. Therefore, pain specialists and urologists are advised to consider the use of a red low-level laser (wavelength of 650 nm, 50 mW) and infrared low-level laser (wavelength of 820 nm, 100 mW) treatment for 15 minutes, three times a week, for only 12 sessions in these patients.

The limitations of the study included the subjective expression of pain severity and pain relief and tools used to evaluate study endpoints, which significantly affects the evaluation of the effectiveness of therapeutic interventions and patients response.

It is suggested that in the future, for definitive clinical recommendations, such studies should be carried out with a larger sample size and long-term follow-up, and they should take into account the optimal treatment parameters of the red light/infrared spectra range of the low-power laser.

Conclusion

The study showed that low-level laser therapy is a safe, noninvasive, and useful method for treating patients with chronic testicular pain. Therefore, red (650 nm, 50 mW) and infrared (820 nm, 100 mW) spectra low-level laser therapies improve testicular pain and sexual satisfaction.

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Authors' Contribution

Conceptualization: Cyrus Momenzadeh.
Data curation: Cyrus Momenzadeh.
Formal analysis: Cyrus Momenzadeh.
Investigation: Cyrus Momenzadeh.
Methodology: Cyrus Momenzadeh, Mohammad Reza Razzaghi.
Project administration: Cyrus Momenzadeh, Mohammad Reza Razzaghi, Mohammad Zaki Abbasi.
Resources: Cyrus Momenzadeh.
Software: Cyrus Momenzadeh.
Supervision: Cyrus Momenzadeh, Mohammad Reza Razzaghi.
Validation: Cyrus Momenzadeh.
Writing–original draft: Mohammad Reza Razzaghi, Mahmoud Dehghani-Ghorbi.
Writing–review & editing: Cyrus Momenzadeh, Mohammad Reza Razzaghi, Mohammad Zaki Abbasi, Alireza Jaffari.

Competing Interests

The authors claim no conflict of interest.

Ethical Approval

This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.REC.1396.110) and registered at Iranian Registry of Clinical Trials (identifier: IRCT201710038146N24; https://irct.behdasht.gov.ir/).

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