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SAFETY AND EFFICACY OF ULTRASOUND GUIDED RADIOFREQUENCY OF DORSAL NERVE OF THE PENIS IN LIFELONG PREMATURE EJACULATION REFRACTORY TO CONVENTIONAL TREATMENT

By

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ABSTRACT

Background: Premature ejaculation (PE) is a significant and common medical problem affecting many men worldwide. While PE is not a life- threatening disorder, its effect on quality-of-life (QoL) issues is significant.

Objective: To evaluate the feasibility, safety and efficacy of pulse radiofrequency (PRF) of dorsal nerve of the penis in lifelong premature ejaculation refractory to conventional treatment.

Patients and Methods: In this prospective study, all adult males complaining from lifelong PE resistant to conventional treatment, and seeking treatment of PE, at Al-Azhar University Hospitals [Al-Hussein and Sayed Galal]; Cairo; Egypt during the period from December 2019 to July 2020 were studied. Detailed history, physical examination, serum testosterone, serum prolactin were obtained. Patients underwent ultrasound guided pulsed radiofrequency of dorsal nerve of the penis. Any operative complications were recorded. To assess the efficacy of the procedure, patients were evaluated by intra vaginal ejaculatory latency time (IELT) and sex satisfaction scale (SSS).

Results: As regard SSS, 3 weeks before intervention, all the subjects (20 subjects) were unsatisfied. Three weeks post intervention, 9 (45%) of subjects were satisfied, while 11 (55%) were unsatisfied. Four months post intervention, 8 (40%) subjects were satisfied, and 12 (60%) were unsatisfied SSS 3 weeks post intervention was significantly different from SSS 3 weeks before intervention and 4 months post intervention ($p<0.001$). The mean of IELT was 33.4±19, 188.4±154.9, and 141.5±129.7 seconds at 3 weeks before PRF, 3 weeks after PRF, and 4 months after PRF, respectively. A significant difference was found between IELT pre intervention, 3 weeks and 4 months post intervention ($p<0.001$). A strong positive correlation was found between IELT and SSS at 3 weeks and 4 months post intervention ($p < 0.001$& $r = 0.78$) and ($p < 0.001$& $r = 0.91$) respectively. In our study, 4 (20%) patients had pain that relieved by analgesic and 2 (10%) patients had minimal bleeding at site of needle insertion & resolved by compression. No subjects complained of erectile dysfunction nor loss of sensation, while 2 (10%) patients reported superficial infection in first week post intervention which may contribute to uncontrolled DM, 4 (20%) patients had tingling within the first 3 weeks, and 2 (10%) had numbness within the first 3 weeks. All these complications resolved with conservative treatment.

Conclusion: PRF is a hopeful treatments in life long PE. Objective data on change in sensation (biothesiometry) and the short term of objective follow-up data are the significant limitations of this study.

Key words: Safety, efficacy, ultrasound guided pulsed radiofrequency, dorsal nerve, penis, lifelong premature ejaculation.

INTRODUCTION

Premature ejaculation (PE) is the inability to delay ejaculation time from penetration to ejaculation that always or nearly always occurs before or within 1 minute of vaginal penetration *(Serefoglu et al., 2014)*.

Patients with primary PE have penile hypersensitivity, which provides further evidence for an organic basis of PE *(Guo et al., 2017)*.

It was hypothesized that reducing the sensitivity of the glans penis with topical desensitizing agents (eg, local anesthetics) would delay ejaculatory latency without adversely affecting the sensation of ejaculation however, in applying a local anesthetic to the penis, there is, of course, the theoretical possibility of penile hypoesthesia, transvaginal contamination, and female genital anesthesia *(Waldinger, 2018)*.

Despite its side effects, such as numbness, paresthesia, pain for neuroma, and erectile dysfunctions, dorsal neurectomy is still performed to decrease the sensitivity of glans penis in selected patients resistant to conventional treatments *(Moon, 2016)*.

Pulsed radiofrequency (PRF) neuromodulation has been shown to be an effective treatment for a wide range of pain conditions *(Cohen and Soriano, 2018)*.

Reported 3 patients with groin pain or orchialgia who were successfully treated using PRF of the nerves innervating the area to reduce sensitivity of glans penis, so we used PRF for neuromodulation of dorsal penile nerves (DPNs) in patients with PE who were resistant to conventional treatments of PE *(Basal et al., 2010)*.

The present work aimed to evaluate the feasibility, safety and efficacy of PRF of dorsal nerve of the penis in lifelong PE refractory to conventional treatment.

PATIENTS AND METHODS

The studies included 20 adult male patients complaining from lifelong PE resistant to conventional treatment, and seeked for delay of ejaculation time during intercourse.

The research ethics committee of our institution approved the study protocol and all participants provided an informed written consent before inclusion.

Patients with congenital anomalies as (hypospadias and undescended testicle), erectile dysfunction, secondary PE, and hormonal PE were excluded.

All subjects who agreed to participate in the study underwent the following:

1. **Full History:** including age, medical co-morbidities e.g. Hypertension (HTN), diabetes mellitus (DM) Ischemic heart disease (IHD), Special habits (smoking, drug abusing, etc.), and erectile function.
2. **Physical Examination:** General, abdominal and genital examination.
3. **Laboratory Investigations:** (Complete blood cell count, hemoglobin A1C, coagulation profile,

lipid profile, thyroid profile, serum testosterone, Serum prolactin.

4. **Intravaginal ejaculatory latency time (IELT):** Is the time between the start of vaginal insertion and the start of intravaginal ejaculation PE, defined as an IELT of less than 1 minute that occurred in more than 90% of acts of intercourse and was resistant to conventional treatments (selective serotonin reuptake inhibitors, topical agents, psychological treatments, behavioral training techniques) *(Janssen and Waldinger, 2016)*.
5. **Sexual satisfaction:** The sexual satisfaction was evaluated using the sexual satisfaction scale (SSS) questionnaire (*Štulhofer et al. (2010)*, that translated to the patients into Arabic words by the physician.

PRF procedure:

Using aseptic technique and real-time sonographic guidance, a 22-gauge, 5-cm-long RF cannula with a 5-mm active tip (Neuro Therm, USA) was introduced under ultrasound guidance (M-turbo scanner (Sonosite, USA) equipped with a high-frequency L38 (13–6 MHz) linear transducer was used.) into the skin of the flaccid penis at the 11-o'clock position to apply pulsed radiofrequency to the right DPN.

The stylet was then removed and the radiofrequency probe inserted through the needle. The energy used in both situations (the sensory stimulation testing and the application of actual PRF), was lower than 0.45 V. First sensory stimulation testing was performed at 50 Hz, and the needle location was redirected based on the patient's identification of the point of maximal stimulation where the patient reported the most intense sensation.

We considered the intense sensation point is the most appropriate place for PRF neuromodulation of DPN at 11-o'clock. Afterwards, the PRF procedure was performed. The impedance ranged from 200 to 450 ohms. PRF procedures were performed with a setting of 2 x20 ms/s with a generator output (Neuro Term radiofrequency generator 1100, USA) of 45 V for duration of 180 seconds at 42C.

The RF cannula was introduced into the skin of the flaccid penis at the 1-O'clock position to apply PRF to the left DPN and the same procedure was repeated on the right DPN. By this procedure, we aimed to ablate sensation over as large an area of the glans penis as possible.PRF was performed by the same physician to avoid interpersonal variations.

All patients were assessed to evaluate the outcomes and satisfaction after surgery using IELT and SSS at three weeks and four months after intervention.

Statistical analysis:

Data management and statistical analysis were performed using the Statistical Package for the Social Sciences (SPSS) version 24.

Numerical data were summarized using means and standard deviations or medians and ranges. Data were explored for normality using Kolmogrov-Smirnov test and Shapiro-Wilk test. Categorical data were summarized as percentages. Comparisons overtime was done by Friedman test followed by Dunn post hoc test for pairwise comparisons. Correlation between SSS and ILET was done using

spearman rho correlation coefficient. P-values ≤ 0.05 were considered significant.

RESULTS

The mean age of the studied patients was 38.4±6.0 years. 6 (30%) patients had a history of diabetes mellitus, 8 (40%) were hypertensive and 24 (23.3%) had ischemic heart disease.

Three weeks before the intervention, the median IELT was 34 sec. (range: 4 to 62 sec.). Three weeks post-intervention, the median IELT was 127 sec. (range: 41 to 556 sec.). Four months post-intervention, the median IELT was 62 sec. (range: 20 to 401 sec.). A significant difference was found between IELT pre-intervention, three weeks, and four months post-intervention ($p<0.001$). Pairwise comparisons revealed that the IELT was significantly longer at the three-week and the four-month post-intervention compared to the baseline value ($p<0.001$). However, the IELT was significantly shorter at the four-month post-intervention compared to that reported at the three-week post-intervention time ($p<0.001$). The IELT at baseline and different follow-up time points **(Figure 1)**.

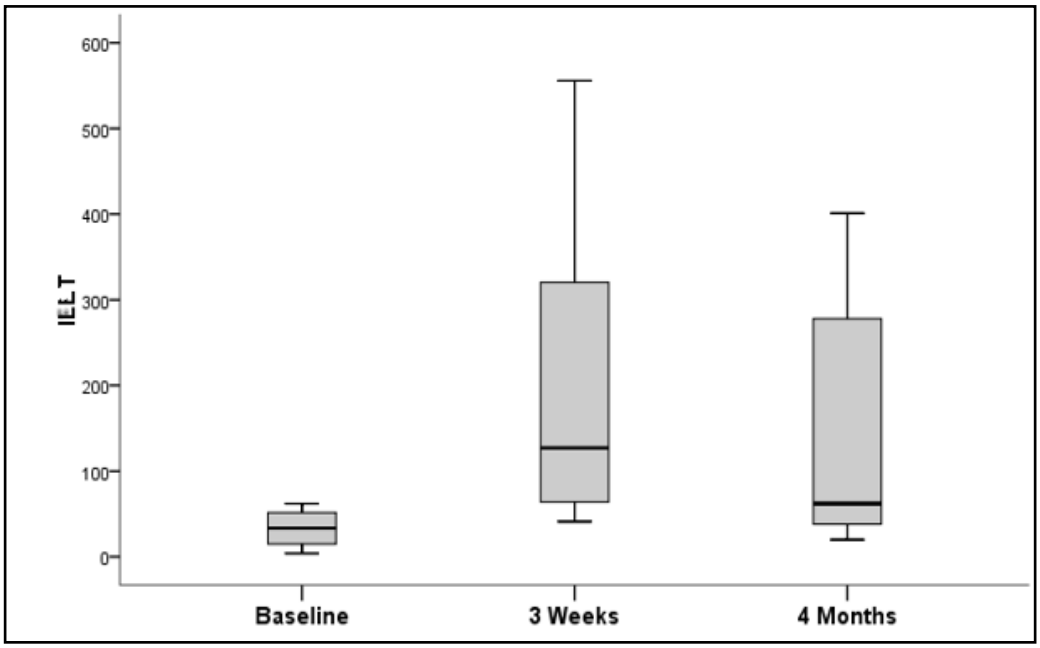

Figure (1): Box and Whisker plot demonstrating the IELT at the baseline and the two follow-up time points

The SSS at baseline and different follow-up time points are demonstrated in figure 4. All patients were unsatisfied pre-intervention. Three weeks post-intervention, 9 (45%) subjects were satisfied while 11 (55%) were unsatisfied. Four months post-intervention, 8 (40%) subjects were satisfied, and 12 (60%) were unsatisfied. A significant difference was found between pre-intervention, three-week, and four-month post-intervention sexual satisfaction rates ($p<0.001$). The pairwise comparison revealed that the satisfaction rate was significantly higher at the two follow-up time points than the baseline value ($p<0.001$). The satisfaction rate was significantly lower at the four-month post-intervention time than the three-week post-intervention rate ($p<0.001$).

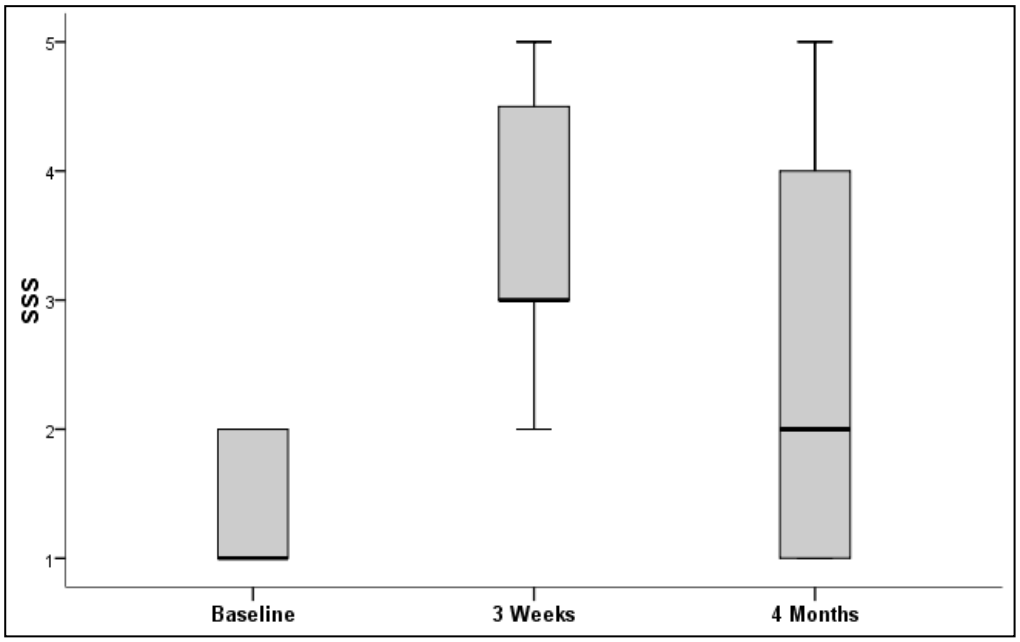

Figure (2): Box and Whisker plot demonstrating the SSS at baseline and the two follow-up time points

Strong positive correlation was found between IELT and SSS at three-week and four-month post intervention time points ($p < 0.001$; $r = 0.78$ and $p < 0.001$; $r = 0.91$, respectively).

Four (20%) patients had pain, and 2 (10%) had minimal bleeding at the needle insertion site. Two (10%) patients reported superficial infection in the first-week post-intervention, which may contribute to uncontrolled DM. Four (20%) patients had penile tingling, and 2 (10%) had penile numbness within the first three weeks (Figure 5). All complications were treated conservatively.

DISCUSSION

Success with systemic agents for treatment of PE has been variable and is associated with side effects. As regard topical agents, *McMahon et al., (2019)* reported a significant increase in IELT for topical treatments compared with baseline or placebo.

The main limitation of these treatments for PE is recurrence after withdrawal of medication. There are some difficulties with medical treatment. A patient must use drugs (local or oral) before every instance of sexual intercourse. The drugs may cause systemic (allergic reactions, sedation, effects on cognitive functions, and limitations using with other drugs) and local (penile hypoesthesia, transvaginal contamination, and female genital anesthesia) problems *(Hu et al., 2019)*.

Theoretically, selective penile dorsal nerve neurotomy (SDN) may be the solution as it blocks hypersensitive peripheral sexual stimulation signals, inhibits penile hypersensitivity and central excitability, which may help improve ejaculation threshold, and extend IELT *(Althof et al., 2010)*.

PRF is often used to treat pain in a variety of areas, which regulates neural activity primarily through electric fields without causing nerve damage *(Basal et al., 2010)*.

Similarly, PRF is used as a novel therapy for PE through modulation of the activity of the dorsal nerves of the penis and reduction its sensitivity *(Hu et al., 2019)*.

In our study we used PRF to treat PE by desensitizing DPNs. The study included 20 patients complaining from lifelong PE resistant to conventional treatment.

PRF was a simple maneuver with minimal complications rate, as 2 patients had minimal bleeding at the site of needle insertion that resolved by compression. Four patients had pain during the procedure that relieved by analgesics. Two patients reported superficial infection in first week post intervention which may contribute to uncontrolled DM, 4 patients had tingling within first 3 weeks, and 2 had numbness with first 3 weeks. All these complications resolved with conservative treatment.

In our study, no subjects complained of neither erectile dysfunction nor loss of sensation, thus confirming studies that have reported that no patients had any erection problem, penile hypoesthesia or pain after the procedure *(Basal et al., 2010)*.

In our study, a significant difference was found between ILET pre intervention, 3 weeks and 4 months post intervention, thus confirming other studies that have reported that all patients experienced a change in IELT, which significantly increased when compared with initial values *(Basal et al., 2010)*. They also reported a significant increase in SSS of all patients.

In our study, three weeks post intervention, 45% of subjects were satisfied, while 55% were unsatisfied. Four months post intervention, 40% of subjects were satisfied, and 60% were unsatisfied. SSS 3 weeks post intervention is significantly different from SSS 3 weeks before intervention and 4 months post intervention.

A strong positive correlation was found between IELT and SSS at 3 weeks post intervention, and 4 months post intervention. Inaccurate or unrealistic expectations were the most frequently cited reasons for patient dissatisfaction.

Small sample size due to many patients refused participation in study, and subjective assessment of patients by ILET and SSS affected by many factors that lead to false result.

CONCLUSION

PRF is a hopeful treatments in life long PE but, It is early to conclude that this new treatment modality might be used widely for the treatment of PE. Objective data on change in sensation (biothesiometry) and the short term of objective follow-up data are the significant limitations of this study. So, the need for placebo-controlled studies (eg, sham procedure), with larger numbers of patients, including assessment of penile sensitivity (eg, biothesiometry) is considered.

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سلامة وفعالية الترددات الراديوية النبضية للعصب الظهرى للقضيب فى علاج القذف المبكر بتوجيه الموجات فوق الصوتية

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خلفية البحث: ان سرعة القذف مشكلة طبية شائعة تؤثر على العديد من الرجال فى شتى انحاء العالم وبالرغم من كونها لا تعد خطرا يهدد الحياة، الا ان سرعة القذف تؤثر سلبا على نمط الحياة الصحية والنفسية.

الهدف من البحث: تقييم جدوى وسلامة وفعالية التردد الراديوي النبضي (التحور العصبي) للعصب الظهري للقضيب في علاج سرعة القذف طويل المدى المقاوم للعلاج التقليدي.

المرضى وطرق البحث: تم إجراء هذه الدراسة المستقبلية على المرضى الذين يسعون للعلاج من القذف المبكر، في مستشفيات جامعة الأزهر [الحسين وسيد جلال]؛ القاهرة؛ مصر. أجريت هذه الدراسة خلال الفترة من ديسمبر 2019 إلى يوليو 2020، حيث تم أخذ تاريخ مرضى كامل من جميع المرضى وتم فحصهم ظاهريا وخضعوا جميعهم لجلسات التردد الراديوي النبضي للعصب الظهري للقضيب بتوجيه الموجات فوق الصوتية وتم تقييم فاعلية هذه الجلسات باستخدام مقياس الرضا الجنسى وحساب زمن كمون القذف داخل المهبل.

نتائج البحث: علاج سرعة القذف باستخدام جلسات التردد الراديوي النبضي للعصب الظهري للقضيب بتوجيه الموجات فوق الصوتية يعد علاجا فعالا، فيما يتعلق بمقياس الرضا الجنسي، وقبل 3 أسابيع من التدخل كان جميع الأشخاص غير راضين. أما بعد ثلاثة أسابيع من التدخل، فقد كان 45٪

راضين بينما كان 55٪ غير راضين. وبعد أربعة أشهر من التدخل، كان 40٪ راضين و 60٪ غير راضين. وفيما يتعلق بزمن كمون القذف داخل المهبل، كان المتوسط قبل 3 أسابيع من التدخل 34 ثانية، أما بعد 3 أسابيع بعد التدخل فقد كان المتوسط 127 ثانية وبعد 4 أشهر بعد التدخل كان المتوسط 62 ثانية، كان هناك فارقا ذو دلالة احصائية بين الزمن قبل التدخل، 3 أسابيع و 4 أشهر بعد التدخل. كما كان هناك علاقة طردية بين زمن كمون القذف داخل المهبل ومدى رضا المريض.

الاستنتاج: يُعتبر التردد النبضوي للعصب الظهري كعلاج سرعة القذف هو بالنسبة للنتائج الأولية التي توصلنا لها أمراً مبشرا جداً إلا أنه يحتاج لبعض التعديلات في بروتوكولات البحث مثل زيادة عدد الحالات محل الدراسة، واستخدام الطرق المادية لتقييم النتائج مثل قياس حساسية حشفة القضيب وعدم الاعتماد على وصف المريض فقط للتاكد من إمكانية إعتماد التردد النبضوي كأحد طرق العلاج الفعالة والآمنه لسرعة القذف.

الكلمات داله: سرعة القذف، التردد النبضوى للعصب الظهرى للقضيب.