EVALUATION OF ERECTILE FUNCTION USING SIMULTANEOUS AUDIOVISUAL STIMULATION WITH SILDENAFIL AND RIGISCAN®: A PILOT STUDY

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ABSTRACT

Aim: To evaluate diagnosis and prediction of ED by using nocturnal penile tumescence, rigidity (NPTR) combined with audiovisual sexual stimulation (AVSS) and Sildenafil.

Materials and Methods: Multicentre study was conducted. Penile rigidity was recorded by NPTR test during 1 hour. AVSS test was performed in 3 steps; First step involved no medical treatment whereas the 2nd and 3rd steps involved 50mg and 100mg Sildenafil, respectively. NPTR test combined with AVSS and Sildenafil was accepted as positive if sufficient erection was observed in any step (Group 1, n=33), if vice versa the patient was included in Group 2 (n=19). Then, each patient underwent intracavernosal injection test (ICE), penile Doppler ultrasonography (PDU), and NPTR.

Results: Mean age was 55±7.4 years. AVSS-NPTR with Sildenafil was positive in 33 (63.5%) patients (Group1) and negative (Group 2) in 19 (36.5%) patients. In Group 1, sufficient erection was achieved in 5 (9.6%), in terms of 18 (34.6%) and 10 (19.2%) patients at the 1st and 2nd steps, respectively. AVSS test showed similar diagnostic efficacy with only NPT (p=0.02) and ICE (p<0.001).

Conclusions: AVSS-NPTR with Sildenafil can be strong candidate for a practical in evaluation of ED and its treatment effectivity.

Key Words: Audiovisual sexual stimulation, Erectile dysfunction, Nocturnal penile tumescence, Sildenafil

INTRODUCTION

The rate of erectile dysfunction (ED) has been growing [1]. The ED is not a life-threatening disease, however it may cause in loss of manpower. Notably, the diagnosis processes of ED can be annoying and also treatment modalities may be ineffective. Nevertheless, phosphodiesterase type 5 (PDE-5) inhibitors are recently used for ED treatment as empirical and the first choice treatments, in daily clinical practise worldwide [1]. Investigation for aetiology of ED is performed by completion of international index of erectile function (IIEF) questionnaire and questioning the presence of nocturnal erection, at the first step of diagnosis. Most of the patients with ED can be managed within the sexual care settings; conversely, however some of them may need specific diagnostic tests. Hatzichristou et al. reported importance of nocturnal penile tumescence and rigidity (NPTR) in evaluation of ED [2]. Thereafter, PDE-5 inhibitors are used for treatment of ED, and efficacy of treatment is assessed by IIEF questionnaires [3]. However, this questionnaire may not provide objective evaluation as reliability of the answers to the questions, and may vary from patient to patient [4]. Although, diagnostic tests such as NPTR, intracavernosal injection (ICE), and penile Doppler ultrasonography (PDU) can allow complete assessment of ED, these tests are difficult to be performed and have a low positive predictive value, in daily clinical practise [4-6]. Additionally, ICE test is invasive [4]. The combination

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of NPTR test with audiovisual sexual stimulation (AVSS) is non-invasive and can be practical alternative to these tests.

In the view of these above, it is hypothesized that Sildenafil might be used along standard AVSS-NPTR in incremental doses (50 mg and 100 mg). Besides, this modality may not only boost the diagnostic accuracy but also may help to predict response to Sildenafil, in patients with ED.

In the present study, we aimed to assess the diagnostic yield of AVSS-NPTR with Sildenafil tests by comparing this new methodology with conventional tests such as self-evaluation questionnaire, overnight NPTR, PDU, and ICE. In the second phase, we compared clinical outcome of Sildenafil treatment at home experience with the outcome of AVSS-NPTR with Sildenafil.

MATERIALS AND METHODS

This is a multicentre study that included retrospective view of prospective recorded data. Fifty-two ED patients were enrolled into the study. Of 13 patients had diabetes mellitus type-2, and 16 patients had previous coronary artery diseases. Between May 2013 and April 2016, men aged 32-73 underwent the first evaluation; the detailed histories were asked. Signed informed consents were obtained from all patients. Ethical approval was obtained from our institute and ethical committee. The IIEF-5 questionnaires were filled and nocturnal erection were asked.

Hormone analysis was performed in laboratory [7]. Then, each patient was invited to an isolated room for AVSS test. All patients watched video films of sexual content and penile erection were recorded by RigiScan® Plus (Timm Medical Technologies, Eden Prairie, MN) for 1 hour. In AVSS-NPTR test, penile erection lasting more than 10 minutes or rigidity of at least 70% were considered as sufficient whereas penile erection less than 10 minutes or penile rigidity less than 70% were accepted as insufficient penile rigidity [8]. This session of AVSS-NPTR test (1st step) was performed without any medical treatment. In the second session, each patient received oral 50 mg Sildenafil citrate 1 hour before the test (All the study groups underwent 2nd step). Then, patients who failed to achieve sufficient penile rigidity in the 1st and 2nd sessions underwent 3rd session. This subgroup of patients received oral 100 mg Sildenafil citrate 1 hour before the AVSS-NPTR tests. Patients who had sufficient erection or rigidity in any step were accepted as "rigidity positive" group (Group 1), and patients who failed to achieve sufficient penile erection and rigidity assessed by RigiScan® Plus during any step of the study were accepted as "rigidity negative" group (Group 2).

The patients were evaluated for their own erection or rigidity during AVSS-NPTR with Sildenafil as "sufficient" or "insufficient", and these reports were recorded, at each session. All patients watched the same video film, in the same room and environment, under the same conditions, at the same time period of the day. Inter-session intervals varied between 3 days to 14 days. After the patients completed all steps in AVSS-NPTR test, ICE, PDU, and 2 consecutive nights NPT test were applied before starting the therapy. The results were evaluated and recorded, individually for each patient.

The efficacy of AVSS-NPTR with Sildenafil in diagnosing of ED was evaluated by IIEF-5 scores, presence of nocturnal erection, self-assessment in AVSS test, ICE, NPT, and PDU results. In the second phase of our study, we evaluated the efficiency of AVSS-NPTR with Sildenafil to predict the response to Sildenafil treatment at home experience. During this phase, each patient received oral maximum 8 pills of Sildenafil in the same dose that induced a positive response in AVSS-NPTR with Sildenafil. If, the test result was negative after 50 mg Sildenafil in the test, the patient received maximal dose of Sildenafil citrate as 100 mg. The patients were then asked to use pills in a maximum dose of 2/week or in a minimum dose of 1/2week. After, using the drugs in specified dosing schedule, the patients reported their erection during sexual intercourse as "adequate" or "inadequate". Then, these results were compared to previous AVSS-NPTR with Sildenafil test findings for all patients, individually.

The Statistical Package for Social Sciences (SPSS, Chicago, IL) version 15.0 was used for statistical analyses. Univariate analysis was performed. The mean values of the parameters were compared by using One-way ANOVA. The significant p was $p \leq 0.05$.

RESULTS

The mean age was 55±7.4 years. Five (9.6%) patients achieved sufficient erection monitored by RigiScan® imaging in both 1st and 2nd steps, in the AVSS-NPTR with Sildenafil test. Additionally, these patients were coded as 1-1. Eighteen (34.6%) patients achieved sufficient erection in only 2nd step with the aid of 50 mg Sildenafil citrate. These patients were coded as 0-1. Of 10 (19.2%) patients were achieved sufficient rigidity at the 3rd step with the aid of 100 mg Sildenafil. These patients were coded as 0-0-1. In total, 33 (63.5%) patients were AVSS-NPTR with Sildenafil test positive (Group 1) and 19 (36.5%) patients were negative (Group 2) as RigiScan® imaging showed no sufficient erection. Patients who were negative in 3 steps were coded as 0-0-0.

Only standard NPT ($p=0.02$) and ICE ($p<0.001$) provided more diagnostic efficacy in Group 1 than Group 2 (Table 1). Besides, patients' experiences at home were compared with other diagnostic methods of ED. According to these, only AVSS-

Table 1. Comparison of audio-visual sexual stimulation (AVSS) test with other diagnostic tests used in erectile dysfunction is summarized.

Parameters	Group 1 (AVSS positive, n=33)	Group 2 (AVSS negative, n=19)	P value
Mean IIEF-5 score	10.9(0-19)	11 (3-20)	N.A.
Positive nocturnal erection, n(%)	24 (68.6)	11 (31.4)	N.A.
SE in self-evaluation of AVSS test, n(%)	29 (67.4)	14 (32.6)	N.A.
Normal VS in PDU, n(%)	22 (59.5)	15 (40.5)	N.A.
Positive NPT test, n(%)	19 (79.2)	5 (20.8)	0.02*
Positive ICE test, n(%)	28 (82.4)	6 (17.6)	<0.001*

AVSS: Audio-visual sexual stimulation, **NPT:** Nocturnal penile tumescence, **ICE:** Intracavernosal injection, **PDU:** Penile Doppler Ultrasonography, **IIEF:** International index of erectile function, **VS:** Vascular structure, **SE:** Sufficient erection, **N.A.:** Not applicable. *Statistical significant p value.

NPTR with Sildenafil test was significant related with home experiences (p=0.01).

There was no significant difference for laboratory analyses including hormone profiles in the groups. All hormone profiles were also in the normal range.

DISCUSSION

Sildenafil citrate is used as a one of the medical treatment options in ED, since the beginning of 2000 [9]. It broke a new ground by leaving behind many other treatment modalities [9]. Besides these, differential diagnoses between psychogenic and organic aetiologies of ED are very important for the clinicians [10]. Therefore, many tests are used for diagnosis and aetiological factors for ED. Subjective assessments of ED can be made by using IIEF-5 scoring, questioning nocturnal erection, and objective tests such as PDU, ICE, NPT, and AVSS, in clinical practise [11]. Although, all these tests are employed during clinical decision period, AVSS is somewhat less commonly used, owing to its low sensitivity. On the other hand widely usage of PDE-5 inhibitors may reduce the aetiological investigations of ED [12]. Additionally, clinical evaluation tests for ED can give us little information to predict the response to PDE-5 inhibitors. Therefore, a test which allows prediction of response to the ED treatment, along with a better diagnostic accuracy and well-suited for daily practice would be invaluable for clinical practise. Herein, we evaluated clinical usage of AVSS-NPTR with Sildenafil test for predicting benefit of Sildenafil in ED. We think that the non-invasive protocol can help us to improve non-invasive diagnostic tools for ED.

The IIEF-5 scoring is cheap, easy-to-apply, and commonly used in clinics for the first-line evaluation of ED. Besides, this is the easiest way to assess the ED and its treatment efficacy. Unfortunately, this test is based on subjective patient reports and may be misleading. The AVSS-NPTR with Sildenafil test can provide objective results for erectile functions. Additionally, it is more objective than IIEF-5 scores and questioning nocturnal erection.

Fitzgerald et al. [13] reported the diagnostic value of PDU and Collins et al. [14] revealed that ICE was commonly used in literature for ED diagnosis. In our multicenter study, patients who are unresponsive to Sildenafil treatment were evaluated by PDU and treated by ICE. This approach provided successful results. However, ICE may be effective method for diagnosis and treatment of ED, it is invasive [15]. The PDU may be a useful for evaluating cavernosal arteries as a screening tool in patients with suspected arteriogenic impotence only when acceleration is evaluated in addition to peak systolic velocity [16]. The specificity of the method may be partially limited by the inability to distinguish between arterial and arteriolar disease [17]. Because of the ICE test is invasive and PDU has low sensitivity and specificity in ED diagnosis, a new better diagnostic tool is needed. These tests may also lead to anxiety in ED patients. Meuleman et al. reported that ICE might lead to attenuation in erection through increasing adrenergic tension [18]. On the other hand, AVSS-NPTR with Sildenafil test is non-invasive and more practical and faster than other invasive tests. In addition, AVSS test is performed under the surveillance of physician, which reduces methodological flaws.

Tang et al. reported diagnosis of ED's vasculogenic subtypes could be improved by adding AVSS test during PDU [19]. Ku et al. measured the degree of rigidity by RigiScan® Plus during sexual intercourse [20]. However, NPT evaluation requires at least 2 days. Bock et al. reported diagnosis of ED might be misleading by using NPT, as NPT may not reflect the real erectile capacity [5]. Although, NPT test is considered one of the acceptable tests for the differential diagnosis of psychogenic versus organic ED, clinicians criticized for its cost effectiveness and time consuming features [21]. Mizuno et al. concluded that the AVSS test should be the examination of choice for the primary aetiological diagnosis in ED [22]. We performed AVSS-

NPTR with Sildenafil citrate administration in the hospital. We found that the diagnostic value of AVSS-NPTR with Sildenafil was comparable to ICE and NPTR tests. The goal of this trial was to present a non-invasive method for ED. Besides, the steps of the test might also compensate the defects of NPTR test in estimation of erectile performance. In addition, AVSS-NPTR with Sildenafil test was superior in predicting clinical response during actual treatment with Sildenafil, in our clinical aspect. Moreover, the efficacy of Sildenafil citrate may be measured by asking home experience of patients. The AVSS-NPTR with Sildenafil test may better show the efficacy of Sildenafil citrate and may reduce misleading resulting from subjective patient reports. In our study, self-assessment scores were not effective as ICE and NPT tests in determining sufficient erection. Thus, the AVSS-NPTR with Sildenafil test may show better diagnostic and prediction features.

There are some limitations in the present study. Firstly, there were low numbers of the patients. Nonetheless, AVSS-NPTR with Sildenafil test was comparable with ICE and NPT tests. We only focused the accuracy of the AVSS-NPTR with Sildenafil test and predicting benefits of Sildenafil in ED patients.

CONCLUSION

The AVSS-NPTR with Sildenafil test can be a strong candidate test for investigating aetiology of ED and predicting results of using Sildenafil in patients with ED. Additionally, the test is non-invasive. However, further studies are needed for more accurate results and to discover easy to apply diagnostic tools in ED.

COMPETING INTERESTS AND AUTHORS CONTRIBUTIONS

-All authors declare that there is no competing interest.

-MA designed the study; YA and MA collected the data and wrote the manuscript. MA and TI provided logistics, and checked the manuscript. OK and MFU made critical check and revised the manuscript.

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