



ANDUROLOGY/SEXUAL MEDICINE

REVIEW

Erectile dysfunction in Arab countries. Part II: Diagnosis and treatment

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KEYWORDS

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ABBREVIATIONS

ED, erectile dysfunction;
DM, diabetes mellitus;
IIEF, International Index of Erectile Function;
IHD, ischaemic heart disease;
PE, premature ejaculation;
PDE-5, phosphodiesterase-5;
EECP, enhanced external counterpulsation

Abstract Objective: To review local published data on the diagnosis and treatment of erectile dysfunction (ED) in Arab countries.

Methods: MEDLINE was searched for English-language articles published from 2000 to 2011, using the search terms 'Arab countries', 'sexual dysfunction', 'diagnosis' and 'treatment'.

Results: In all, 86 articles were found to be relevant to this review; only a few had a high level of evidence and the remaining studies used an uncontrolled design. Several local studies were consistent with previous reports showing that a customised diagnostic pathway, with full consideration of the patient's goals, is adopted by most clinicians to treat ED. For an effective treatment, the evaluation methods should answer important questions about the aetiology and severity of ED, as well as the patient's and partner's goals and expectations. As ED is known to be associated with many common medical comorbidities and medications, careful questioning can yield information about peripheral vascular disease, coronary artery disease, diabetes, hypertension, dyslipidaemia, and tobacco and alcohol use. The presence of psychological, neurological or chronic debilitating diseases can direct further evaluation.

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tion; PGE1, prostaglandin E1

Conclusion: The methods used for the diagnosis and treatment of ED need more investigation, especially in Arab countries. Only a few studies addressed the results of different methods of investigating and treating ED among Arab men.

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Introduction

A two-level diagnostic approach is a logical guide for treating patients with erectile dysfunction (ED). Currently, although various treatment options are available, a tailored diagnostic pathway with full consideration of the patient's goals is recommended. Lue [1] proposed the 'goal-directed approach to diagnose and treat ED' more than 20 years ago, and this approach is still valid. In general, the following should be obtained in every patient: (1) a detailed medical and psycho-sexual history; (2) a thorough physical examination; and (3) appropriate laboratory tests (complete blood count, fasting glucose, lipid profile, kidney function and testosterone, and others if indicated) [2,3].

For a satisfactory and cost-effective treatment the evaluation methods should answer these inquiries: (1) whether the cause of ED is organic or psychogenic; (2) the severity and possible reversibility of ED; (3) the patient's and probably the partner's goals and expectations.

Many classifications have been proposed for ED; the classification that integrates the various causes of ED with erectile physiology and functional anatomy is the recommended one [4]. Clinically, an older patient with a long history of diabetes mellitus (DM) and vascular disease is likely to have ED secondary to vascular and neuropathic disease. However, a young patient with psychiatric illness is more likely to have psychogenic ED.

Considering the increasing life-expectancy and the high incidence of ED in an ageing population, a further increase in patients with ED should be expected. The tailored diagnosis of ED not only allows the physician to avoid further costly evaluation, but also saves the patient from unnecessary and sometime invasive diagnostic techniques.

The diagnostic pathway and treatment of ED have been reported in many studies, but they are not yet well addressed in the Arab region. This provoked several investigators in Arab countries to assess different methods for the diagnosis and treatment of sexual dysfunction among patients in this region. The objective of this review is to address the published data in the last 10 years on the diagnosis and treatment of ED in Arab countries.

Diagnosis

Physical examination and special investigations

A thorough physical examination with particular attention to the genital area can sometimes reveal an obvious

cause (e.g. micropenis, penile chordee, Peyronie's plaque). The finding of small soft atrophic testes or gynecomastia should prompt an endocrine evaluation for hypogonadism or hyperprolactinaemia. Patients with some genetic syndromes, e.g. Kallmann's or Klinefelter's, can present with obvious physical signs of hypogonadism or a distinctive body habitus. A careful neurological examination should also be conducted. Testing for genital and perineal sensation and the bulbocavernosus reflex is also useful in assessing possible neurogenic ED. A history and physical examination had 95% sensitivity but only 50% specificity in diagnosing organic ED [5]. A multifaceted comprehensive approach is required for a full evaluation to diagnose ED. However, in many cases, a careful history and physical examination will direct the physician to the most expedient and cost-effective approach, and eliminate the need for unnecessary diagnostic tests [5].

Local data. In one study, El-Sakka [6] investigated the association between the International Index of Erectile Function (IIEF) and axial penile rigidity values in patients with ED from a total of 516 men. There was a significant association between the overall presence of ED and low axial penile rigidity. The IIEF score is associated with axial penile rigidity and can differentiate between patients with and without ED. In another study, the same author reported a significant association between increasing severity of ED and increased values of end diastolic velocity, and decreased values of peak systolic velocity and resistive index on penile Doppler ultrasonography and rigidometer tests [7]. In addition, El-Sakka [8] showed that a low peak systolic velocity can be used as a screening tool for ischaemic heart disease (IHD) in patients with ED. Al Turki [9] tried to determine the valid clinical question of whether an inquiry about sexual health, as a reflection of vascular health, should be part of routine physical examinations for young men. He concluded that facilitating patients to talk with their treating physicians about sensitive issues such as ED during consultation will help patients to seek appropriate and safe medical advice.

Laboratory investigation

The routine laboratory investigation should be directed at identifying treatable conditions or previously undetected medical illnesses that might be contributory, e.g. renal insufficiency, DM and endocrine abnormalities (hypogonadism, hyperprolactinaemia) [10]. A complete

laboratory evaluation includes serum chemistry, renal function, a complete blood count, urine analysis and hormonal evaluation (generally serum testosterone and prolactin), and should be done in the initial evaluation.

Local data Zohdy et al. [11] evaluated the effect of obesity on serum total testosterone levels and penile duplex ultrasonography variables in men with ED, and concluded that obesity is associated with lower total testosterone levels and disturbances of penile haemodynamics. El-Sakka et al. [12] reported a possible association between sexual dysfunction, e.g. ED, premature ejaculation (PE) and low desire, and hypogonadism. They also found that 23.8% of patients had endocrinopathy. The most frequent endocrine changes were a low testosterone level (15%), hyperprolactinaemia (13.7%), and hypothyroidism (3.1%). There were significant associations between endocrinopathy and obesity, smoking, low desire, and PE ($P < 0.05$ for each). Also, there were significant associations between low desire and low testosterone level, hyperprolactinaemia and hypothyroidism ($P < 0.05$ for each). Hyperprolactinaemia was significantly associated with PE ($P < 0.05$) but not with a low testosterone level. Furthermore, they investigated the effect of testosterone-replacement therapy on the PSA level in hypogonadal men with ED [13].

Treatment

The therapeutic strategy for treating ED could be a direct interference with the underlying cause or to bypass the cause and offer a nonspecific but personally and socially acceptable treatment. Nevertheless, patient age, general health, associated comorbidities, as well as patient and partner needs and expectations, are all important concerns. The association between ED and some categories of commonly used medications for the treatment of concomitant conditions, especially diuretics, antiandrogens and antihypertensive medications, should be considered.

Local data Levinson et al. [14] reported on the efficacy and safety of sildenafil citrate for treating ED in men in Egypt and South Africa. This was a 12-week randomised, double-blind, placebo-controlled, parallel-group, flexible-dose study. Improved erections were reported by 74% of patients receiving sildenafil and 27% of those receiving placebo ($P < 0.001$). Headache, dyspepsia and flushing were the most common adverse events in sildenafil-treated patients.

In a recent study El-Sakka et al. [15] reported on the use of sildenafil for men with ED in the Middle East, in an observational analysis of patients with DM and/or hypertension treated in the clinical-practice setting. They reported that overall effectiveness was rated as good or very good by 91.4% of patients, with 93.9% rating their sexual activity as spontaneous and 91.4% as

'natural'. Discontinuation of sildenafil due to adverse events was infrequent (0.5%). Tolerability was rated as good or very good by 95.7% of patients. It was concluded that sildenafil was a well-tolerated and highly effective treatment for ED in outpatients with DM and/or hypertension from the studied Middle Eastern countries.

In another study on phosphodiesterase-5 (PDE-5) inhibitors, Ali [16] reported on the effectiveness, in routine clinical practice, of sildenafil citrate and tadalafil on the sexual responses of Saudi men with ED, and concluded that both agents can assist an individual in extending/enhancing the excitement phase or prolonging the sexual interaction. This study emphasised the difference between the short-acting agent sildenafil and the longer-acting tadalafil. El-Sakka [17] assessed the effect of type 2 DM on the efficacy of sildenafil citrate for treating ED. He concluded that sildenafil is an effective treatment for diabetic patients with ED. Although the efficacy of sildenafil was negatively affected by factors such as poor control and longer duration of DM, and the presence of more than one DM-related complication, the overall efficacy and overall patient satisfaction were high. El-Sakka also assessed the effect of PE and low desire on the efficacy and satisfaction rate of sildenafil in the treatment of ED. The efficacy of sildenafil was negatively affected by an increased duration and severity of ED, but the overall efficacy and overall patient satisfaction were not attenuated by PE or low desire [18].

El Khat et al. [19] reported an observational comparative study on patients in Saudi Arabia, Kuwait and the United Arab Emirates, to assess psychosocial and efficacy outcomes of tadalafil 20 mg on-demand, over a period of 20 weeks, in men with ED who were treatment-naive vs. men pre-treated with an ED treatment other than tadalafil. The authors concluded that patients with ED and treated with tadalafil in a naturalistic setting reported improvements in both psychosocial outcomes and erectile function, with some differences between the treatment-naive and pre-treated groups. The results of this study might assist physicians in tailoring tadalafil therapy and setting realistic treatment expectations.

On a selected group of patients reporting ED on their honeymoon, Ghanem et al. [20] reported that tadalafil therapy was safe and effective as a short-term management. Of 45 patients included in that study, 41 (91%) were able to achieve vaginal intromission and perform sexually. Thirty-four patients (76%) needed tadalafil for < 1 month, five (11%) for up to 3 months, and two (4%) for > 3 months.

In another randomised, double-blind, parallel, placebo-controlled 12-week study carried out to evaluate the efficacy and safety of 20-mg tadalafil taken 'as needed' in a population of men with ED from Egypt and Turkey, Saylan et al. [21] reported that tadalafil

was better than placebo for all three co-primary efficacy endpoints. The mean (SD) change from baseline for the Erectile Function domain of the IIEF was 9.3 (0.8) for the tadalafil group and 2.3 (1.6) for the placebo group. Tadalafil-treated patients reported a significantly greater improvement in the mean (SD) percentage of successful penetrations, of 34.5 (4.1) vs. 4.6 (8.1) for placebo, and successful intercourse attempts, of 52.2 (3.8) vs. 16.8 (7.8) for placebo.

Kamel et al. [22] assessed the safety, efficacy and patient acceptability of vardenafil treatment under 'real-life' conditions in 2824 patients in the Middle East. They concluded that an overall improvement in erections was reported in 94.3% of patients. In most patients the treatment was successful after the first (67.0%) or second (83.6% cumulative) tablet, and the authors concluded that vardenafil was effective, reliable and well-tolerated in patients with ED treated under real-life conditions.

As to the complications of PDE-5 inhibitors, El-Domyati et al. [23] reported the case of a 48-year-old man who had acute vision loss 36 h after taking 50 mg sildenafil citrate; they concluded that when such drugs are used for ED, a condition that must be considered is non-arteritic ischaemic optic neuropathy, even though the users might have neither predisposing nor precipitating factors for this disease, even if occurring when there is a minimal blood level of these drugs.

In a previous review, El-Sakka [24] reported on the future directions and potential utility for PDE-5 inhibitors in alleviating cavernous fibrosis after radical prostatectomy. He concluded that despite the encouraging recent results of the role of PDE-5 inhibitors in preventing ED after prostatectomy, debate remains on the exact mechanism of PDE-5 inhibitors in the prevention, amelioration and reversion of penile fibrosis. Future studies are warranted to establish when to start PDE-5 inhibitor treatment in each of the conditions associated with penile fibrosis. Mosbah et al. [25] reported a study that compared early vs. late penile rehabilitation in patients with nerve-sparing radical cystoprostatectomy, based on a prospective randomised trial, and concluded that early erectile rehabilitation advances the natural healing time of potency and maintains erectile function.

In another study on a special category of patients with intractable angina refractory to aggressive surgical and medical treatment, El-Sakka et al. [26,27] assessed the effect of the duration of refractory IHD and number of enhanced external counterpulsation (EECP) courses on the efficacy and satisfaction rate of EECP in patients with IHD-associated ED. EECP is a noninvasive outpatient treatment used for patients with intractable angina refractory to aggressive surgical and medical treatment. They concluded that EECP could improve ED in patients with refractory IHD. The efficacy and satisfaction rate of EECP in patients with IHD-associated ED were

negatively influenced by longer duration of IHD and requirement of a second course of EECP.

In a report of other methods of treating ED, Mahmoud et al. [28] assessed the comparative value of prostaglandin E1 (PGE1) and papaverine for treating erectile failure, in a double-blind crossover study among Egyptian patients. As evidence of its reliability and effectiveness, PGE1 (20 µg/mL) induced a significant positive erectile response in 42 of 52 patients (81%). This rate reached 100% with neurogenic, hyperprolactinaemic and/or psychogenic ED. However, with papaverine hydrochloride (30 mg/mL) and exclusively in cases of vasculogenic (most probably arteriogenic) ED, there was a negative response, with no erection in six of 52 patients (12%) and a non-rigid tumescence in 13 (25%), vs. two (4%) and eight (15%), respectively, with PGE1. Moreover, with PGE1 the regional pain was tolerable and transient, and the positive erectile response was not associated with priapism even in patients who formerly had priapism with papaverine hydrochloride.

With the same method of treatment El-Sakka [29] investigated the reliability of intracavernosal PGE1 administered in the office vs. self-injection therapy, in patients with ED. There were significant differences between the number of injections and amount of PGE1 per month, total number of injections, and total amount of PGE1, between the office and self-injection programmes. There was a significant increase in the discontinuation rate in the office-injection group compared with the self-injection group. There was more penile fibrosis in the self-injection than in the office-based group. A self-injection programme is reliable; an office-injection programme can be reserved for a subset of patients with ED who have specific preferences.

On the surgical treatment of ED, Salama [30], using a reliable questionnaire, investigated satisfaction with a malleable penile prosthesis among couples in the Middle East; 70% of the patients and 57% of the partners were satisfied with the prosthesis. There was an increase in the frequency of intercourse, in sexual desire, and ability to achieve orgasm. Dislike for the device was the most common cause in patients for dissatisfaction with the device, while a sense of unnaturalness was the main cause in partners. Results from this evaluation highlight the obvious need for proper preoperative counselling for both the patient and his partner to minimise unrealistic expectations.

In the special category of renal transplant recipients, El-Assmy et al. [31] reported that penile vascular insufficiency is less common in recipients than previously reported. They concluded that early transplantation can delay or prevent the development of penile vasculopathy. El-Bahnasawy et al. [32] reported that in the absence of associated vascular risk factors, unilateral interruption of the internal iliac artery decreases arterial

penile blood flow, but not to a degree that compromises erectile function.

Miscellaneous

Kamel et al. [33] compared penile measurements in normal subjects and patients with ED. The average fully stretched penile length in normal men was 12.9 cm, but was 11.2 cm in patients with ED (significantly different, $P < 0.001$), although the mean fully stretched penile girths were not statistically different between the groups.

Awwad et al. [34] also determined penile size in normal Jordanian men (group 1, 271) and men with ED (group 2, 109). They found that in group 1 the mean (SD) mid-shaft circumference was 8.98 (1.4) cm, the flaccid length was 9.3 (1.9) cm, and the stretched length was 13.5 (2.3) cm. In group 2 the flaccid length was 7.7 (1.3) cm and the stretched length was 11.6 (1.4) cm. The mean fully erect penile length after trimix injection was 11.8 (1.5) cm. In group 1 there was no correlation between length and flaccid length or stretched length, but there was a significant correlation between patient height and midpoint circumference, flaccid and stretched lengths, and between stretched lengths and midpoint circumference. In group 2 there was no correlation between height and flaccid, stretched, or fully erect lengths. However, there was a significant correlation between the flaccid, stretched and fully erect lengths. Comparing group 1 and group 2, the patients in group 1 were slightly older than in group 2 ($P = 0.035$), but there was no significant difference in their height. However, there was a significant difference in the mean flaccid length, at 9.3 vs. 7.7 ($P = 0.001$), and the mean stretched length 13.5 vs. 11.6 ($P < 0.001$).

Summary and conclusion

A detailed medical and psychosexual history remains the mainstay in the diagnosis of ED. In general, all investigations are conducted in an artificial (nonsexual) setting with little privacy. This sometimes leads to a high anxiety level and an increased sympathetic overriding response, which might significantly influence the test results. In addition, the variations in technique and lack of normative values from a large group of normal subjects resulted in the inaccurate interpretation of test results. Therefore, some patients undergoing evaluation might require more than one study to arrive at a diagnosis.

In the past three decades there has been significant progress in understanding penile physiology, and furthermore, several revolutionary new treatments for patients with ED have become available. With the advances in molecular biological techniques and their introduction into the field, instead of symptomatic

treatment, there might be cures for the various types of ED in the near future.

As new drugs are developed for ED, new issues will arise that are relevant to their safety, efficacy, tolerability and certainly their cost. Undoubtedly the emergence of PDE-5 inhibitors has opened a new area of research in oral treatments for ED. The clinical implications of all these advances in diagnosis and treatment might result in another breakthrough in the management of ED.

Conflict of interest

No conflict of interest to declare.

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