POSSIBLE ROLE OF BULBOCAVERNOSUS REFLEX LATENCY IN PREDICTING SEXUAL ADVERSE EFFECTS OF ANTIDEPRESSANT MEDICATION

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ЗНАЧЕНИЕ ВРЕМЕНИ БУЛЬБОКАВЕРНОЗНОГО РЕФЛЕКСА В ПРОГНОЗИРОВАНИИ НАРУШЕНИЙ СЕКСУАЛЬНОЙ ФУНКЦИИ ПРИ АНТИДЕПРЕССАНТНОЙ ТЕРАПИИ

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It is a well-known fact that psychotropic medication often results genitourinary and sexual adverse effects [1]. Accurate estimation of medication induced sexual dysfunction is difficult to obtain because many patients fail to report them and clinicians neglect to inquire about them. Sexual dysfunction may be idiosyncratic or associated with medical or psychiatric illness as well, making assessment of medication related dysfunction difficult.

Authors used the technique of bulbocavernosus reflex latency measurement as a routine procedure in checking the functional innervation of the genital area. Coaxial needle electrodes are inserted into the bulbocavernosus muscle. Stimulation is on the dorsal side of the penile shaft and can be done using ring electrodes of a surface stimulator. The intensity required in this case is usually 5 to 20 mA and the duration is 0.1 ms. Values are measured to the onset of the negative peak. We consider the values 34 ± 3 ms (mean ± 1 SD) as fully normal, 38—42 ms as dubious. Values > 42 ms are pathological.

We found that 69 % of the men presenting > 42 ms values complain about disturbed or missing erection, while only 17 % of the dubious group (DG) and 13 % of the males with normal values (NVG) do the same. When receiving a psychotropic medication the overall rate of erectile dysfunction increases to 16 % in NVG, while to 77 % in DG.

While initial and after-drug-induction percentages do not differ too much in NVG, they show a great difference in DG. On the basis of these preliminary findings we suggest that bulbocavernosus reflex latency should be screened before initiating a psychotropic medication and, if there is a choice, drugs with less sexual side effects should be given to patients with dubious latency values, predicting a greater likelihood of the development of a drug-induced erectile dysfunction.

Key words: sacral reflexes, bulbocavernosus reflex latency, erectile disorder, psychotropic drugs.

Introduction

Sexual health and function are highly important determinants of quality of life. Disorders such as erectile dysfunction (ED) and female sexual dysfunction are getting more and more highlighted, partially as a result of the aging of the population [2].

Penile erections involve an integration of complex physiologic processes involving the central nervous system (CNS), peripheral nervous system, and vascular and hormonal systems as well. Any abnormality involving these systems, whether caused by disease or certain medications, has a significant impact on the ability to develop and sustain an erection, ejaculate, or experience a sexual orgasm. The filling of the cavernous bodies by blood relies upon neural and hormonal mechanisms operating at various levels of the neural axis. The regulation of penile tumescence seems to be unique among visceral functions, as it inevitably requires central neurological input.

Erections occur in response to tactile, olfactory and visual stimuli. The penile portion of the process leading to erections represents only a single component. The ability to achieve and maintain a full erection also depends on the status of the peripheral nerves.The hypothalamic and limbic pathways play an important role, too. The medial preoptic center, the paraventricular nucleus, and anterior hypothalamic regions modulate erections and coordinate autonomic events associated with sexual responses. Afferent information is assessed in the forebrain and relayed to the hypothalamus.

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The efferent pathways from the hypothalamus enter the medial forebrain bundle and project caudally near the lateral part of the substantia nigra into the tegmental region of the midbrain.

Several pathways have been described to explain how information travels from the hypothalamus to the sacral autonomic centers. One of them travels from the dorsomedial hypothalamus through the dorsal and central gray matter, descends to the locus ceruleus, and projects ventrally in the mesencephalic reticular formation. Input from the brain is conveyed through the dorsal spinal columns to the thoracolumbar and sacral autonomic nuclei. The primary nerve fibers to the penis are from the dorsal nerve of the penis, a branch of the pudendal nerve. The cavernosal nerves are a part of the autonomic nervous system and incorporate both sympathetic and parasympathetic fibers. They travel posterolaterally along the prostate and enter the corpora cavernosa and corpus spongiosum to regulate blood flow during erection and detumescens.

The dorsal somatic nerves are also branches of the pudendal nerves. They are primarily responsible for the sensation experienced when sexually stimulating the penis. This stimulation causes the release of neurotransmitters from the cavernosal nerve endings and relaxing factors from the endothelial cells of the sinusoids. Nitric oxide (NO) synthase produces NO from arginine. This in turn produces cyclic guanosine monophosphate (cGMP) and cyclic adenosine monophosphate (cAMP), which, working via calcium channel and protein kinase mechanisms, cause smooth muscle relaxation in the arteries supplying the erectile tissue, producing a dramatic increase in penile blood flow. Relaxation of the sinusoidal smooth muscle (round a half of the corpora cavernosa tissue is composed of smooth muscle cells) increases its complience, facilitating fast filling and expansion. The venules beneath the rigid tunica albuginea are compressed, resulting in near total occlusion of venal outflow. All these events result in a mean intracavernosal pressure of 100 mmHg.

Additional stimulation of the glans initiates the bulbocavernosus reflex. The ischiocavernosus muscles strongly compress the base of the blood-filled corpora cavernosa, and the intracavernosal pressure reaches at least 200 mmHg, resulting in a full erection and hardness.

Sacral reflexes are electrophysiologically recordable responses of perineal and pelvic floor muscles to electrical stimulation in the uro-genito-anal region. The clinically most elicited two sacral reflexes are the anal and the bulbocavernosus one.

The bulbocavernosus reflex has been widely used for the diagnosis of neurogenic erectile dysfunction, elicited clinically by squeezing the glans penis. A neurophysiological method for recording the bulbocavernosus reflex was first reported in 1967 [3]. The method tests the integrity of the large myelinated nerve fibers in the S_2—S_4 segments. The minimum latency response was measured and values greater than 45 ms were considered abnormal.

Material and methods

It is a well-known fact that a large number of various drugs may cause erectile disorder [4]. Antihypertensive agents like atenolol, benazepril, debrisoquin, enalapril, guanfacin, methyldopa, nisoldipin, perindopril or prazosin, antiarrhythmics like atenolol or propafenon, diuretics like amilorid, antihypercholesterolemic drugs like bezafibrat or fenofibrat, anti-inflammatory drugs like diclofenac, a series of hormones, hormone-analogues and anti-hormones, antihistamines, cytostatic drugs and other widely used agents. In our own clinical practice, antidepressants (AD) and other psychopharmacologically active agents (such as fluoxetin,imipramin,paroxetin, sertralin, thioridazin, tiaprid, trimipramin, etc.) are the most common drugs often causing or worsening male erectile disorder [5].

The aim of our study was to find out whether there is any relation between the bulbocavernosus reflex latency values (checked prior to initiating a psychoactive drug therapy) and the likelihood of developing an erectile disorder during the drug treatment.

56 consecutive male patients aged 35—54 requiring an antidepressant therapy and willing to undergo a bulbocavernosus reflex latency measurement procedure were involved in our study.

Prior to beginning the medication (clomipramin in 5 patients, paroxetin in 28 patients and sertralin in 23 patients), a bulbocavernosus reflex latency measurement was performed in each patient. We inserted coaxial needle electrodes into the bulbocavernosus muscle. Stimulation was given on the dorsal side of the penile shaft by using ring electrodes of a surface stimulator. The required slightly suprathreshold intensity was usually 5 to 20 mA and the duration was 0,1 ms. Values were measured to the onset of the first negative peak [Figure 1].

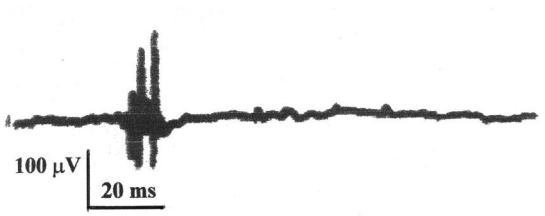

Figure 1. Bulbocavernosus reflex response by slightly suprathreshold stimulation

By stronger stimulation (threshold + cca 30 %), a second component [Figure 2] can be observed, while the latency of the relevant first negative peak slightly shortens [6]. Siroky et al.[7] found the average latency 35 ± 2 ms, while Dick et al.[8] found 31 ms to be average. According to our reference data, we considered the values 34 ± 3 ms (mean ± 1 SD) as fully normal, 38—42 ms as «dubious». Values > 42 ms are thought to be undoubtedly pathological.

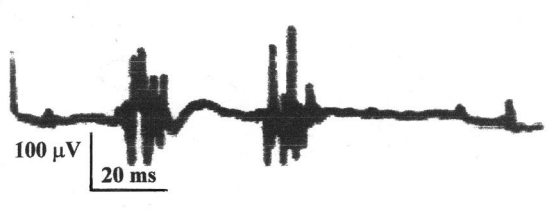

Figure 2. Bulbocavernosus reflex response by stronger (threshold + 30%) stimulation

After that, patients were carefully inquired about their sexual life and complaints, using even an abbreviated form (9 questions related to erectile capability of the total 23) of The Massachusetts Male Aging Study (MMAS)[9].

After 6 weeks, antidepressant treatment patients were once again inquired about their erectile capability and sexual complaints.

Results and discussion

Based on the initial reflex latency values patients could artificially be divided into three groups. 13 patients of the 56 were divided into the «pathological group» (PG), presenting > 42 ms values. 12 patients belonged to the «dubious group» (DG) with values between 27—41 ms, while 31 patients presented fully normal values less than 27 ms («normal value group»; NVG).

Not too surprisingly, 9 of the 13 PG patients (69 %) complained about disturbed or missing erection prior to the AD therapy, while complaints concerning erectile capability proved to be 17 % (2 of 12 patients) only in the DG and 13 % (4 of 31 patients) in the NVG.

After 6 weeks treatment we found that 5 of the 31 NVG patients (16 %) presented erectile disorder, showing only 3 % increment compared with the pre-treatment percentage. 10 of the 13 PG patients (77 %) complained about sexual difficulties after 6 weeks of treatment, which means 8 % increment. 7 of the 12 DG patients (58 %) presented erectile difficulties after the 6 weeks treatment period, which means an increment of 39 %.

With other words we found that antidepressant treatment does not have a great impact on the prevalence of erectile disorder, neither among men with fully normal (≤ 37 ms) latencies, nor among men with poor (≥ 42 ms) bulbocavernosus reflex latency values. On the other hand «dubious», transitory latency values seem to predispose men to antidepressant-induced erectile disorder: more than three times as many DG patients present erectile disorder after 6 weeks of AD-treatment as before the treatment.

These preliminary findings should be handled with caution because of the small number of patients. Nevertheless, we suggest that bulbocavernosus reflex latency should be screened before initiating a psychotropic medication and, if there is a choice, drugs with less sexual side effects should be given to patients with «dubious» latency values.

Аннотация

Известно, что психотропные препараты часто вызывают побочные эффекты в виде нарушений сексуальной функции [1]. Точная оценка подобных нарушений крайне затруднена из-за того, что больные о них, как правило, не сообщают, а клиницисты не обращают пристального внимания. Кроме того, сексуальные нарушения могут быть обусловлены идиосинкразией, либо соматическими или психологическими заболеваниями, что затрудняет оценку побочных медикаментозных эффектов.

Авторы использовали стандартную методику исследования продолжительности бульбокавернозного рефлекса для функциональной оценки иннервации генитальной зоны.

В бульбокавернозную мышцу вводили игольчатые электроды, поверхностную стимуляцию можно было осуществлять с помощью кольцевых электродов. Интенсивность раздражения составляла от 5 до 20 ма, а продолжительность воздействия — 0,1 ма. Оценку проводили по отрицательному пику. Продолжительность ответа 34 ± 3 мсек рассматривали как нормальную, 38—42 мсек — как промежуточную, а более 42 мсек — как патологическую.

Обнаружено, что у 69 % обследуемых с продолжительностью реакции более 42 мсек отмечены жалобы на нарушение эрекции, в то время как в промежуточной группе их число составило 17 %, а в группе с нормальным временем — 13 %. При приеме психотропных препаратов симптомы эректильной дисфункции увеличились до 16 % у лиц с нормальной реакцией и до 27 % — у лиц с промежуточной реакцией.

Тогда как в группе с нормальной продолжительностью реакции процент лиц с нарушением функции до и после приема препаратов практически не изменился, в промежуточной группе выявлены резкие различия. На основе этих предварительных данных представляется целесообразным исследовать время бульбокавернозного рефлекса до назначения психотропных препаратов и при возможности выбора отдавать предпочтение средствам с менее выраженным отрицательным сексуальным эффектом. В первую очередь это относится к лицам с промежуточным временем рефлекса, т. к. у них наиболее вероятна возможность неблагоприятных проявлений.

Ключевые слова: крестцовые рефлексы, время бульбокавернозного рефлекса, нарушение эректильной функции, психотропные вещества.

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