COMPARISON OF BIOTHESIOMETRY AND NEURO- UROPHYSIOLOGICAL INVESTIGATIONS FOR THE CLINICAL EVALUATION OF PATIENTS WITH ERECTILE DYSFUNCTION

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ABSTRACT

In the literature the determination of the vibration sensitivity threshold of the penile glans by means of biothesiometry has been introduced as a cost-effective office test for the evaluation of penile neuropathy in impotent men. At our facility we have gained extensive experience with neuro-urophysiological tests for the evaluation of penile innervation. These neuro-urophysiological tests have the disadvantage of complexity, invasiveness and time consumption. In our study both methods were compared in 31 impotent patients. The results showed that penile glans biothesiometry yields consistent results when measurements are repeated during 1 session. However, no relationship was found between the outcome of penile glans biothesiometry and neuro-urophysiological tests of the dorsal penile nerve, which is probably due to the fact that vibration is not an adequate stimulus to the skin of the penile glans that contains free nerve endings (that is pain receptors) only, and hardly any vibration receptors. We conclude that biothesiometric investigation of penile glans innervation is unsuited for the evaluation of penile innervation and cannot replace neuro-urophysiological tests.

KEY WORDS: neurophysiology, penis, penile erection, impotence, evoked potentials

Penile erection is a complex physiological response that depends upon the integration of neurological, vascular and hormonal mechanisms. The neurological processes responsible for penile erection originate in the central nervous system through integration of sexual stimuli (tactile, audio-visual, gustatory and olfactory), and through mechanical and reflexogenic stimulation of the genital organs. Several studies have directly or indirectly demonstrated the importance of penile sensory input for sexual function. Herbert showed that sexual activity and ejaculation in the rhesus monkey are dependent upon dorsal penile nerve function.1 Newman found a correlation between sexual activity and vibratory perception.2 Previously, we found that erectile dysfunction in the elderly man is associated with erectile dysfunction in the central nervous system through integration of sexual stimuli (tactile, audio-visual, gustatory and olfactory), and through mechanical and reflexogenic stimulation of the genital organs. Several studies have directly or indirectly demonstrated the importance of penile sensory input for sexual function. Herbert showed that sexual activity and ejaculation in the rhesus monkey are dependent upon dorsal penile nerve function.1 Newman found a correlation between sexual activity and vibratory perception.2

From each patient we obtained a detailed history focusing on factors associated with neurogenic erectile dysfunction, such as pelvic surgery, alcohol abuse, diabetes mellitus as well as medication and intoxications. Furthermore, we measured height and weight to calculate body mass index. Extensive neurological testing of each patient consisted of biothesiometry followed by neuro-urophysiological investigations. Each patient was tested during 1 session to avoid time related variations. Before the investigation patients were informed about both procedures and from all patients written informed consent was obtained.

During the investigations each patient was in the supine position in a room with a constant temperature of 25°C. A commercially available biothesiometer was used. Vibratory stimuli were given through a 1 cm. wide tactor at a fixed frequency of 120 cycles per minute with variable amplitude. Amplitude adaption is possible by turning a control knob. Electromagnetic energy is transformed into vibratory motion of the tactor, which is placed on the skin. Vibration amplitude is linearly related to the applied voltage. For statistical analysis the applied voltages, which can range from 0 to 50 volts, were recorded.

To avoid adaptation the tactor should be at rest when it is placed on the site selected for analysis. On every test site a clear noticeable stimulus was given so patients would know what type of stimulus to which they were supposed to respond. After this initial stimulation the apparatus was turned to zero. The amplitude was increased stepwise with increments of 1 to 2 volts, and the patient was told to respond with a clear "yes" when he first perceived the vibration, at which point he was supposed to respond again with a clear

PATIENTS AND METHODS

For this study we examined 31 patients (mean age 49 years, range 17 to 71) with complaints of erectile dysfunction. Accepted for publication October 7, 1994.
measurements were used. Results of biothesiometry are because they provide information about general neuropathy. Furthermore, they tend to relax the patient before he is tested on the glans penis. Furthermore, they tend to relax the patient before he is tested on the glans penis.

Three different areas on the body were tested, starting with “yes.” This upper threshold was also determined 3 times. This upper threshold was also determined 3 times. The somato-sensory potentials were obtained with bipolar percutaneous stimulation (stimulus duration 0.2 msec., frequency 2.7 Hz.) of the posterior tibial nerve at the ankle of the right foot. Fingertip measurements were considered useful during 1 session is excellent. Comparison of upper and lower threshold measurements the 2-sided Wilcoxon test, vibratory stimuli were applied to the index finger of the dominant hand, glans penis and medial malleolus of the right foot. Fingertip measurements were considered useful.

The neuro-urophysiological investigations were done next. Evoked potentials were obtained with a commercially available stimulation and registration apparatus. Neuro-urophysiological investigations consisted of measurement of the tibial evoked potential, pudendal evoked potential and bulbocavernous reflex latency. The somatosensory potentials were obtained with bipolar percutaneous stimulation (stimulus duration 0.2 msec., frequency 2.7 Hz.) of the posterior tibial nerve at the ankle of the right foot (tibial evoked potential) and the dorsal penile nerve on the dorsum of the shaft of the penis (pudendal evoked potential). Stimulation of the posterior tibial nerve was considered accurate if twitching of the toes was clearly visible. Pudendal stimulation intensity was at least twice the sensory threshold. The evoked potentials were recorded from the Cz-2 point according to the international 10 to 20 system. We averaged at least 200 stimuli and measured each curve twice.

To measure bulbocavernous reflex latency, penile stimulation was done on the penile shaft as in the pudendal evoked potential. Recording was in the right ventral quadrant of the external anal sphincter muscle with a concentric needle electrode. For bulbocavernous reflex latency 4 separate measurements were recorded with supramaximal square-wave stimuli (60 mamp.). The shortest latency was used for further evaluation.

Smoking was recorded as units per day, and drinking habits were noted as positive or negative. Body mass index was calculated as body weight divided by (height)$^2$ (kg./m.$^2$).

For statistical analysis distribution-free methods are used due to the skewness of the sample distributions for the study parameters. For statistical comparison of biothesiometric lower and upper threshold measurements the 2-sided Wilcoxon 1-sample test was used. For judging correlation of biothesiometry and neuro-urophysiological investigations Kendall's coefficient of correlation ($\tau$) was appropriate. A $p$ value of $\leq 0.05$ was considered statistically significant. Furthermore, we calculated the coefficient of replication reliability for the separate measurements of biothesiometry.$^{10}$

RESULTS

Our study group consisted of 31 patients with complaints of erectile dysfunction, of whom 9 were suffering from diabetes mellitus. No patient had undergone pelvic surgery, or experienced intoxications or alcohol abuse. The coefficient of replication reliability for the separate measurements was 0.99 for measurement of the index finger, 0.98 for the glans penis and 0.99 for the ankle. Therefore, repeatability of biothesiometric measurements in 1 patient during 1 session is excellent. Comparison of upper and lower threshold measurements of the index finger, glans penis and ankle showed no statistically significant difference between mean lower and upper measurement ($t = 0.59$, $p = 0.10$ and 0.98, respectively). For further analysis overall averaged measurements were used. Results of biothesiometry are given in table 1.

Table 2 indicates the age dependency of biothesiometric parameters. There was a statistically significant increase in ankle vibratory threshold in older patients ($\tau = 0.38$, $p = 0.003$). Fair correlation between patient age and index finger measurements was found ($\tau = 0.23$, $p = 0.07$). There was no significant correlation between patient age and biothesiometric data derived from the glans penis ($\tau = 0.17$, $p = 0.19$).

Comparison of biothesiometric and neuro-urophysiological data showed fair correlation between tibial evoked potential latency and ankle vibratory threshold ($\tau = 0.28$, $p = 0.03$). Comparison of pudendal evoked potential latency and penile vibratory threshold showed no significant correlation ($\tau = 0.11$, $p = 0.39$), as did comparison of bulbocavernous reflex latency and penile vibratory threshold ($\tau = 0.20$, $p = 0.12$).

For our study, correlation between neuro-urophysiological parameters and patient age was fair for tibial evoked potential ($\tau = 0.29$, $p = 0.05$) and pudendal evoked potential ($\tau = 0.24$, $p = 0.06$). No relationship was found between patient age and bulbocavernous reflex ($\tau = 0.02$, $p = 0.86$). For the other parameters evaluated in our study, such as diabetes mellitus, body mass index, smoking and drinking habits, and medication, no statistically significant correlation was found with the outcome of biothesiometry and neuro-urophysiological investigations.

DISCUSSION

We compared the results of 2 testing modalities for the evaluation of peripheral nerve function. Biothesiometry, an inexpensive and simple method for the determination of vibratory thresholds of any area of the body surface, was compared with neuro-urophysiological tests. For the former test, vibratory stimuli were applied to the index finger of the dominant hand, glans penis and medial malleolus of the ankle of the right foot. For the latter test, latencies of tibial and pudendal evoked potential as well as bulbocavernous reflexes were measured.

The value of neuro-urophysiological tests for the diagnosis of neurogenic erectile dysfunction has been proved in many studies. One study showed aged-dependent pudendal nerve neuropathy in clinically unsuspected patients with erectile dysfunction.$^3$ That study proved that repeatability and reproducibility of neuro-urophysiological investigations are excellent. Combination of the test results of pudendal evoked potential and bulbocavernous reflex latency measurements allows for differentiation between peripheral and central pudendal nerve neuropathy. The combination of an abnormal pudendal evoked response with a normal bulbocavernous reflex is compatible with central neuropathy, whereas an abnormal bulbocavernous reflex together with a normal pudendal evoked potential latency suggests peripheral or sacral neuropathy.$^5$

Although neurophysiological tests are undoubtedly valid, some questions must be raised concerning the value of biothesiometry. In the literature the topic of intra-individual variation of biothesiometric data has been discussed extensively. Aaserud et al.$^{14}$ and Fagius and Wahren$^{15}$ demonstrated a marked inter-individual and intra-individual variation in vibration sensitivity threshold measurements. Both studies concluded that repeatability, meaning within 1 session, and reproducibility, meaning at different occasions, of biothesiometric measurements are questionable. In our study, when

Table 1. Biothesiometric data

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>Volts</th>
<th>Mean ± SD (range)</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finger</td>
<td>31</td>
<td>5.5</td>
<td>2.6 (1.0—11.0)</td>
<td>5.0</td>
</tr>
<tr>
<td>Penis</td>
<td>31</td>
<td>21.2</td>
<td>15.0 (9.9—no response*)</td>
<td>16.7</td>
</tr>
<tr>
<td>Ankle</td>
<td>31</td>
<td>28.4</td>
<td>14.8 (9.3—no response*)</td>
<td>18.8</td>
</tr>
</tbody>
</table>

* No response is set at 55.0 volts.
we assessed only intra-individual repeatability of biothesiometric measurements, we found that it was good. The coefficients of replication reliability for the index finger, glans penis and ankle were 0.99, 0.98 and 0.99, respectively. Reproducibility of biothesiometry, however, was not investigated in our study but it is judged to be poor by the aforementioned studies. This poor reproducibility of biothesiometry is attributed to methodological problems, such as varying pressure exerted for the hand-held probe, variation in the exact locus that is stimulated at different moments, and psychological variability in alertness and attentiveness.

We found fair correlation between ankle vibratory threshold and tibial evoked potential latency ($r = 0.28$), which was to be expected regarding neuroanatomy of the sensory portion of the posterior tibial nerve that consists mainly of large diameter myelinated fibers with gnostic (vibration, touch) sensory properties. Direct electrical stimulation, as in tibial evoked potential measurement, and indirect vibratory stimulation via vibration sensors, as in ankle biothesiometry, are adequate stimuli for the posterior tibial nerve. Both techniques investigate the same sensory modality and neuroanatomical tracts. Therefore, we were likely to find a correlation between the outcome of both investigations.

On the other hand, there was no significant correlation between penile vibratory threshold and pudendal evoked potential or bulbocavernous reflex latency ($r = 0.11$ and 0.20, respectively). This lack of correlation between penile biothesiometry and neuro-urophysiological measurements of the dorsal penile nerve (pudendal evoked potential and bulbocavernous reflex) can be explained by the fact that both tests investigate distinct parts of penile innervation. In an anatomical study of the innervation of the human glans penis, Halata and Munger found the most numerous nerve terminals to be free nerve endings ($A\beta$ or $C$ type). The unique corpuscular receptors of the glans penis, the so-called genital end bulbs, proved to be numerously coiled free nerve endings. From a neurophysiological viewpoint, these genital end bulbs, proved to be numerously coiled free nerve endings. Pacini and Ruffini corpuscles were occasionally identified, whereas mechanoreceptors were not found at all. From this study it must be concluded that the human glans penis is highly sensitive to pain but relatively insensitive to touch and vibration. These neuroanatomical data most certainly account for the differences in outcome of penile biothesiometry and neuro-urophysiological tests. Vibration seems to be an inadequate stimulus to the skin of the penile glans, whereas electrical stimulation directly activates the major area of penile sensory innervation, albeit in a crude, unphysiological manner.

The finding that biothesiometry is an unsuitable investigative tool for the assessment of penile glans innervation is further corroborated by the fact that the penile vibratory threshold did not correlate with patient age ($p = 0.19$), whereas for the other measurements (index finger and ankle) an age dependency was found. The latter finding is in accordance with the results of Aaserud et al, who demonstrated a clear age-related increase in vibration thresholds of the knuckle of the second metacarpophalangeal joint and of the medial malleolus. In a similar study of the penile shaft, Rowland et al found a good correlation between vibrotactile threshold and patient age. The main and important difference between their study and ours was the location of stimulation. Rowland et al stimulated the ventral penile shaft, whereas we stimulated the penile glans.

**CONCLUSIONS**

From our study it must be concluded that penile glans biothesiometry and neuro-urophysiological studies of the dorsal penile nerve investigate different sensory modalities, with the latter covering the larger part and yielding the more consistent results. Therefore, we conclude that penile glans biothesiometry cannot replace laborious studies, such as somatosensory evoked potentials and sacral reflex latency measurements. Whether biothesiometric investigation of the penile shaft might prove useful as an office test should be a subject for further research.

The issue of the clinical use of neurophysiological investigations (either evoked potential studies or biothesiometry) in the diagnostic evaluation of erectile dysfunction needs some further comment. Our previous studies have shown that the outcome of neuro-urophysiological investigations correlates well with the clinical presentation and pathogenesis of erectile dysfunction. These studies also have an important impact on our understanding of the etiology of male impotence. Neuro-urophysiological investigations can be beneficial to the clinician in many ways. These tests can be helpful in establishing a differential diagnosis, and an abnormal test can determine those patients who need special precautions with respect to the dose of intracavernous pharmacological agents. The diagnosis of a somatic cause for the erectile dysfunction can help a patient and partner to accept the problem more easily. The proof of neurogenic impotence can predict the possible success of other therapies. When laborious or invasive therapies, such as psychotherapy or penile revascularization, are planned a thorough neuro-urophysiological evaluation is indispensable because these therapies should not be performed in patients with combined neurogenic and psychogenic/vasculogenic impotence. On the other hand, however, it is important to state that neuro-urophysiological tests, including biothesiometry, have no therapeutic implication per se. The finding of neurogenic impotence has no therapeutic consequences to date. It can only keep physicians and patients from embarking on therapeutic strategies that are bound to fail. In conclusion, our bias is that a comprehensive neurophysiological investigation should not be replaced by simple biothesiometry and that the test should be done within the context of special scientific protocols or whenever elucidation of a certain individual problem is warranted, either by the physician or patient.

**REFERENCES**