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INFUSION PHARMACOCAVERNOSOMETRY AND NOCTURNAL PENILE TUMESCENCE FINDINGS IN MEN WITH ERECTILE DYSFUNCTION

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ABSTRACT

Infusion pharmacocavernosometry and nocturnal penile tumescence findings were compared in 50 men with erectile dysfunction of either organic or psychogenic etiology. Of the men 29 had abnormal and 21 had normal nocturnal penile tumescence. Infusion pharmacocavernosometry parameters (equilibrium pressure, maintenance flow rate and 30-second pressure fall) were compared to nocturnal penile tumescence status (normal versus abnormal). When traditional normal values were used for infusion pharmacocavernosometry parameters poor correlation with nocturnal penile tumescence status was found. When new cutpoints for infusion pharmacocavernosometry parameters were chosen a stronger correlation was noted. This study suggests that when vasoactive drugs are injected intracavernously for diagnostic purposes, anxiety and/or the absence of sexual stimulation following the injection may prevent complete cavernous smooth muscle relaxation resulting in falsely abnormal values. Therefore, over reliance on infusion pharmacocavernosometry as a single test for evaluation and treatment decisions concerning erectile dysfunction should be avoided.

KEY WORDS: penile erection, pharmacokinetics

Since reports of intracavernous injection of papaverine hydrochloride by Virag[1] and phenoxybenzamine by Brindley[2] intracorporeal injection of vasoactive drugs for diagnostic and therapeutic purposes has become widespread. Papaverine hydrochloride injected intracorporeally produces erections by causing arterial vasodilatation, corporeal smooth muscle relaxation and an increase in venous outflow resistance.[3] However, anxiety mediated sympathetic tone can maintain the corporeal smooth muscle in a state of contraction, partially or fully blunting the effects of papaverine. The intracorporeal injection of a mixture of papaverine hydrochloride and phentolamine mesylate, an α-adrenergic blocking agent, produces better erections than does the injection of either agent alone.[4] However, it has not been established whether this combination of agents in doses commonly used completely overcomes anxiety mediated sympathetic responses. For therapeutic purposes incomplete suppression of anxiety mediated responses is less important, since drug dosage can be altered to achieve the desired response and since alternative methods of treatment are available should intracavernous pharmacotherapy prove to be ineffective. However, for test purposes variation in response to intracavernous injection of vasoactive drugs is important, since the response to these agents usually is interpreted as an index of arterial and venous circulatory integrity.

To refine the diagnosis of erectile failure owing to corporeal-venous occlusive dysfunction, infusion cavernosometry after the intracorporeal injection of vasoactive drugs (infusion pharmacocavernosometry) has been used.[5,6] While the results of infusion pharmacocavernosometry appear to be useful, normative data for men with adequate erectile function have not been established. In addition, this diagnostic technique has not been compared to more traditional methods used in impotence diagnosis, such as nocturnal penile tumescence where much normative data already exist. We compare infusion pharmacocavernosometry and nocturnal penile tumescence findings in men with erectile dysfunction of either psychogenic or organic etiologies.

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MATERIALS AND METHODS

The study included 50 men presenting with the chief complaint of erectile dysfunction who were evaluated by history, physical examination, routine and endocrine blood tests, as well as nocturnal penile tumescence and infusion pharmacocavernosometry studies. Nocturnal penile tumescence studies were performed on 2 consecutive nights with a Rigiscan device.† Nocturnal penile tumescence was considered normal, regardless of patient age, if more than 1 erection episode with 60% or greater rigidity (at base and tip) sustained for 15 minutes or more was recorded.[7] Infusion pharmacocavernosometry was performed with the patient in the supine position by a technique modified after that described by Padma-Nathan et al.[8] After 1% lidocaine (2 to 3 ml.) was injected subcutaneously in the dorsal precoronal area, a 21 gauge butterfly needle was inserted into each distal corpus cavernosum. A needle was attached to a pressure transducer for the continuous monitoring of intracorporeal pressure. Another needle was attached to a pressure regulated infusion pump.‡ Papaverine hydrochloride (60 mg.) and phentolamine mesylate (2 mg.) in a volume of 2 ml. were injected through 1 of the butterfly needles into the corpora cavernosa. The maximum intracorporeal pressure obtained (equilibrium pressure) usually occurred 10 to 20 minutes after drug injection. After the equilibrium pressure was noted, room temperature heparinized saline (1 unit per ml.) was infused to obtain, if possible, an intracorporeal pressure (maximum infusion pressure) of 145 mm. Hg. The infusion rate necessary to maintain this intracorporeal pressure (maintenance flow rate) was noted once its equilibrium had been obtained. The infusion was then stopped and the intracorporeal pressure 30 seconds later was noted and subtracted from 145 mm. Hg. The resulting figure was termed the 30-second pressure fall. The 30-second pressure fall value was not applicable if a maximum infusion pressure of 145 mm. Hg was not achieved.

Initially age and infusion pharmacocavernosometry factors (equilibrium pressure, maintenance flow rate and 30-second

† Dacomed Corp., Minneapolis, Minnesota.
‡ Cavrolab 1720, Life Tech Corp., Houston, Texas.

pressure fall) were described and compared for patients with normal and abnormal nocturnal penile tumescence results using the t test and the Wilcoxon test. Infusion pharmacocavernosometry factors were categorized into normal and abnormal groups based on conventional normal values (cutpoints). The chi-square and Fisher exact tests were used to determine if the infusion pharmacocavernosometry factor categories were associated with nocturnal penile tumescence outcome. Additional cutpoints for infusion pharmacocavernosometry factors were investigated using logistic regression techniques. These cutpoints were chosen to produce the best combination of sensitivity and specificity for predicting nocturnal penile tumescence status. In this context sensitivity was defined as the percent of those with an abnormal nocturnal penile tumescence status who had abnormal infusion pharmacocavernosometry values, and specificity was defined as the percent of those with a normal nocturnal penile tumescence status who had normal infusion pharmacocavernosometry factors.

RESULTS

Of the total 50 patients 29 had abnormal and 21 had normal nocturnal penile tumescence. Table 1 summarizes the descriptive information for the study group. Mean patient age was 51.2 years with a range of 30 to 70 years. Patients with abnormal nocturnal penile tumescence results were significantly older and had significantly lower equilibrium pressures but significantly higher maintenance flow rates and 30-second pressure falls than those with normal nocturnal penile tumescence results.

Initially, an equilibrium pressure of greater than 90 mm. Hg and a 30-second pressure fall of less than 30 mm. Hg were considered normal.[5] A maintenance flow rate of less than 10 ml. per minute was arbitrarily selected as normal. Using these guidelines for normal values, the relationships between nocturnal penile tumescence status and infusion pharmacocavernosometry data are given in table 2. Note that only 1 patient had an equilibrium pressure of 90 mm. Hg or greater. Sensitivity and specificity of infusion pharmacocavernosometry using these guidelines for normal values also are presented. Note that for the equilibrium and 30-second fall pressures the sensitivities are high and the specificities are low. The maintenance flow rate has the best combination of sensitivity and specificity with a sensitivity of 65.5% and a specificity of 61.9%. Since these norms appeared inappropriate for our group, new cutpoints obtained by logistic regression were chosen, and higher values for sensitivity and specificity were obtained (table 3). Individual as well as combinations of infusion pharmacocavernosometry factors were examined with respect to their relationship with nocturnal penile tumescence status. The 30-second pressure fall had the best combination of sensitivity and specificity of any of the individual factors. In general, combining the various infusion pharmacocavernosometry factors resulted in a higher sensitivity but lower specificity than was seen with the individual infusion pharmacocavernosometry factors.

No hematomas were seen but in 9 patients ecchymoses developed at a needle site. Six patients had a full, sustained erection at the conclusion of the study. The erections in all 6 of these patients resolved promptly after intracavernous injection of 3 to 5 mg. metaraminol bitartrate. No other complications were noted.

TABLE 1. *Descriptive information*

Factor	No.	Mean (standard deviation)	Median	T Test/ Wilcoxon p Value
Age (yrs.):				
Abnormal nocturnal penile tumescence	29	55.0 (10.6)	56	
Normal nocturnal penile tumescence	21	45.9 (9.8)	45	0.01
Total	50	51.2 (11.1)	53	
Equilibrium pressure (mm. Hg):				
Abnormal nocturnal penile tumescence	29	17.9 (13.2)	16	
Normal nocturnal penile tumescence	21	32.6 (21.7)	26	0.01
Total	50	24.1 (18.6)	19	
Maintenance flow rate (ml./ min.):				
Abnormal nocturnal penile tumescence	29	34.5 (47.7)	20	
Normal nocturnal penile tumescence	21	19.3 (34.9)	6	0.003
Total	50	34.5 (44.3)	10	
30-sec. pressure fall (mm. Hg):				
Abnormal nocturnal penile tumescence	22	93.1 (28.4)	96.5	
Normal nocturnal penile tumescence	19	62.7 (29.1)	70	0.002
Total	41	79.0 (32.2)	82	

CASE HISTORIES

Case 1. R. K., a 44-year-old man, presented with a 4-year history of erectile dysfunction. Equilibrium pressure was 9 mm. Hg, maximum infusion pressure was 67 mm. Hg and maintenance flow rate was 120 ml. per minute. Nocturnal penile tumescence study was normal (part *A* of figure). The findings from the infusion pharmacocavernosometry study suggested marked corporeal-venous occlusive dysfunction but sex history and nocturnal penile tumescence findings suggested that the erectile dysfunction was psychogenic. Sex therapy was begun and after 5 sessions the patient and his wife reported that they were having normal coitus.

Case 2. F. S., a 60-year-old man, presented with a 5-year history of erectile dysfunction. Equilibrium pressure was 19 mm. Hg, maximum infusion pressure was 113 mm. Hg and maintenance flow rate was 120 ml. per minute. Nocturnal penile tumescence findings were normal (part *B* of figure). Although the infusion pharmacocavernosometry study suggested marked corporeal-venous occlusive dysfunction, the nocturnal penile

TABLE 2. *Categorical information by nocturnal penile tumescence status*

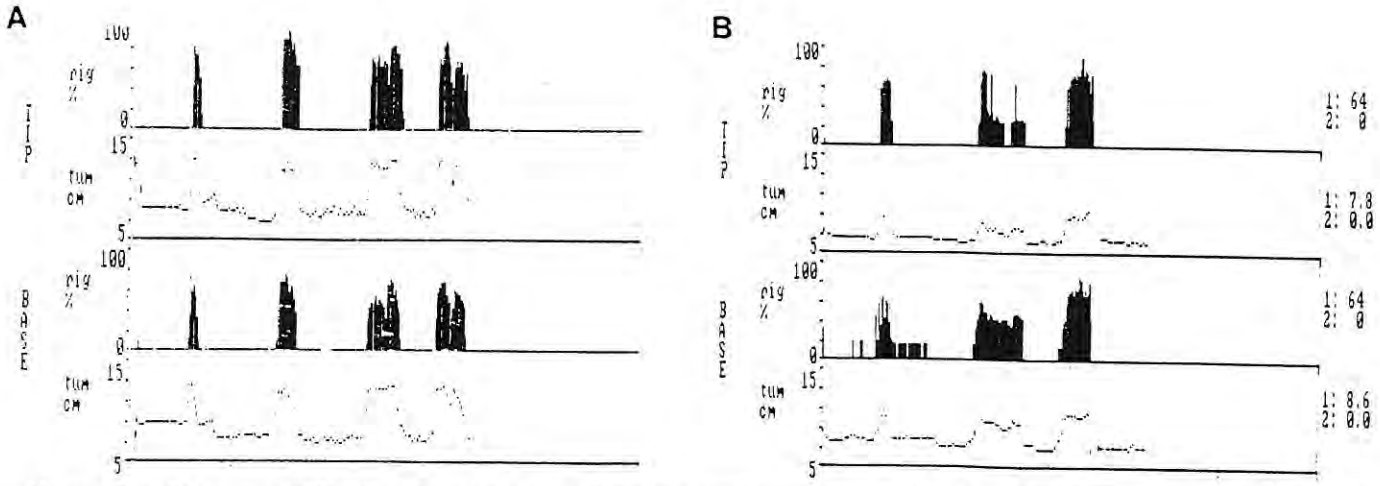
Infusion Pharmacocavernosometry Factor	Nocturnal Penile Tumescence Normal No. (%)	Nocturnal Penile Tumescence Abnormal No. (%)	Fisher's Exact/ Chi-Square Test p Value
Equilibrium pressure (mm. Hg):			
<90	20 (95.2)	29 (100.0†)	0.42
≧90*	1 (4.8‡)	0	
Maintenance flow rate (ml./ min.):			
≧10	8 (38.1)	19 (65.5†)	0.06
<10*	13 (61.9‡)	10 (34.5)	
30-sec. pressure fall (mm. Hg):			
>30	16 (84.2)	22 (100.0†)	0.10
≦30*	3 (15.8‡)	0	

* Normal results.
† Sensitivity.
‡ Specificity.

TABLE 3. *Categorical information by nocturnal penile tumescence status using cutpoints suggested by logistic regression*

Infusion Pharmacocavernosometry Factors	Nocturnal Penile Tumescence Normal No. (%)	Nocturnal Penile Tumescence Abnormal No. (%)	Fisher's Exact/ Chi-Square Test p Value
Equilibrium pressure (mm. Hg):			
<21	7 (33.3)	20 (69.0†)	0.01
≧21*	14 (66.7‡)	9 (31.0)	
Maintenance flow rate (ml./min.):			
≧12	6 (28.6)	18 (62.1†)	0.02
<12*	15 (71.4‡)	1 (37.9)	
30-sec. pressure fall (mm. Hg):			
>75	6 (31.6)	16 (72.7†)	0.01
≦75*	13 (68.4‡)	6 (27.3)	
Any of 3 abnormal:			
Any	9 (42.8)	26 (89.7†)	0.001
None	12 (57.2‡)	3 (10.3)	
Equilibrium or maintenance flow rate abnormal:			
Either	8 (38.1)	24 (82.8†)	0.001
Neither	13 (61.9‡)	5 (17.2)	
Equilibrium or 30-sec. fall abnormal:			
Either	9 (42.9)	25 (89.3†)	0.001
Neither	12 (57.1‡)	3 (10.7)	
Maintenance flow or 30-sec. fall abnormal:			
Either	8 (38.1)	23 (79.3†)	0.003
Neither	13 (61.9‡)	6 (20.7)	

* Normal value.
† Sensitivity.
‡ Specificity.



Nocturnal penile tumescence findings. Tumescence (*tum*) is penile circumference in cm. and rigidity (*rig*) is in percentage on relative scale. *A*, case 1. *B*, case 2.

tumescence study and sex history indicated that he was capable of achieving adequate erections under certain circumstances. The patient elected to enter the intracavernous injection program. He injects himself with 9 mg. papaverine hydrochloride plus 0.3 mg. phentolamine mesylate (total dose 0.3 ml.), and obtains erections that he rates as 9 or 10 on a scale of 10. Using these pharmacologically assisted erections, the patient has had coitus approximately 2 times a week for the last 9 months.

DISCUSSION

As the data in table 2 show, there is poor correlation between nocturnal penile tumescence and infusion pharmacocavernosometry results when traditional cutpoints for infusion pharmacocavernosometry factors are used. While there was a strong correlation between the 2 testing procedures when new cutpoints were chosen (table 3), the correlation was not strong enough to suggest that clinicians should rely solely on 1 test or the other. Nocturnal penile tumescence results must be interpreted with caution, since men with normal erections may have abnormal nocturnal penile tumescence, especially if a sleep disorder or depression is present. Furthermore, nocturnal penile tumescence may not be always be an indicator of erectile potential in erotic and sexual circumstances.[9] Despite these limitations of nocturnal penile tumescence, one would not expect a man to have normal nocturnal penile tumescence if the erectile dysfunction is owing to severe corporeal-venous occlusive dysfunction.

The direct injection of high doses of vasoactive drugs into the corpora cavernosa for diagnostic purposes is an attempt to substitute neural input by stimulating neurotransmitters to initiate an erection whose quality is presumably dependent on both sides of the vascular system (arterial and venous). However, anxiety, the absence of ongoing neural stimulation (as would be provided through sexual stimulation) and perhaps other unknown factors may blunt the effects of smooth muscle relaxants. The addition of an adrenergic blocking agent, such as phentolamine, may not always be sufficient to overcome sympathetically mediated smooth muscle constriction.

Buvat et al found that only 1 of 6 patients with normal nocturnal penile tumescence had a normal erection after the intracavernous injection of 80 mg. papaverine.[10] Their study differs from ours in that only papaverine and not papaverine and phentolamine were injected. Also infusion cavernosometry was not performed after drug injection. Allen and Brendler

found that the response to intracorporeal pharmacological testing was accurately predicted by nocturnal penile tumescence measurements.[11] In their study papaverine and phentolamine were used but after injection the men were sent home and asked to attempt coitus. The response to injection was considered positive if erection adequate for vaginal penetration was reported. Like others using intracorporeal drugs for testing and therapeutic purposes, we have found that the response is better if the patient assumes a standing position following injection. The response is even better if sexual stimulation follows drug injection. In our study the patient was in the supine position for the duration of infusion pharmacocavernosometry and no sexual stimulation was used.

We believe that infusion pharmacocavernosometry, as described herein, may be a useful test in the evaluation of men with erectile insufficiency. However, like all other components of impotence evaluation infusion pharmacocavernosometry has its uncertainties and limitations. Only when a careful history, physical examination, psychological assessment and all other parts of the impotence evaluation (including nocturnal penile tumescence and infusion pharmacocavernosometry) are considered together, can a reasonably accurate diagnostic assessment be made. In particular we view with concern recent over reliance on new and unvalidated tests, such as infusion pharmacocavernosometry, without an attempt to correlate them to more traditional testing, such as nocturnal penile tumescence.

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