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A multidisciplinary study was performed on 200 consecutive patients with erectile dysfunction more than 1 year in duration, which included a standardized intracavernous injection of a vasoactive substance mixture (15 mg. per ml. papaverine plus 0.5 mg. per ml. phentolamine). The multidisciplinary findings correlated well with the intracavernous dose needed for full erection. The group without pathological hemodynamic findings (36 patients) needed an average of 0.67 ml. and the group with pathological inflow (107) needed an average of 1.07 ml. In the venous insufficiency group (57 patients) only 18 achieved full erections with an average of 2.1 ml. (39 achieved tumescence only to 3 ml.). The results show that standardized intracavernous injection of a vasoactive substance mixture is a useful method to evaluate penile hemodynamics. This pharmacological test appears to be effective in the differential diagnosis of nonvascular and vascular erectile dysfunction. (J. Urol., 139: 734–737, 1988)
the patients and the maximum dose was set at 3 ml. At least 3 injections (1 injection per day) per patient were performed at the hospital without psychogenic or reflexogenic stimulation. The interval until maximum onset of action as well as quality and duration of maximum response were recorded by the urologist. The penile reaction was divided into 6 degrees according to the palpatory findings: 0—no reaction, 1—slight tumescence, 2—medium tumescence, 3—complete tumescence with no rigidity, 4—complete tumescence with medium rigidity and 5—complete rigidity.

Severe hypoplasia or aplasia of both penile arteries on angiography and/or Doppler ultrasound was considered an arterial etiology. A bulbocavernous reflex latency exceeding 42 msec. was regarded as a neurogenic etiology. On dynamic cavernosography, a maintenance flow greater than 80 ml. per minute was considered a venous etiology.

RESULTS

During the diagnostic use of vasoactive substances in the 200 patients studied 19 experienced 21 prolonged erections (duration of more than 6 hours). The first 4 erections were treated successfully by aspiration of blood from both corpora cavernosa, while the remainder were treated by intracavernous injection of 2 mg. of the α-adrenergic stimulator metaraminol.

According to the results of the multidisciplinary evaluation, the etiology was purely arterial in 58 patients, arterio-neurogenic in 42, arteriovenous plus neurogenic in 11, arteriovenous in 19, arterio-psychogenic in 7, neurogenic in 27, venous in 24, psychogenic in 9 and neurogenic-venous in 3. The doses required by the individual patients to achieve a complete erection at least 30 minutes in duration are shown in figure 1.

If one arranges these groups under hemodynamic aspects, basically different reactions to the intracavernous injection can be classified as 1—no effect on hemodynamics, 36 patients (fig. 1, 1 and h), 2—disturbance of arterial inflow with venous competence, 107 patients (fig. 1, a, b and e) and 3—excessive outflow, 57 patients (fig. 1, c, d, g and i). Mean patient age in these 3 groups was 44.7, 46.9 and 45.3 years, respectively. The age distribution curves showed no significant differences. In contrast to the normal subjects, 20 of 36 patients without pathological hemodynamic findings achieved a complete erection after administration of 0.5 ml or less within 5 to 8 minutes. In this group a mean dose of 0.67 ml. was needed to achieve a complete erection (fig. 2, a). All patients with arterial insufficiency achieved a complete erection by means of vasoactive substances. The response time was markedly prolonged (up to 40 minutes) and the mean dose was 1.07 ml. (fig. 2, b). Only in 18 of 57 patients with venous insufficiency (maintenance flow more than 100 ml. per minute) could a complete erection be achieved by intracavernous injection of vasoactive substances and the mean dose was 2.1 ml. in these patients (fig. 2, c).

DISCUSSION

Intracavernous injection of a papaverine-phenolamine mixture induces an erection with complete rigidity provided the penile hemodynamics are intact and the dosage is adequate. This effect is achieved mainly by relaxation of the smooth muscles of the cavernous sinus. Juennemann and associates demonstrated the importance of a decrease in penile outflow to achieve complete rigidity as a result of this cavernous relaxation. Patients in whom the erectile dysfunction is not of arterial or venous etiology have a complete erection in response to a standardized intracavernous injection of vasoactive substances. Arterial insufficiency produces prolongation in the response time from a normal of 5 to 8 minutes up to 40 minutes and, depending upon the extent of the inflow disturbance, an increase in dosage is required to achieve complete rigidity. A mild inflow disturbance cannot be differentiated from an intact penile blood supply by means of this test. If complete rigidity cannot be achieved even by maximum doses (45 mg. papaverine and 1.5 mg. phenolamine) marked insufficiency of the smooth cavernous muscles or abnormal venous channels must be assumed based on the results of animal experiments. The insufficient reduction in venous outflow prevents the intracavernous pressures that are necessary to achieve complete rigidity and it can be demonstrated as venous leakage by means of dynamic cavernosography. This cavernous reaction to intracavernous injection of vasoactive substances can be modulated by external and psychological factors, respectively, in terms of an increase adrenergic tone but it can be inhibited completely only in rare cases. This penile response to certain intracavernous doses of vasoactive substances is well reproducible in the same

![Fig. 1. Etiology of erectile dysfunction according to results of multidisciplinary approach (200 patients) in correlation to dosage required for full erection. a, arterial etiology, 58 patients. b, arterio-neurogenic etiology, 42 patients. c, arteriovenous plus neurogenic etiology, 11 patients. d, arteriovenous etiology, 19 patients. e, arterio-psychogenic etiology, 7 patients. f, neurogenic etiology, 27 patients. g, venous etiology, 24 patients. h, psychogenic etiology, 9 patients. i, neurogenic-venous etiology, 3 patients.](image-url)
Intracavernous injection of vasoactive substances in a standardized form represents a simple and reliable method to evaluate penile hemodynamics. To avoid serious side effects such injection should be performed only by physicians experienced with this technique. By means of this pharmacological test a rationalized 3-step program was developed to answer therapy relevant questions: 1) baseline examination included history, physical examination and laboratory testing, 2) specific non-invasive examinations included pharmacological testing, Doppler sonography and sexual history plus psychometry, and abdominal and pelvic sonography, and 3) specific invasive examinations (only in certain indications) included dynamic cavernosography, angiography, bulbocavernous reflex latency testing and evaluation of the somatosensory evoked potential.

REFERENCES


EDITORIAL COMMENTS

The authors support serial intracavernous injections of vasoactive agents in the differential diagnosis of impotence and evaluation of penile hemodynamics. The diagnosis of impotence is based on the quality of the response, time required to achieve the response and dose required to induce a full erection. Men with intact penile vasculature responded to vasoactive agents with full, rigid erections. Men with vasculogenic impotence (that is venous, arterial or mixed), if they respond at all, usually require higher doses of medication to induce this response, the onset of which may be delayed.

Several factors should be considered when vasoactive agents are used intracavernously in the differential diagnosis of and screening for impotence. The same dose administered to the same patient at different times may induce a different response. The response may differ if the patient is in the supine, standing or sitting position during injection, if he is anxious or if there is sexual stimulation. Patients with penile arterial insufficiency may have a normal response. An attenuated response may occur in up to 44 per cent of the patients with normal vasculature despite repeated injection.1

Vasoactive agents injected intravenously have great potential for the differential diagnosis of impotence. However, this potential is not yet realized. More test standardization is required so that specificity, sensitivity and accuracy can be defined. Factors that should be standardized include the vasoactive agent used, dose, whether single or multiple injections are given, test conditions, use of visual sexual stimulation, position during injection and methods to assess the response.

Currently, it appears that a diagnosis of severe venous incompetence or severe arterial insufficiency can be excluded with certainty if a full erection is achieved after carefully performed intracavernous injection. The significance of a partial response or no response still is uncertain.

The authors agree with the authors that intracavernous injection of pharmacological agents is useful in the evaluation of penile hemodynamics. However, owing to the imprecise nature of most of our current diagnostic tests to differentiate various types of impotence, the etiological classification in this article is oversimplified. A prolonged bulbarcavernous reflex only implies that the patient may have some neurological deficit and not necessarily neurogenic impotence. During evaluation of the cavernous artery, penile arteriography and Doppler analysis currently are imprecise and there will be large numbers of false negative or positive results in the diagnosis of arteriogenic impotence.

It must be emphasized that the dosage mentioned by the authors is for diagnostic purposes (without sexual stimulation). If the patient is to perform self-injection before sexual intercourse the dosage required would be much lower. We prefer to start with 0.1 ml. (3 mg.) papaverine alone in patients with neurogenic impotence and 0.5 ml. (15 mg.) in those with other types, and then we increase the dosage gradually until a desirable result is obtained. Use of 2 to 4 mg. metaraminol to treat priapism is dangerous. Two deaths have been reported in France owing to complications from acute severe hypertension. We prefer a small dose of epinephrine (10 μg./1 ml. normal saline) repeated every 5 minutes after aspiration of 15 to 20 ml. blood. Others prefer irrigation with phenylephrine solution.

Standardization of a dynamic test for erectile dysfunction is a difficult task owing to the psychological inhibition that invariably occurs in such an artificial environment. I congratulate the authors on this endeavor and I stress that when results are equivocal the test should be repeated 2 or 3 times to rule out psychological overshadowing of organic disease.

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REPLY BY AUTHORS

We appreciate the editorial comments and are in complete agreement that, although techniques may be standardized, patients will never be. In particular, psychogenic influences may alter the individual response to standardized intracavernous pharmacological testing. Accordingly, to avoid an attenuated response in an anxious or nervous patient, we recommend that pharmacological testing not be performed as the first diagnostic procedure for erectile dysfunction. Rather, it should be introduced after the urologist has gained the confidence of the patient. It should be performed in a secure, quiet environment and it should be repeated to prove reproducibility. The complexity of the erectile phenomenon and the current gaps in our knowledge of it currently make a precise diagnostic method unavailable. However, we believe that standardized intracavernous pharmacological testing, besides minimizing the use of invasive techniques, provides a useful evaluation of penile hemodynamics as an aid to choosing the appropriate therapeutic option.