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ERECTILE RESPONSES TO INTRACAVERNOUS PAPAVERINE AND PHENTOLAMINE: COMPARISON OF SINGLE AND COMBINED DELIVERY

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ABSTRACT

In a prospective study of 15 consecutive impotent patients we evaluated the erectile responses to intracavernous injections of standardized doses of papaverine and phentolamine alone and in combination. Of the 15 patients 13 achieved a full erection with the drug combination, whereas only 6 achieved a full erection with papaverine and 1 with phentolamine. Our results suggest an effective alternative to the use of papaverine alone, whose long-term sequelae have been shown to be deleterious. (*J. Urol.*, 140: 1415-1416, 1988)

After Virag reported the intracavernous application of papaverine for erectile dysfunction in 1982¹ Brindley introduced autoinjection therapy with the α -blocker phenoxybenzamine.² Since then Zorgniotti and LeFleur have described the use of a combination of papaverine and the α -blocker phentolamine for autoinjection,³ and many intracavernous injection protocols for impotence now use this combination.⁴⁻⁹ Despite its popularity, the superiority of the combination of papaverine and phentolamine compared to either drug alone has never been proved. We examined the possible synergistic effects of a combination of papaverine and phentolamine used for intracavernous injection in the treatment of erectile dysfunction.

PATIENTS AND METHODS

Fifteen consecutive patients between 24 and 59 years old with erectile dysfunction lasting at least 1 year were seen in our impotence clinic. For each patient a detailed history was taken based on a standard questionnaire that emphasized sexual function. A physical examination, including a neurological examination, blood chemistry studies, including SMA 12, testosterone and prolactin, nocturnal penile tumescence monitoring with a Snap-Gauge^{*10} and Doppler analysis of the 4 penile arteries before and after intracavernous injection of the vasoactive drugs also were performed.¹¹ Pharmacocavernosometry and pharmacocavernosography were done in 9 patients¹² and bulbocavernosus reflex latency testing in 3.¹¹ Penile arterialization was considered abnormal if the Doppler study showed significantly reduced flow (or none) in both cavernous arteries. Pharmacocavernosometry was interpreted as abnormal when the maintenance flow rate exceeded 14 ml. per minute, thus suggesting venogenic impotence. A bulbocavernosus reflex latency exceeding 42 msec. was considered abnormal.

Each patient consented to participate in the study. Intracavernous injections were done once a day in the hospital by a urologist, and the patients remained supine during and after injection. On day 1 a combined 0.5 ml. dosage was delivered (15 mg./ml. papaverine and 0.5 mg./ml. phentolamine). The patient was advised to avoid any psychogenic or reflexogenic stimulation. The response was evaluated by inspection and palpation by a urologist and classified into 6 categories (table 1). Depending on the response, the dose was doubled or reduced the following day(s) until a full erection lasting at least 15 minutes was reached (intracavernous pressure 80 mm. Hg). The maximal dose was 3 ml. If combined delivery induced a full erection that was reproducible the following day, a doubled

amount of papaverine (30 mg./ml.) was injected singly the next day. The following day a doubled amount of phentolamine (1 mg./ml.) likewise was injected singly. All solutions had the same pH (4.5) and they were iso-osmolar.

RESULTS

Of the 15 patients 13 (87 per cent) reached a full erection (E5) with the papaverine-phentolamine combination. The mean amount of the solution injected was 0.81 ml., corresponding to 12.1 mg. papaverine and 0.4 mg. phentolamine. Of the remaining 2 patients 1 reached full tumescence (E3) and 1 medium tumescence (E2).

With the double dose of papaverine alone 6 patients (40 per cent) reached a full erection and only 1 achieved a better response with papaverine (15 mg.) than with the combination of papaverine (7.5 mg.) and phentolamine (0.25 mg.). With phentolamine alone 1 patient (7 per cent) reached full erection.

Injection of the combination induced a full erection in 4 of 6 patients with venous leakage diagnosed by pharmacocavernosography,¹² whereas papaverine alone induced a full erection in only 2 of these patients (table 2). The only complication was prolonged erection (greater than 300 minutes) in 1 patient, which was treated successfully by 2 mg. metamamol intracavernously.

DISCUSSION

Papaverine and phentolamine induced erection more frequently when given in combination than when either drug was given alone. The response to the combination was superior to the additive effect of the substances alone and superior to the effect of a doubled dosage of either drug. Delivered singly, papaverine was more effective than phentolamine. Our results support the use of a combination of papaverine and phentolamine rather than papaverine alone. In addition to a physiologically adapted pH and osmolarity, another benefit of combined delivery would be the diminution not only of systemic but also of local side effects. This possible reduction of local

TABLE 1

Response to Intracavernosal Injection	Classification
No response	E0
Slight tumescence	E1
Medium tumescence	E2
Full tumescence	E3
Full tumescence + medium rigidity	E4
Full rigidity	E5

TABLE 2. *Erectile responses to papaverine and phentolamine alone and in combination*

Pt. No.—Age	Diagnosis*	Amount Injected (ml.)	Response (mins.)		
			Combination	Papaverine	Phentolamine
1—56	Arteriogenic	1	E5 (15)	E4 (5)	E5 (3)
2—45	Arteriogenic	0.5	E5 (150)	E5 (240)	E3 (30)
3—33	Venogenic	0.5	E5 (240)	E4 (20)	E3 (5)
4—29	Neurogenic	0.25	E5 (60)	E1 (5)	E1 (5)
5—54	Arteriogenic + venogenic	1	E5 (45)	E5 (45)	E1 (5)
6—53	Arteriogenic	1	E5 (90)	E4 (90)	E3 (60)
7—56	Arteriogenic	1	E5 (30)	E4 (12)	E2 (3)
8—53	Arteriogenic + venogenic	1	E5 (90)	E3 (30)	E1 (5)
9—59	Arteriogenic + hormonal	1	E5 (55)	E5 (30)	E1 (2)
10†—44	Venogenic + neurogenic	1	E5 (180)	E2 (5)	E2 (5)
11—51	Arteriogenic + venogenic	1	E5 (60)	E5 (20)	E2 (3)
12†—35	Venogenic	1	E5 (60)	E5 (25)	E2 (10)
13—44	Venogenic	3	E3 (50)	E2 (25)	E1 (4)
14—26	Venogenic	3	E2 (40)	E1 (30)	E0
15—24	Neurogenic	0.25	E5 (120)	E5 (10)	E2 (10)

* Etiology based on findings of our studies, including Doppler analysis, pharmacocavernosometry, pharmacocavernosography and bulbocavernosus reflex latency.

† Penile venous surgery also was performed.

side effects seems to be the more important, since recent experimental findings in monkeys that underwent 100 intracavernous injections of papaverine showed extensive intracavernous fibrosis and ultrastructural changes of the cavernous smooth muscles.¹³

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