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CAN AN INTRACAVERNOUS PAPAVERINE INJECTION BE USED TO DIAGNOSE ARTERIOGENIC IMPOTENCE?

Akio IMAGAWA and Yasuo KAWANISHI

From the Department of Urology, Takamatsu Red Cross Hospital
(Chief: Dr. A. Imagawa)

We injected papaverine into the corpus cavernosum of 93 patients with impotence, and compared the results with findings from nocturnal penile tumescence monitoring, psychogenic erection monitoring after sexual stimulation, penile-brachial indexes, and dynamic cavernosography. There was a significant correlation between the findings from papaverine injection and dynamic cavernosography, but there was no correlation between the papaverine findings and other tests including the penile-brachial index. We conclude that we can disregard the possibility of venous abnormality in those who respond to papaverine injection, but we cannot disregard the possibility of arteriogenic abnormality. We proved that papaverine injection cannot diagnose arteriogenic abnormality.

Key words: Impotence, Papaverine test, Penile-brachial index, Dynamic cavernosography, Vasculogenic impotence

INTRODUCTION

Papaverine hydrochloride was first injected accidentally into the intracavernous body by Virag[1]. He observed and reported the interesting phenomenon of a prolonged, fully rigid erection of two hours duration. Since then many clinical observations[2-4] and fundamental studies[5,6] have been reported, and an intracavernous papaverine injection has become widely used for the diagnosis and treatment of impotence[7,8].

Men capable of erection after papaverine use were considered to have normal vasculogenic function. To reappraise this theory, we compared the results from a number of papaverine tests with findings from a penile-brachial index, dynamic cavernosography, and tumescence monitoring at night and/or after sexual stimulation.

PATIENTS AND METHODS

Ninety-three consenting patients between 23 and 79 (mean age 51.0 years) were registered in this investigation. All patients underwent routine history and physical examinations, and an evaluation of hormone deficiency.

For the papaverine test, the patients was placed in the supine position. Forty mg. of papaverine hydrochloride (1 ml.) was injected slowly using a 23-gauge single needle inserted at a 90 degree angle into the lateral corpus cavernosum at midshaft. There was no dilution of the papaverine, and no use of a constrictive technique at the base of the penis. After 5 minutes the patients were asked to stand, and the changes in the penis were evaluated. The patients were then asked to walk for about 5 minutes, followed by a second evaluation.

The changes in the penis were evaluated as follows:

P1 (full erection) when turgidity was firm to palpatation, the angle of erection was over 90 degrees, and the patient felt his erection could penetrate.

P2 (tumescence only) when the erection was evaluated as tumescence only without rigidity to palpatation.

P3 (minimal change) when no erection occurred.

If detumescence occurred within 10 min-

utes, then patients were graded one point lower on the scale. A continuous erection for over 6 hours was diagnosed as priapism.

For the penile-brachial index a 9.5 MHz doppler device and a 42 mm. cuff were used to measure the systolic pressure in both penile dorsal arteries. The penile-brachial index was calculated by dividing the systolic pressure in the penile dorsal arteries by the systolic brachial pressure. We recorded the higher of the left and right indices.

Nocturnal penile tumescence was monitored with a mercury strain-guage, and full records were kept of sleep patterns. Monitoring was done on one night only after the patients were asked to stay awake for 24 hours. However, if the REM-sleep phase was not observed at least three times, then the recording was abandoned, and re-done on the second or third night. The results of nocturnal penile tumescence monitoring were classified as follows:

MS1a: There were periodic occurrences of tumescence involving changes of over 16 mm in the circumference of the penis.

MS1b: There were periodic occurrences of tumescence but involving changes of less than 16 mm.

MS2a: There were occurrences of tumescence involving changes of over 16 mm but without periodicity.

MS2b: There were occurrences of tumes cence involving changes of less than 16 mm without periodicity.

MS3: There was only a slight change in the penis.

MS4: There was no change in the penis.

We performed and evaluated tumescence monitoring using a method previously reported[9] after audiovisual sexual stimulation involving a sexual stimulation score.

In dynamic cavernosography, a single 19 gauge needle was inserted into the corpus cavernosum at a lateral position. A contrast medium diluted with warm normal saline solution was injected at an initial rate of 10 ml/min. The rate was increased gradually until the intracorporeal pressure, measured through a 21 gauge single needle inserted into the opposite corpus cavernosum, reached 80 mmHg. After the flow rate required to reach this point ('flow rate to produce') was recorded, the minimal flow rate required to maintain erection ('flow rate to maintain') was measured. We did not use anesthesia or heparin at all during the test.

RESULTS

Table 1 shows the underlying causes of the patients' impotence, as evaluated by medical history and physical examinations. Of the 93 men, impotence was diagnosed to be due to organic causes in 36: 11 had diabetes, 6 had urethral or pelvic trauma, 4 had undergone intrapelvic surgery, 3 had vascular disease, 1 had a whip lash injury, 1 had induration of the corpus cavernosum, 1 had gynecomastia, and 9 were over 60 years old. The cause of impotence was considered to be psychogenic or unknown in the other 57 patients: 4 had psychiatric disease, 11 had episodes of first coital failure, 2 had remarried, 1 had prostatism, while 39 had no apparent disease or traumatic episode. None of the patients, including the gynecomastic patient, showed any abnormality on an endocrine examination.

Table 1. Underlying cause of impotence.

Organic :		**36**
	Diabetes	11
	Urethral or Pelvic Trauma	6
	Intrapelvic Surgery	4
	Vascular Disease	3
	Whip-lash Injury	1
	Induration of Cavernosum	1
	Gynecomastia	1
	Old Age (Over 60)	9
Psychogenic		18
	Psychiatric Disease	4
	First Coital Failure	11
	Remarriage	2
	Prostatism	1
Unknown		39

On the papaverine test, 45 of the 93 patients were evaluated as P1, 39 as P2, and 9 as P3. Priapism occurred in 8 patients, but was successfully treated in each case by a dopamine injection into the corpus cavernosum.

Nocturnal penile tumescence monitoring

Table 2. The relationship between papaverine test results and NPT monitoring.

	P1	P2	P3
MS1a	16	2	
MS1b	8	7	
MS2a	3	4	
MS2b	2	0	
MS3		6	1
MS4		3	3

Table 3. The relationship between papaverine test results and psychogenic erection monitoring after sexual stimulations.

	P1	P2	P3
A	8	3	2
B	5	5	0
C	9	13	3
D	4	7	2
N	10	5	2

was performed on 62 of the 93 patients; 19 were evaluated as MS1a, 16 as MS1b, 8 as MS2a, 2 as MS2b, 9 as MS3, and 8 as MS4. Table 2 shows the results and findings of the papaverine test and nocturnal penile tumescence monitoring. Twenty-seven of the 33 patients evaluated as P1 on the papaverine test were classified according to the findings of nocturnal penile tumescence monitoring as functional (MS1a) or functional-suspected (MS1b and MS2a). The remaining 6 patients were classified as organic-suspected (MS2b and MS3) or organic (MS4). Thirteen of the 22 patients evaluated as P2 were classified as functional or functional-suspected, while the remaining 9 were organic or suspected organic. Three of the 7 patients evaluated as P3 were classified as functional or suspected functional, while the remaining 4 were organic or suspected organic.

Monitoring for erotic erection using a sexual stimulation score was performed in 78 of the 93 patients. Thirteen patients were classified as A, 10 as B, 25 as C, 13 as D, and 17 as N. Table 3 shows the results in comparison with those of the papaverine test. The correlation of papaverine results to the sexual stimulation score in Table 3 is very similar to that of papaverine to NPT shown in Table 2.

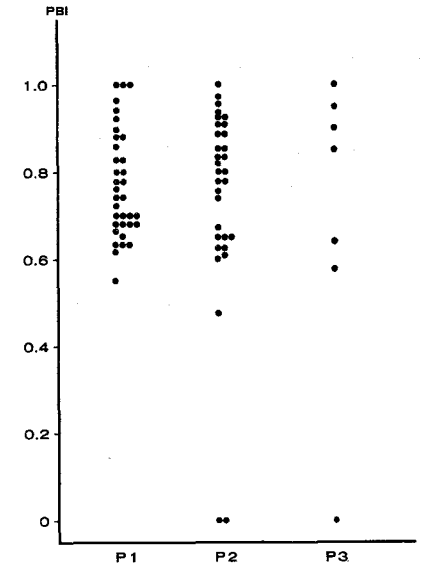

Fig. 1. The relationship between the penile-brachial index and papaverine test results. No correlation was seen among the three groups.

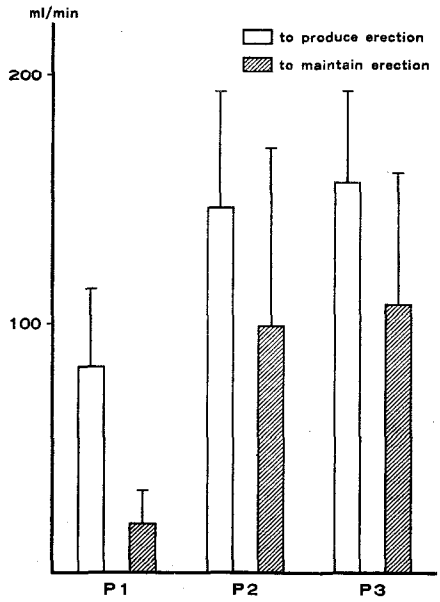

Fig. 2. The relationship between dynamic cavernosography and papaverine test results. The uppermost bar with vertical line in each case indicates one standard deviation. The flow rate in P1 is significantly lower than in the other groups. ($p<0.001$)

Penile-brachial indices were calculated for 71 of the 93 patients. The results of the penile-brachial index are shown and compared with the papaverine test in Figure 1. The penile-brachial index was less than 0.7 in 11 of the 35 patients classified as P1 on the papaverine test, in 9 of the 30 patients classified as P2, and in 2 of the 6 patients classified as P3.

A dynamic cavernosography was performed on 77 patients. Figure 2 shows the flow rates to produce and maintain an erection in each group for the papaverine test. The mean flow rate and standard deviation to produce an erection in each group were 81.8±31.7 ml/min in P1, 146.7 ±46.3 ml/min in P2, and 157.5±34.5 ml/min in P3, (where flow rate was set at 200 ml/min when the erection was not achieved). The mean flow rate and standard deviation to maintain an erection in each group were 19.5±13.4 ml/min in P1, 99.4±70.8 ml/min in P2, and 107.5± 52.8 ml/min in P3. Both mean flow rates for P1 were significantly lower than those for the other groups.

DISCUSSION AND CONCLUSIONS

Papaverine hydrochloride is a nonspecific, smooth muscle relaxant. In a man with normal cavernous function, an erection occurs within several minutes and continues for several hours when papaverine is injected directly into the corpus cavernosum. The mechanism for this phenomenon is considered to be the increase in blood volume in the corpus cavernosum due to the relaxation of the smooth muscle of the corpus cavernosum.

Juenemann et al.[5] in dogs, and Leu et al.[10] and Kawanishi and Imagawa[6] in men investigated the hemodynamics of the penis after papaverine injection into the corpus cavernosum. Juenemann et al.[5] reported that papaverine profoundly increased the resistance to venous outflow, and increased arterial inflow by 300 to 700 percent over baseline levels in dogs. In man, Leu et al.[10] observed that the flow and diameter of the deep arteries increased in all subjects before the onset of full rigidity after papaverine use.

These observations suggest that an increase in blood flow and an increase in resistance to venous outflow are the mechanism by which erection is achieved after papaverine injection into the corpus cavernosum. In the present clinical study the findings after papaverine injection correlate significantly with the results of dynamic cavernosography. However, no correlation was seen between the findings after papaverine injection and the penile-brachial index. Abber et al.[4] also recognized the lack of correlation between the 2 tests. They suggest that the discrepancy may be because the dorsal artery flow, measured by the penile-brachial index, does not supply the corpus cavernosum. It is true that the penile-brachial index does not detect the direct supply to the corpus cavernosum, but the discrepancy was too large to be explained by this reason alone.

We were unable to detect by the thermal diffusion method any increase in blood flow in the corpus cavernosum during erection after papaverine injection[6]. However we could detect a marked increase just before full erection was achieved following sexual stimulation. We think therefore that erection after papaverine use is achieved with a smaller volume of blood compared with normal physical erection. The apparent change in blood flow after papaverine use is a secondary effect, following an increase in the volume of the sinusoidal space. Thus full rigidity can be achieved in a papaverine test, even in patients who have mild arterial abnormalities. However, for normal physical erection, a large volume of blood flow is necessary. Even men who can achieve erection after papaverine use may have arteriogenic impotence. We therefore think that a papaverine injection into the corpus cavernosum cannot detect arteriogenic impotence.

Men who can achieve erection after papaverine use, but have a low penile-brachial index, especially with peripheral vascular disease[11] should undergo further examination such as arteriography.

On the other hand, however, because

the findings of the papaverine test show good correlation with the results of dynamic cavernosography, subsequent cavernosography becomes unnecessary when a hard erection is achieved with the papaverine test. The possibility of venous abnormalities as a cause of impotence can be rejected in patients with P1 results.

Men with normal results on a papaverine test, but with abnormal findings on nocturnal penile tumescence monitoring probably have arteriogenic or neurogenic causes for their impotence. However, the reason why men with normal findings from nocturnal penile tumescence monitoring have abnormal responses on a papaverine test is not understood. It may be because nocturnal penile tumescence monitoring does not measure actual rigidity.

In conclusion, the papaverine test is useful for detecting venous abnormalities, and as a means of decreasing the frequency of dynamic cavernosography. However, it does not diagnose arteriogenic impotence.

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和文抄録

パパベリンテストは動脈性インポテンスを診断し得るか？

高松赤十字病院泌尿器科（部長：今川章夫）
今川章夫，川西泰夫

インポテンスを訴える93例に塩酸パパベリンの陰茎海綿体内投与による勃起状態を観察（パパベリンテスト）し，夜間陰茎勃起現象の記録，性的視聴覚刺激による勃起の記録，penile-brachial index，海綿体灌流による人工勃起の結果と比較検討した．

パパベリンテストの結果は海綿体灌流による勃起発現流量および勃起維持流量と強い相関を示したが，penile-brachial index とはまったく相関を示さなかった．したがって，パパベリンテスト陽性は流出路の閉鎖不全である静脈性インポテンスを否定し，陰性は静脈性インポテンスを強く疑わせるが，パパベリンテストの結果から動脈性インポテンスを診断することはできないと考えられた．

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