Radionuclide Assessment of Penile Corporal Venous Leak Using Technetium-99m-Labeled Red Blood Cells

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In an attempt to evaluate penile corporal venous outflow, a method that utilizes intracorporal injection of Tc-RBC was developed and used in 20 patients with erectile dysfunction. Seven patients showed venous leak and 13 had normal venous outflow. Technetium-labeled RBC corporal clearance in the flaccid state and after intracorporal injection of papaverine (30 mg) and regitine (1 mg) were assessed in sequence by two separate injections of 18.5 MBq of Tc-RBC each. The time for 50% corporal clearance (T50%) was determined from the time activity curves obtained in flaccid state and after intracorporal injection of the vasoactive agent. There were no statistically significant differences in T50% measured in the flaccid state between normal venous outflow (202 ± 139 sec) and venous leak (92 ± 35 sec, $p = 0.1$). However, after intracorporal injection of papaverine and regitine a significant increase in the T50% was noted in normal venous outflow (2892 ± 1899 sec) as compared to venous leak (213 ± 123 sec, $p < 0.001$). The results suggest that measurement of corporal clearance of Tc-RBC after intracorporal injection of papaverine may be a useful method in detecting venous leak, and could be used as a screening test in patients with erectile dysfunction.

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The most common organic cause of impotence is vasculogenic and results from arterial insufficiency and/or incompetence of the veno-occlusive mechanism (venous leak) (*1*). Nuclear medicine techniques have been used in the evaluation of patients with erectile dysfunction. Radioisotope penile plethysmography measures intrapenile blood volume during pharmacologically-induced tumescence (*2,3*). It has been reported to be useful in detecting arterial insufficiency, but not venous leak (*3*). The ^{133}Xe washout method has also been used to evaluate penile blood flow. Although it has been demonstrated that delayed xenon washout after subcutaneous injection is a good indicator of arterial insufficiency (*4,5*), the intracorporal xenon washout method has been shown unreliable in the prediction of venous leak (*6,7*).

In an attempt to quantitate corporal venous drainage, a technique that measures the clearance of Tc-RBC from the corpora was developed. The present study evaluated the clearance of intracorporally injected Tc-RBC in patients with normal venous outflow and in patients with venous leak. The study was performed both in the flaccid state and after intracorporal injection of a vasoactive agent in order to assess the ability of the method in detecting venous leak.

MATERIALS AND METHODS

Patient Population

A radionuclide study of corporal venous outflow was performed in 20 patients with erectile dysfunction. All patients underwent a comprehensive evaluation by a careful history and physical examination, hormonal and neurological tests, penile-brachial pressure index (PBI), papaverine test and dynamic infusion cavernosometry and cavernosography (DICC). Their ages ranged from 28 to 63 yr (mean = 45 yr), with symptoms of impotence varying from 8 mo to 10 yr (mean 4 yr). Seven patients showed venous leak as a cause of erectile dysfunction. None had evidence of arterial insufficiency with a PBI ≥ 0.86. The remaining 13 patients had normal venous outflow and the causes of erectile dysfunction were neurogenic (n = 7), psychogenic (n = 5) and arterial (n = 1).

Radionuclide Study

The radionuclide study of the corporal venous outflow was carried out in the flaccid state and after intracorporal injection of a vasoactive agent (papaverine 30 mg and regitine 1 mg). With the patient in the supine position, a 21-gauge butterfly needle was placed in the mid-portion of the corpora and the patient was allowed to rest for 10–15 min to reduce anxiety. The dynamics of corporal venous outflow were studied with the detector of a digital gamma-camera (Apex-415, Elscint-Haifa, Israel) imaging the pelvis in the anterior view. Previously prepared Tc-RBCs (18.5 MBq) using the in-vitro technique (*8*) were injected via the intracorporal needle and data acquisition with computer images of 1 frame/15 sec was recorded for 20 min. At the end of acquisition in this flaccid state, the vasoactive agent was slowly injected via the same intracorporal needle for approximately 1

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min. Then, another intracorporal injection of 18.5 MBq of Tc-RBC was performed and data acquisition was repeated as before.

At the end of the acquisition, the penis was examined by palpation and the degree of tumescence: (a) rigid, full response; (b) partial, short-lived erection response; and (c) no response recorded.

For data analysis, a region of interest was defined for the penis and a time-activity curve (TAC) was generated after background subtraction for both the flaccid state and after papaverine injection (Fig. 1). Study results were assessed qualitatively based on curve morphology and by the quantitative assessment of the clearance of the labeled blood from the corpora by measuring the time to half outflow (T50%). T50% was defined as the time in seconds required for the corpora to empty half of the maximum counts and was obtained from the exponential fit of the curve after the injection of the Tc-RBC.

Statistical Analysis

The paired t-test was used to compare between T50% in the flaccid state with that after papaverine injection in the same group. Student's t-test was performed for comparison between the two groups. Sensitivity, specificity, and accuracy of T50% were calculated between normal venous outflow (n = 13) and venous leak (n = 7) in the flaccid state and after papaverine injection. Values are shown by mean ± s.d. (95% confidence intervals).

RESULTS

Normal Venous Outflow

A rapid clearance curve was demonstrated in the flaccid state in all but two patients. After papaverine injection, 12 of 13 patients showed that the curve was more horizontal with less slope and sometimes flat for the first few minutes. This pattern was obtained in two patients in the flaccid state. The T50% was 202 ± 139 sec (CI = 119 to 286 sec) in the flaccid state. After papaverine, there was a statistically significant increase in the T50% to 2892 ± 1899 sec (CI = 1754 to 4030 sec, t = 4.8, $p < 0.001$). Twelve of these patients had no evidence of arterial unsufficiency and had a PBI ≥ 0.81.

One patient presented with bilateral hypogastric arteries obstruction after pelvic trauma. The T50% of this patient was 87 sec in the flaccid state and after papaverine 4841 sec.

There was a full rigid erection response to papaverine injection in four, no response in one, and partial response in eight patients as assessed by palpation.

Venous Leak

A rapid clearance curve was found in these patients both in the flaccid state and after papaverine injection. The T50% was 92 ± 35 sec (CI = 61 to 123 sec) in the flaccid state and 213 ± 123 sec (CI = 102 to 323) after papaverine injection (t = 2.09, p = 0.1). None of these patients had evidence of arterial insufficiency. Of the seven patients with venous leak, one patient showed no response and six had partial response to papaverine by palpation.

In the flaccid state, there were no significant differences in the T50% between venous leak and normal venous outflow (t = 1.95, p = 0.1). However, a significant difference between the groups was found in the T50% after papaverine injection (t = 3.54, $p < 0.001$) (Fig. 2).

DISCUSSION

Normal penile erection requires relaxation of the smooth muscle of the corpus cavernosum, adequate arterial inflow and reduction of venous outflow (*1*). Relaxation of the smooth muscle of the corpus cavernosum allows expansion of the lacunar spaces. Dilatation of the cavernous and helicine arteries increases the blood flow to the dilated lacunar spaces. The filling and distention of the lacunar spaces against the tunica albuginea results in the compression of the subtunical venous plexus reducing corporal venous outflow with entrapment of blood within the corpora leading to erection (*1*). Incompetence of these veno-occlusive mechanisms (venous leak) has been recognized as a common cause of erectile dysfunction with reported incidence varying from 25% to 78% (*9*).

The usefulness of flow, volume and pressure measurements for the evaluation of vasculogenic impotence in the flaccid state has long been recognized, and the introduction of intracorporal injection of papaverine as a diagnostic tool allowed the functional evaluation of erection (*10,11*).

Papaverine is a nonspecific smooth muscle relaxant which, when injected intracorporally, augments penile

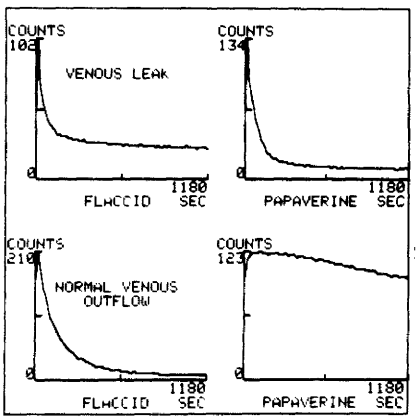

FIGURE 1. Time-activity curve of Tc-RBC corporal clearance representative of venous leak (top) and normal venous outflow (bottom). (Left) flaccid state and (Right) after papaverine injection.

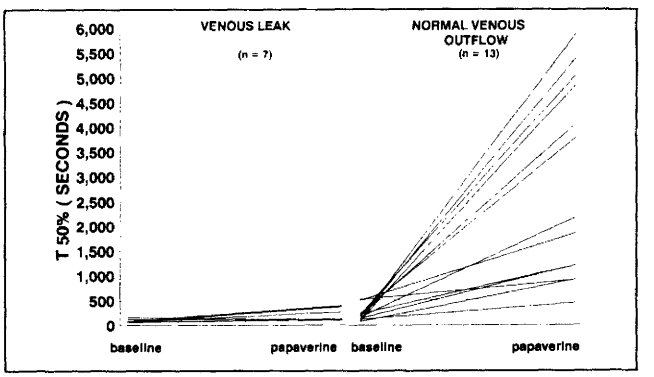

FIGURE 2. T50% measurements in venous leak and normal venous outflow in the flaccid state (baseline) and after intracorporal injection of a vasoactive agent (papaverine).

blood inflow, activates the veno-occlusive mechanism and eventually causes penile erection (*1,10,11*). A normal rigid erection following intracorporal injection of papaverine can rule out vasculogenic impotence (*1*). However, the significance of a partial short-lived erection or no erection is still of uncertain significance. Failure to respond may be due to reduced arterial inflow, augmented venous outflow, a combination of both, or can be due to excessive adrenergic-constrictor tone as a result of anxiety (*1,10–12*).

Arterial insufficiency can be evaluated by penile blood pressure, Doppler pulse-wave analysis, duplex sonography and angiography. Corporal venous outflow can be evaluated by dynamic infusion cavernosometry and cavernosography (*1*). This is an invasive procedure with infusion of large amounts of saline that causes overdistention of the corpora, takes a long time to perform, may be painful, and causes patient discomfort.

Nuclear medicine techniques have been used in the evaluation of patients with erectile dysfunction (*2–7*). Radioisotope penile plethysmography uses intravenous injection of Tc-RBC and pharmacologically-induced tumescence. It measures intrapenile blood volume and has been shown to be useful in the evaluation of arterial inflow disorders (*2,3*), but does not correlate with venous leak (*3*). Nsyeo et al. (*4*) and Lin et al. (*5*) reported that measurement of penile xenon washout is an effective method to evaluate penile arterial insufficiency after injection of the radioactive gas into the subcutaneous prepuce. However, they could not evaluate venous leak since skin blood flow is not related to corporal outflow. Haden et al. (*6*) studied penile xenon washout after intracorporal injection of radioactive gas in the flaccid state. They found no significant difference in penile blood flow between the impotent patients studied and the normal group. However, they suggested that xenon washout measurements can be used to measure penile venous outflow with stimulated or induced erection.

Schwartz and Graham (*7*) used a combined radioisotope penile plethysmography and intracorporal xenon washout method following intracorporal injection of papaverine to induce tumescence. Their study shows that xenon outflow measurements alone could not be used to predict competence of the veno-occlusive mechanism. Xenon-133 washout is a multi-variable function dependent on more than one vascular process, and the washout curve has a slow component that may not be related to blood flow but rather to absorption in adipose tissue (*13*).

The measurement of the clearance of an intravascular agent injected intracorporally may reflect venous blood outflow from the corpus cavernosum. In the present study, corporal venous outflow was evaluated using a radionuclide technique that utilizes intracorporal injection of Tc-RBC both in the flaccid state and after intracorporal injection of papaverine and regitine. In the flaccid state, a rapid clearance of the Tc-RBC was found both in patients with venous leak and normal venous outflow, a finding similar to Haden's study (*6*) with intracorporal xenon washout. However, after intracorporal injection of papaverine, 12 of 13 patients with normal venous outflow showed a more horizontal curve with a steeper slope after the reinjection of the Tc-RBC (Fig. 1). None of the patients with venous leak has demonstrated this characteristic.

Quantitation of T50% provides a criterion for discriminating patients with venous leak from patients with normal venous outflow. The method seems to be of no use in the flaccid state, where the sensitivity was 52%, specificity 92% and accuracy 80% when using threshold of 75 sec. However, after papaverine injection and using a threshold of 500 sec, sensitivity was 100%, specificity 92%, and accuracy was 95% in separating venous leak from normal venous outflow. One patient in the present study had arterial insufficiency and this method showed the presence of a normal venous outflow. However, further work is needed to determine the role of this method in patients with arterial insufficiency. The method is rapid, easy to perform, and uses small amounts of injection that cause no overdistention of the corpora.

In conclusion, the results suggest that the measurement of the corporal clearance of intracorporally injected Tc-RBC after papaverine may be a useful method in detecting significant venous leak and could be used as a screening test in patients with erectile dysfunction.

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