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A Comparison of Colour Duplex Ultrasonography after Transurethral Alprostadil and Intracavernous Alprostadil in the Assessment of Erectile Dysfunction

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This study aimed to investigate whether transurethral alprostadil could be used for the diagnosis of erectile dysfunction using colour duplex ultrasound. The ultrasonography results were compared after transurethral and intracavernous alprostadil administration in 20 patients with erectile dysfunction. There were no significant differences in the mean peak systolic velocities (PSVs) between the two routes of administration, but the mean end diastolic velocities (EDVs) showed significant differences, with patients treated with transurethral alprostadil having higher EDVs. Linear regression analysis of the PSVs reached following the two routes of administration showed a moderate relationship, but linear regression analysis of the EDVs showed no relationship. We concluded that transurethral alprostadil was an inappropriate vasoactive drug to use with colour duplex ultrasonography for the evaluation of patients with erectile dysfunction because it required a longer scan time and it was less effective and less reliable than intracavernous alprostadil at stimulating complete corporeal smooth muscle relaxation.

KEY WORDS: Intracavernous alprostadil; Transurethral alprostadil; Erectile dysfunction; Colour duplex ultrasound

Introduction

Penile erection is a neurovascular event involving relaxation of cavernosal smooth muscle, arterial dilatation and mechanical restriction of venous outflow.[1,2] Vascular erectile dysfunction (ED) is the most common cause of organic erectile impotence.[3] Objective tests of vascular function are required to evaluate patient selection criteria and to measure the success of treatment. Several invasive and non-invasive diagnostic

methods have been used to evaluate vascular ED. To date, high resolution duplex ultrasonography or Doppler and colour duplex ultrasonographies, combined with the pharmacological stimulation of erections, appear to be the best tests for this purpose. Colour duplex ultrasonography provides an objective method for assessing the response to an intracavernous injection of a vasoactive drug. It allows measurement of the size and dilatation of the cavernous arteries and of the blood velocity in the cavernous and dorsal arteries.[4–7] Corporeal smooth muscle relaxation is a prerequisite to the correct diagnosis of ED resulting from vascular dysfunction. Intracavernosal injections might elicit significant anxiety in some patients, thus, inhibiting smooth muscle relaxation.[8] Studies have documented the effects of anxiety, and have described audiovisual, vibratory and manual stimulation techniques that might be employed in an attempt to lessen the effects of anxiety.[9–11]

A transurethral drug delivery system (medicated urethral system for erection [MUSE]) for alprostadil was introduced as an alternative form of pharmacotherapy for ED. Although the efficacy of MUSE in treating patients with organic ED remains controversial,[12,13] this minimally invasive method may be more acceptable to patients, thus, decreasing anxiety.

The purpose of this study was to compare, using colour duplex ultrasonography, the accuracy and efficacy of transurethral alprostadil with intracavernous alprostadil when used for diagnostically evaluating patients with ED.

Patients and methods

PATIENTS

All patients were referred to us for evaluation of ED and were assessed initially in the urology clinic, where full medical histories were taken and physical examinations performed. If the physical examination failed to demonstrate an overt neurological dysfunction, the patient was investigated using colour duplex ultrasonography. All patients gave verbal consent. B-K Medical, Herlev, Denmark approved the study.

COLOUR DUPLEX ULTRASONOGRAPHY

Colour duplex Doppler imaging was performed with the patient in the supine position and the penis in the anatomical position. A Bruel & Kjaer 3535 duplex Doppler ultrasound scanner and a linear array 7.5 MHz transducer were used (B-K Medical, Herlev, Denmark). One operator performed all the ultrasonography to maintain consistency between patient assessments.

Each patient was examined using colour duplex ultrasonography after injection of intracavernous alprostadil (10 μg). Several days later, each patient received a transurethral dose of alprostadil (1000 μg) and the colour duplex ultrasound was repeated. The mean interval between the two duplex ultrasound evaluations was 4.7 days (range 3 – 7 days). The peak systolic velocity (PSV) and end diastolic velocity (EDV) of both cavernosal arteries were measured at 5, 10, 15, 20, 25 and 30 min after pharmacological stimulation. The scan was considered abnormal if the PSV was not 25 cm/s or the EDV was greater than 5 cm/s in response to alprostadil.[14]

ANALYSIS OF SENSITIVITY AND SPECIFICITY

The correlation between intracavernous and transurethral alprostadil treatment was analysed with linear regression to produce estimates of sensitivity and specificity. For the purpose of estimating sensitivity and specificity, we assumed that duplex ultrasonography following intracavernous alprostadil was the

control. Sensitivity was defined as the percentage of abnormal ultrasonography results following intracavernous alprostadil that were also abnormal following transurethral alprostadil. Specificity of this test was defined as the percentage of normal ultrasonography results following intracavernous alprostadil that were also normal following transurethral alprostadil.

STATISTICAL ANALYSIS

Statistical analyses were performed using linear regression and the Student's *t*-test, assuming equal variances. All data were expressed as mean ± SD. A P-value < 0.05 was considered statistically significant.

Results

PATIENTS

From July 1998 to December 1998, we performed colour duplex ultrasound measurements in 20 patients, who were 42 – 77 years old (mean age of 54 years). The mean duration of ED was 4.7 years with a range of 1 – 15 years.

OVERALL VASCULAR FINDINGS

Penile duplex ultrasonography following stimulation with intracavernous alprostadil showed that five patients demonstrated normal vascular findings and 15 patients had abnormal vascular findings, such as arterial insufficiency, venous leakage or a mixture of both types of vascular dysfunction. After transurethral alprostadil, colour duplex ultrasonography showed that 19 patients had abnormal vascular findings and one patient had normal vasculature.

Among the five patients who appeared to have normal penile vasculature following intracavernous alprostadil and duplex ultrasonography, only one showed normal vascular findings after transurethral alprostadil. In the other four patients the EDV was persistently > 5 cm/s.

The sensitivity and specificity of the colour duplex ultrasound after transurethral alprostadil, assuming that the ultrasound findings after intracavernous alprostadil were the control findings, were 93% (14/15) and 20% (1/5), respectively.

PEAK SYSTOLIC VELOCITY AND END DIASTOLIC VELOCITY

The PSVs in the right and left cavernosal arteries were calculated at 5, 10, 15, 20, 25 and 30 min following administration of alprostadil via either the intracavernous or transurethral route of administration in each patient. The study showed that more of the patients treated with intracavernous alprostadil reached the PSV by 5 min than patients in the transurethral alprostadil-treated group (Fig. 1). The mean time to reach the PSV was 7.3 ± 3 min following intracavernous alprostadil compared with 12.3 ± 5.7 min following transurethral alprostadil. The mean PSVs following intracavernous alprostadil were 38.5 ± 11.5 and 36.6 ± 12.7 cm/s in the left and right cavernosal arteries, respectively, compared with 36.6 ± 8.8 and 33.3 ± 11.4 cm/s in the left and right cavernosal arteries, respectively, following transurethral alprostadil. There were no significant differences in the mean PSV between the two routes of administration.

In the most tumescent state, the mean EDVs following intracavernous alprostadil were 8.0 ± 4.1 and 6.9 ± 4.2 cm/s on the left and right side, respectively, compared with 10.7 ± 4.3 and 10.1 ± 5.2 cm/s on the left and right side, respectively, following transurethral alprostadil. The mean EDVs measured after the two routes of administration showed significant differences (P = 0.044, P = 0.038, left and right side, respectively), with patients who received transurethral alprostadil demonstrating the faster EDVs in their left and right cavernosal arteries.

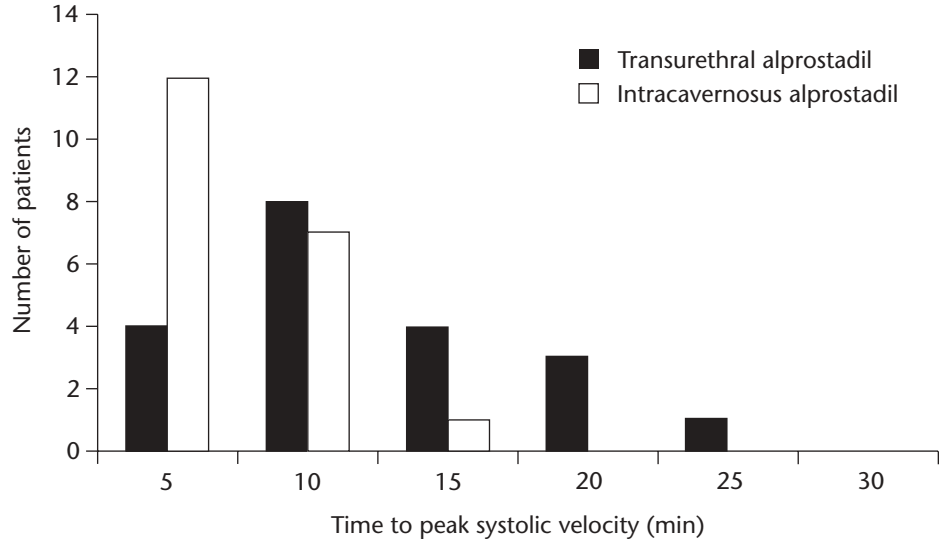

FIGURE 1: Time to reach the peak systolic velocity (PSV) in 20 patients treated with either transurethral or intracavernous alprostadil. The PSVs of the left and right cavernosal arteries were measured at 5, 10, 15, 20, 25 and 30 min after pharmacological stimulation

Linear regression analysis of the PSVs for both cavernous arteries following intracavernous and transurethral alprostadil showed a significant but weak relationship ($P < 0.001$, R = 0.531; Fig. 2). Analysis of the EDVs between the two routes of administration showed no significant relationship (Fig. 3).

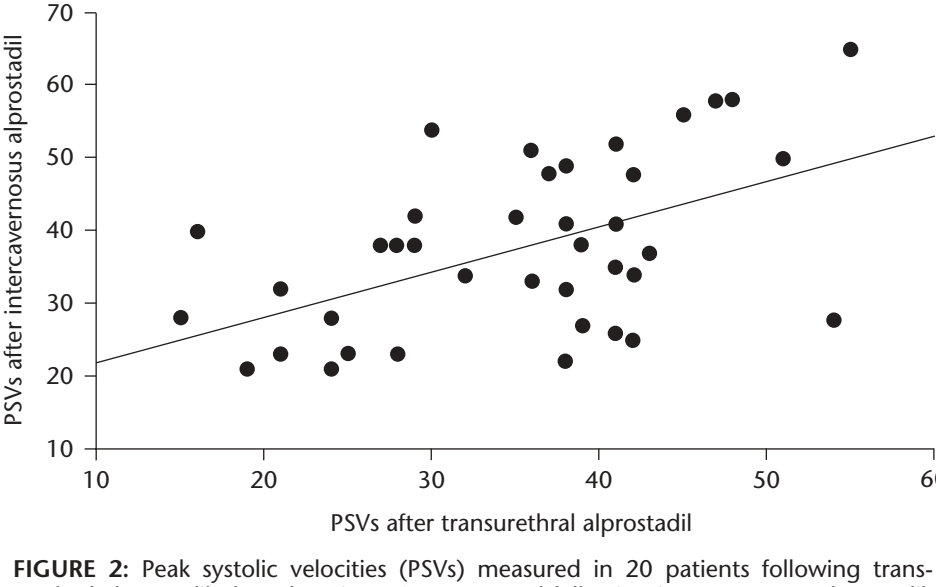

FIGURE 2: Peak systolic velocities (PSVs) measured in 20 patients following transurethral alprostadil plotted against PSVs measured following intracavernous alprostadil. Linear regression analysis showed a significant but weak relationship ($P < 0.001$, R = 0.531)

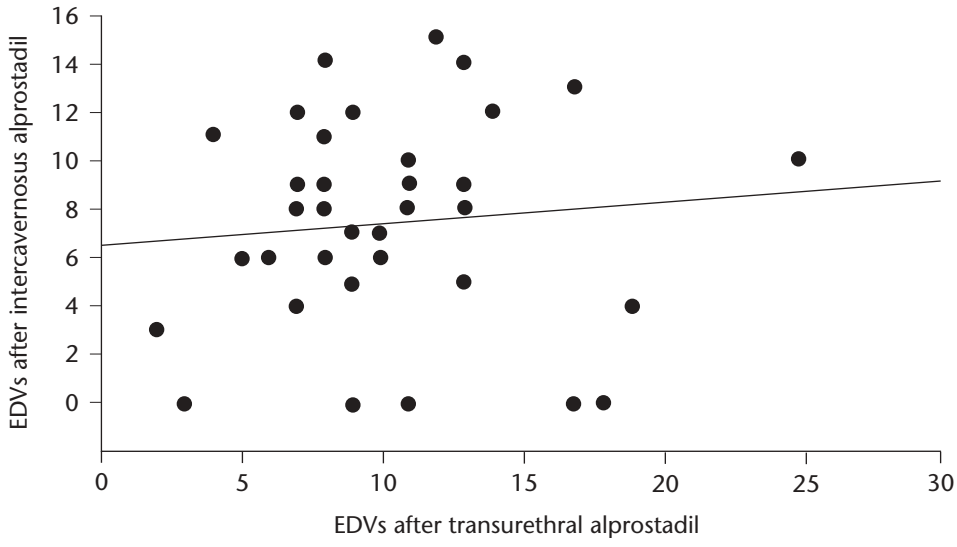

FIGURE 3: End diastolic velocities (EDVs) measured in 20 patients following transurethral alprostadil plotted against EDVs measured following intracavernous alprostadil. Linear regression analysis showed no significant relationship

ADVERSE EVENTS

Two patients complained of slight penile pain after intracavernous alprostadil injections, while nine (38%) felt a painful or burning sensation in the penis or urethra following transurethral alprostadil. Among the nine patients, two complained of severe pain radiating to the scrotum. Prolonged erections occurred in two patients in the intracavernous alprostadil-treated group and pharmacological detumescence was performed.

Discussion

The evaluation of penile circulation is considered of paramount importance in the initial assessment of most patients with ED. Duplex ultrasonography has gained an increasingly important role in the diagnosis of cavernous artery dysfunction. Relaxation of the corporeal smooth muscle by vasoactive agents is essential to evaluate penile vascular function during erectile stimulation. It is especially important that total relaxation of the corporeal smooth muscle is achieved when precise measurements are to be made of the veno-occlusive mechanism of the corpora cavernosa.

The fact that a relatively high percentage of patients have needle phobia prompted several researchers to investigate alternative routes of administration for vasoactive drugs (to avoid intracavernous injection). A transurethral drug delivery system is less invasive than injections and has the advantages of decreasing the patient's anxiety. Reducing anxiety is important as sympathetic tone must be reduced to achieve relaxation of the corporal smooth muscle.[15] The primary route of drug delivery following transurethral alprostadil is most likely via the vascular channels that communicate between the corpus spongiosum and corpora cavernosum. These vascular communications were confirmed by a cast study of a human cadaveric penis using methylene blue dye injected into the glans penis, which

demonstrated that blood can flow directly into the corpora cavernosa via the emissary veins.[16] The degree of vascular communication between the corpus spongiosum and corpora cavernosum is thought to vary from person to person. Therefore, the delivery of transurethral alprostadil to the corpora cavernosa is less consistent between patients than that of intracavernous alprostadil.

Transurethral alprostadil may be more acceptable to patients because it is less invasive, but our data showed that transurethral administration is a less effective method of drug delivery than intracavernous administration. The time to reach the PSV was delayed in the transurethral alprostadil-treated group. In the intracavernous alprostadil-treated group, more patients reached the PSV by 5 min compared with the transurethral alprostadil-treated group. Penile duplex ultrasonography with transurethral alprostadil therefore required more scan time than when used with intracavernous alprostadil. While transurethral administration achieved a comparable arterial dilatation and PSV compared with intracavernous alprostadil injection, the EDVs between the two methods of administration showed significant differences. Linear regression analysis of the PSVs following intracavernous and transurethral alprostadil showed a significant but weak relationship. Analysis of the EDVs between the two routes of administration showed no significant relationship. These findings show that transurethral alprostadil was an inappropriate vasoactive drug.

According to Porst,[17] the total response rates in patients treated with transurethral and intracavernous alprostadil were 43% and 70%, respectively, and completely rigid erections were achieved in 10% and 48% of patients, respectively. Tam *et al.*[18] also reported that the EDVs were significantly higher after transurethral alprostadil than following intracavernous alprostadil injections. In this study, the values of the EDVs provided proof that, in the majority of the patients, the cavernous smooth muscle relaxation stimulated by transurethral alprostadil was less complete than that achieved by intracavernous alprostadil injection.

A transurethral drug delivery system is less invasive than intracavernous injection and has the advantage of decreasing the sympathetic tone induced by anxiety over having an injection in the penis. Delivery of the drug to the corpora cavernosa following transurethral alprostadil was, however, less effective and less reliable than that following intracavernous alprostadil. Furthermore, relaxation of the cavernous smooth muscle induced by transurethral alprostadil was not complete enough to allow a proper diagnosis of vascular ED. We concluded that transurethral alprostadil was an inappropriate vasoactive drug to use when evaluating ED in patients using colour duplex ultrasound. It required a longer scan time and was less effective and less reliable than intracavernous alprostadil in obtaining complete corporeal smooth muscle relaxation.

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