

Physiological interrelationships between the venous shunts of penile corpus spongiosum and cavernous compartments during erection used in the pharmacotherapy of erectile dysfunction.



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Physiological interrelationships between the venous shunts of penile corpus spongiosum and cavernous compartments during erection used in the pharmacotherapy of erectile dysfunction.

AIM OF THE STUDY: *Alprostadil (A) induces smooth-muscle relaxation by stimulating the increasing of intracellular cAMP. Intra-urethral administration is an alternative to its intra-cavernose injection in inducing erection. In order to understand the functional and anatomical basis for drug transfer, the possible communications of the corpus spongiosum with the corpora cavernosa were studied.*

MATERIAL OF STUDY: *A "Spongiogram" (SP) was performed in 44 patients (pt.) by injection of radiological contrast into the glans. The SP visualized drainage of the glans into the deep dorsal vein, as well as that of the spongiosum into the circumflex veins, which in turn drained into the deep dorsal vein.*

RESULTS: *In 34 pt. (77,2%) filling of the corpora was also visualized; in 10 pt. (22.8%), with ectasia of the deep dorsal vein, such a filling was not visualized.*

DISCUSSION: *Filling of the corpora cavernosa, in 34 pt. demonstrated the presence of "spongiosal-cavernosal" shunts.*

CONCLUSIONS: *The presence of "spongiosal-cavernosal" shunts justified the efficacy of A in term of complete penile erection, regarding also corpora cavernosa; in the other cases an increased speed of venous discharge justified the drug's lack of local efficacy, with poor results in terms of erection.*

KEY WORDS: Alprostadil, Erectile Dysfunction, Spongiosography

Introduction

Penile erection represents a complex phenomenon of integrated neuro-vascular events culminating in the accumulation of blood under pressure in corpora cavernosa and organ rigidity.

The efficacy of Alprostadil, chemically identically to PGE 1, by intracavernous injection therapy was widely demon-

strated in inducing erection. The drug induces relaxation of corpus cavernosum musculature through the activation of prostaglandin receptors activating the membrane bound adenylate cyclase and subsequently resulting in an increase in intracellular concentration of cAMP in the cavernous tissue. These effects are completed by the effect of PGE1 to inhibit the release of noradrenaline from sympathetic nerve endings and to block angiotensin II secretion in the cavernosa tissue.

Transurethral application and more recently intraurethral represent two alternative absorptions ways of A. In the first case A is delivered to the corpora cavernosa after it is carried from a semi-solid urethral pellet to corpus spongiosum, across the urethral epithelium. In the second case an A cream must be introduced into the ure-

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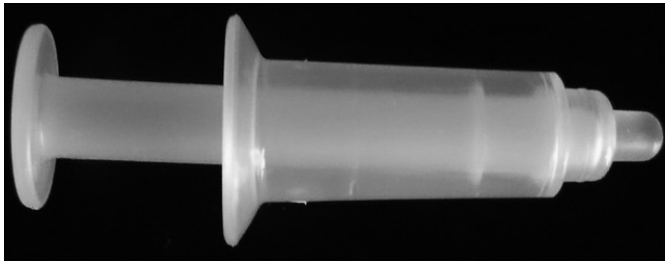


Fig. 1: Intraurethral device.

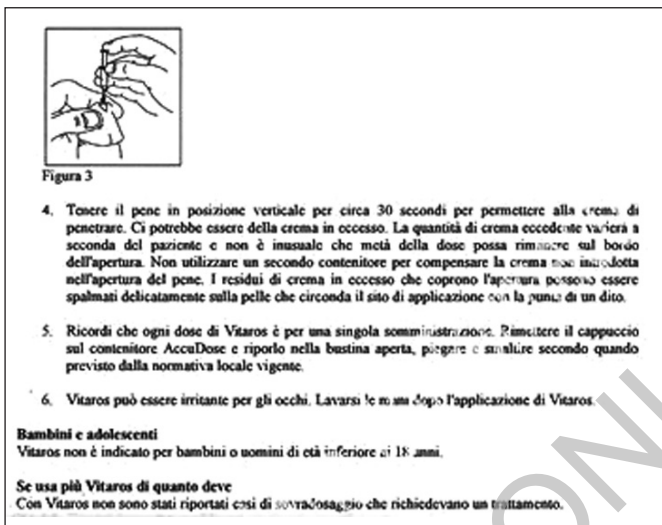


Fig. 2: Device positioned inside the meatus.

thral meatus by a very simple specific device (Fig. 1-2). In order to understand the functional and anatomical basis for drug transfer, we have studied the possible venous communications (shunts) between the corpus spongiosum :glans penis and urethral corpus spongiosum, and cavernosal compartments, in patients suffering from erectile dysfunction (ED).

Anatomic and Physiological Basis of Penile Erection

Arterial component - Blood supply to the corpora cavernosa of the penis is derived from the internal pudendal artery, which in the final branch of the anterior trunk of the internal iliac artery. The former becomes the common penile artery which in turn branches into three: the bulbo-urethral, cavernosal and dorsal penile arteries. The cavernosal artery is the most important determinant of intracavernosal pressure; along its length this artery gives off multiple helicine branches which reach lacunar spaces (Fig. 3).

The corpora cavernosa contain the erectile components and they are surrounded by a thick fibroelastic sheath,

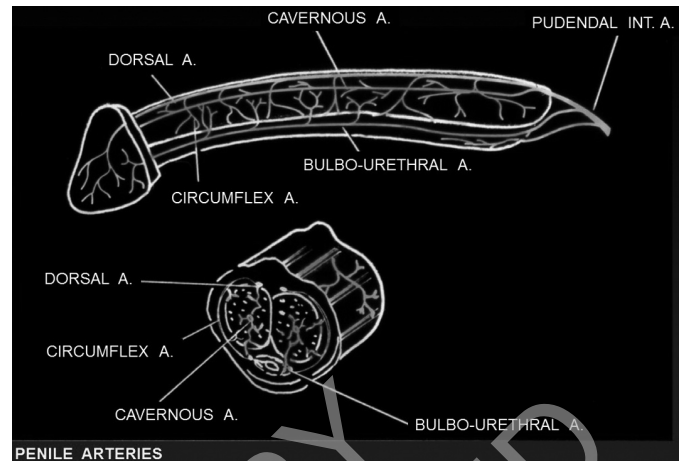


Fig. 3: Penile arteries.

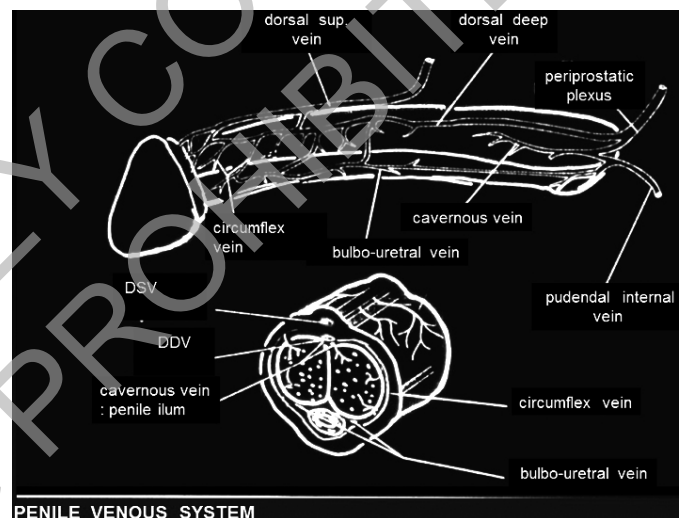


Fig. 4: Penile entire venous system.

the tunica albuginea. The erectile tissue comprises multiple interconnecting sinusoidal spaces or lacunae. The lacunar walls or trabeculae contain the fibromuscular contractile elements, consisting of smooth muscle, elastin and collagen. In basal condition the trabecular smooth is tonically contracted by discharge within the sympathetic noradrenergic nervous system. In these conditions basal arterial inflow is sufficient for the maintenance of cellular metabolism. In this state blood gas level are equivalent only to those found in venous blood.

Venous drainage of the penis comprehends three main venous systems: the superficial system, which drains the skin and subcutaneous tissues, the intermediate system, which drains the pendulus portion of the penis, and the deep system, which drains the proximal corpora cavernosa and the crura (Fig. 4).

The superficial system is the least important system of venous drainage in functional terms. A lot of superficial

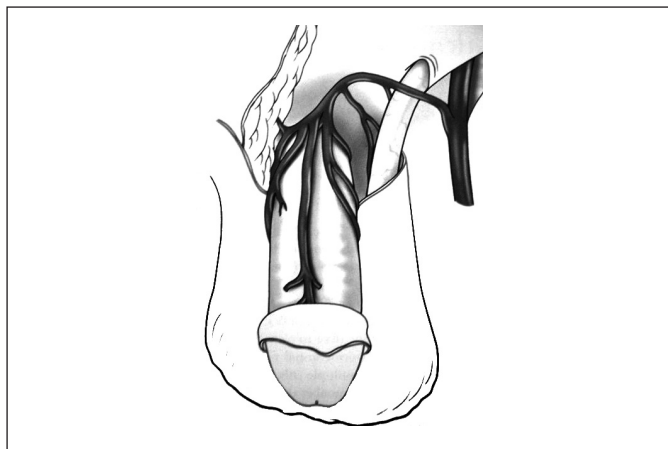


Fig. 5: Superficial venous system.

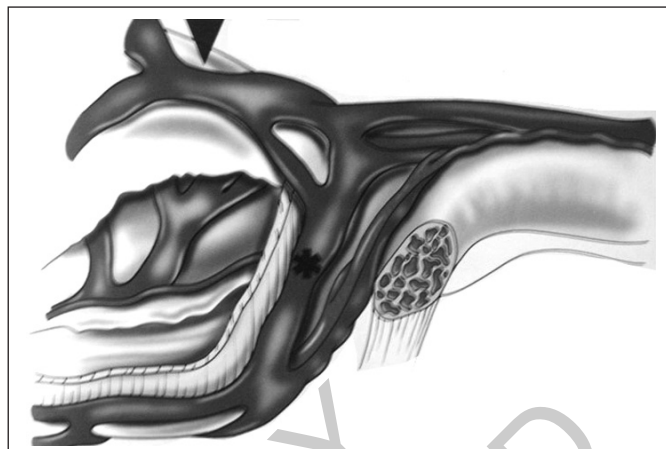


Fig. 7: Deep venous system.

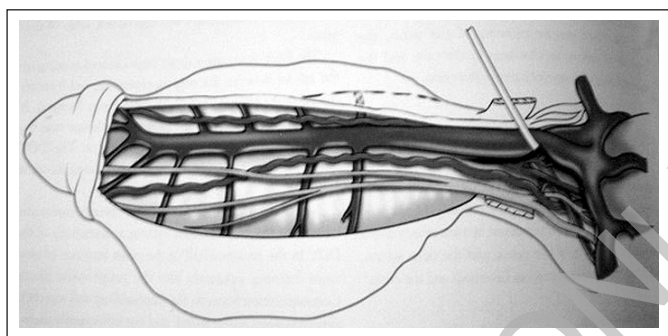


Fig. 6: Intermediate venous system: DDV.

veins run on the dorsolateral surface of the penis between Buck's and Colles' fasciae and unite at the base of the penis to drain into one, normally the left, saphenous vein (Fig. 5).

The intermediate system is focused on the deep dorsal vein (DDV). The DDV arises from multiple small veins (five to eight) emerging from the glans penis. Proximally, the DDV has multiple tributaries: the circumflex veins, normally 3 to 12. These arise from the emissary veins, which pass through the tunica albuginea, carrying blood from the lacunar spaces of the corpora cavernosa. The circumflex veins are visible dorsolaterally on the surface of the tunica albuginea and may communicate with each other, with their contralateral counterparts and the lateral veins of the penis.

The DDV is usually a single vessel running in the deep between the corpora cavernosa; it enters the pelvis by passing thorough the suspensory ligament. It drains into the periprostatic Santorini plexus and then into the perivesical plexus and internal iliac veins. The DDV usually has three to eight bicuspid valves along its entire length (Fig. 6). The deep venous system is constituted by emissary veins in the proximal one-third of the penis and join to create two to five large cavernous veins, which themselves unite to form one or two larger veins

on the dorsomedial surface of the corpora cavernosa. These run deep and medial to the cavernosal arteries, pass between the urethral bulb and crura, and then course laterally for 2-3 cm to drain into the internal pudendal veins¹ (Fig. 7).

In the flaccid state the vascular smooth muscle in these resistance vessels is contracted, allowing limited blood flow into the lacunar spaces. During erection there is a considerable increase (up to seven-eight times) in the global intra penile blood volume, with corresponding relaxation of trabecular walls and lacunar spaces. Intracorporal pressure reaches systemic blood pressure, producing both an increase in penile volume (tumescence) and rigidity. The autonomic nervous system guarantees the integrated control of most of these smooth muscle-dependent changes in local vascular reactivity.

On activation of autonomic system the vascular smooth muscle relaxes and the arteries lengthen and relax, increasing intracorporal blood flow and pressure. Flow rate into the lacunar spaces determines the rate of filling of the corporal bodies; considering this it can be concluded that, under normal conditions, penile rigidity will be more dependent on arterial pressure than on flow. Rarely the cavernosal arteries divide into two or three branches inside the corpus cavernosum and in 30% of men there are communications between cavernosal arteries and connections with dorsal arteries. This is a compensatory physiologic mechanism in cases of cavernosal arteriopathy.

The accumulation of blood inside the corpora cavernosa determines the establishment of an erection. Arterial inflow enters a closed space to expand the lacunae and the trabecular walls against the tunica albuginea, enabling the transmission of the arterial pressure to the tunica albuginea.

The mechanism that maintains the pressurized blood in the corpora is known as the "corpora-veno-occlusive" mechanism² (Fig. 8).

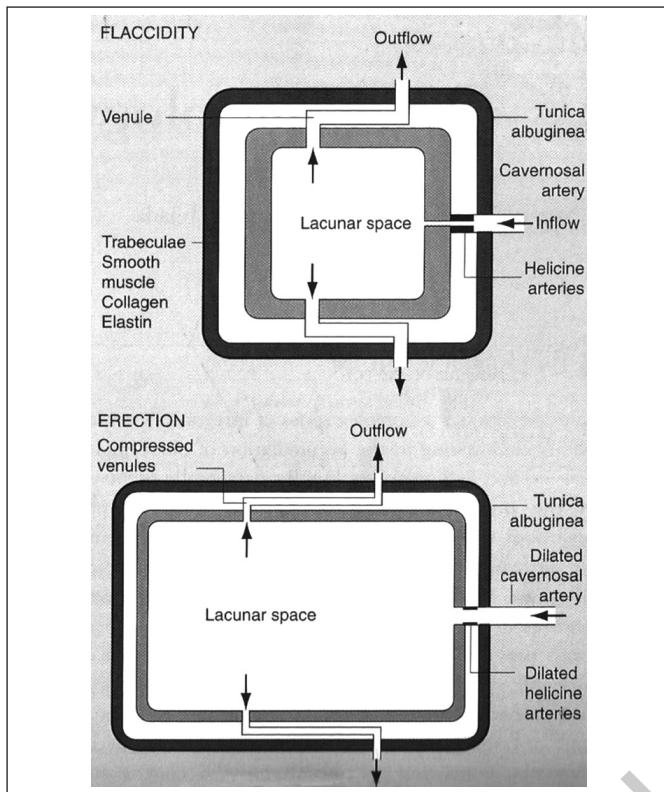


Fig. 8: Diagram of corporoveno-occlusive mechanism.

Material and Methods

The study was done on 44 patients affected by ED of medium degree (15-20 IIEF score), mean age 45.2. They were undergone to SP by injection of radiological contrast into the glans and previously to "penile dynamic Doppler ultrasound" (PDDU) investigation. SP visualized drainage of the glans into the deep dorsal vein, as well as that of the spongiosum into the circumflex veins, which in turn drained into the deep dorsal vein^{3,4}.

Results

In 34pt. (77.2%) filling of the corpora was also visualized, so demonstrating spongiosal-cavernosal communications (Fig. 9).

In 10pt. (22.8%), with ectasia of the deep dorsal vein and increased speed discharge, tested by PDDU examination, such a filling was not visualized (Fig. 10). It was due to an early systemic absorption of contrast medium and, probably, of A with failure of its local efficacy.

Conclusions

The presence of considerable vascular anatomical variations in penile venous circulation is well documented by "Spongiosography". These individual different conditions

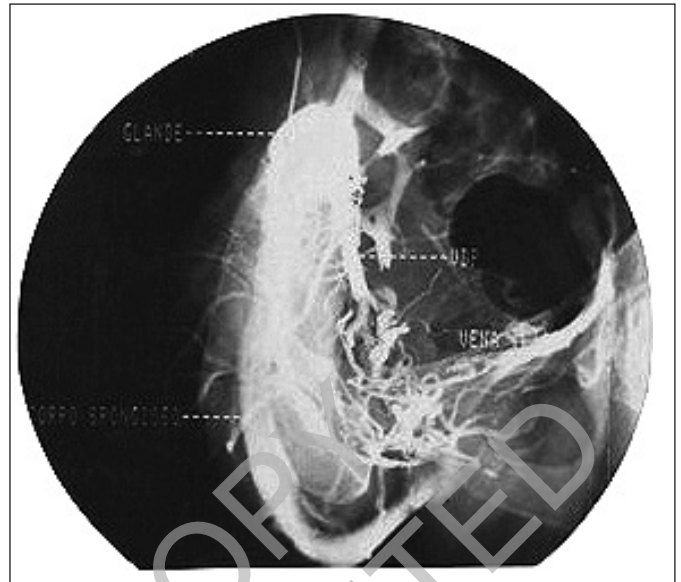


Fig. 9: "Spongiosogram" with cavernous tissue opacized.

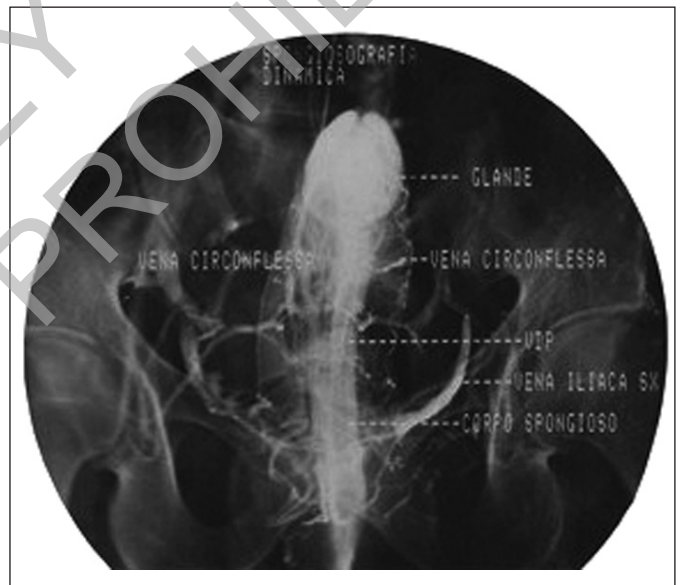


Fig. 10: "Spongiosogram" in absence of cavernous tissue opacization.

would justify, in our opinion: a) the major or minor drug effect in term of inducing a complete erection and not only a glandular-urethral spongiosum tumescence b) the very individually dose related drug response c) the presence of side effects (ipotenive shock, for example) due to an increased speed of venous discharge, rapid systemic absorption and lack of local efficacy of A.

Riassunto

L'Alprostadil, chimicamente identico alla prostaglandina E1, induce il rilassamento della muscolatura liscia endo-

cavernosa, stimolando la produzione di cAMP intracellulare. La sua efficacia nell'indurre l'erezione peniena, dopo somministrazione per via intracavernosa, è stata ampiamente dimostrata.

Esistono però altre modalità particolari di somministrazione dell'Alprostadil, senza ricorrere alla micro-iniezione endocavernosa, o mediante un dispositivo transuretrale consistente di un sistema medicato contenente Alprostadil oppure con un contenitore monodose che veicola una crema con il principio attivo nel meato uretrale mediante uno stantuffo. L'Alprostadil è così distribuito ai corpi cavernosi dopo essere stato veicolato al corpo spongioso attraverso l'epitelio uretrale.

Nei pazienti affetti da disfunzione erettile di media gravità (15-20 score IIEF) è stata esaminata la possibile presenza di "shunts" venosi a livello glandolare e del corpo spongioso con i corpi cavernosi, al fine di comprendere e quantificare le basi anatomo-funzionali riguardanti il passaggio del farmaco da un compartimento all'altro.

44 pazienti sono stati sottoposti a "spongiosografia morfo-funzionale" con iniezione di m.d.c. nel glande e precedentemente ad ecocolordoppler penieno dinamico. Lo spongiosogramma ha dimostrato il drenaggio venoso del glande stesso nella vena dorsale profonda, così come quello del corpo spongioso nelle vene circonflesse, a loro volta tributarie della vena dorsale profonda.

In 34 pazienti (77.2%) è stato possibile visualizzare, in modo più o meno evidente anche il tessuto cavernoso, dimostrando così la presenza di "shunts" venosi spongioso-cavernosi.

In 10 pazienti (22.8%) con marcata ectasia della vena dorsale profonda e pregresso riscontro all'esame ecocolordoppler penieno dinamico di un aumento della velocità di deflusso nella vena stessa, non è comparsa opacizzazione cavernosa, evidente segno di precoce distribuzione sistemica del m.d.c. e verosimilmente dell'Alprostadil, con scarso effetto locale.

La presenza di notevoli varianti anatomiche vascolari a tale livello giustificerebbe la maggiore o minore efficacia del farmaco, la riposta dose-dipendente individuale, nonché l'insorgenza di eventuali effetti collaterali (shock ipotensivo ad esempio) dovuti a precoce ed elevato assorbimento sistemico.

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