

that depends on the relaxation of smooth muscle in the erectile bodies. The relaxation of smooth muscle involves the release of nitric oxide and other mediators, which stimulate the production of intracellular cyclic nucleotides that cause relaxation. With relaxation of the corporal smooth muscle, rapid arterial filling begins, resulting in engorgement of the sinusoids in the cavernosa and veno-occlusion due to the compression of the subtunical venules against the tunica albuginea.

The use of locally applied drugs is a promising and appealing way to treat erectile dysfunction, because it activates the hemodynamic events involved in natural erection. PGE₁ was chosen for local delivery because it increases the intracellular concentration of cyclic AMP and has a short half-life. Previously, therapy for erectile dysfunction with PGE₁ and other drugs involved an intracavernous injection. Alternative methods of delivering drugs to the erectile bodies have been explored. The application of a cream containing PGE₁ to the urethral meatus in 20 men with erectile dysfunction resulted in full penile tumescence in 30% of subjects.¹⁷ In pilot studies, transdermal nitroglycerin, minoxidil, and PGE₁ failed to induce rigid erections, apparently because of insufficient transfer of the drug through the skin.^{18,19}

Although the urethral mucosa is not commonly recognized as a route of drug transfer, it is a more suitable surface for absorption than the skin, because it is lined with complex columnar cells rather than by stratified squamous epithelium. Furthermore, there are submucosal veins that communicate between the corpora spongiosum (surrounding the urethra) and the corpora cavernosa, providing a potential route for drug transfer. In a recent report, the intraurethral administration of PGE₁ proved to be effective in men with erectile dysfunction.²⁰ In that study, a PEG-based medication that melted at body temperature was used. In our study, Gelucire®-based formulations with a very specific melting points and known HLB values were tested.

Analysis of hemodynamic changes after intracavernosal injection of PGE₁ served as a reference to evaluate the efficacy of transurethral delivery of PGE₁. Results revealed that after injection, the blood flow rate and the RI value of the bilateral arteries of

patients with venous leakage syndrome were significantly lower than those of patients with arteriogenic or psychogenic impotence. Patients with diabetes or hypertension showed flow rates similar to those of patients with venous leakage syndrome.

A patient with arteriogenic erectile dysfunction was not responsive to the administration of formulation 1 although a 45° erection with a rigidity grade of 1-2 was noted when formulation 1 was given to a patient with venous leakage. When patients with arteriogenic impotence were given formulation 2, only tumescence resulted, whereas the patient with venous leakage syndrome had no response to this formulation. However, the presence of tumescence indicates that transurethral delivery of PGE₁ occurred was accomplished to some extent. Formulation 3 produced tumescence in 1 patient with venous leakage syndrome, and a 45° erection with a rigidity grade of 2 in another patient with the same etiology. Formulation 4 also caused a 45° erection with a rigidity grade of 2 in 2 patients with venous leakage syndrome.

One of 4 patients who received formulation 5 and who suffered from mild arteriogenic impotence showed a satisfactory erection and rigidity. The blood flow rate of the bilateral arteries was higher than 40 cm/s, which did not statistically differ from results obtained for patients with arteriogenic impotence who received an intracavernosal injection. Furthermore, 2 patients with venous leakage syndrome showed either 45° or 80° erections with rigidity grades of 1 or 2 when given this formulation. Although the fourth patient achieved tumescence only, this finding still indicates that a certain amount of PGE₁ was delivered. The poor response in this patient was probably due to the etiology of dysfunction (arteriogenic and venous leakage).

Formulation 6 failed to induce satisfactory erection in either patient tested; one of them had arteriogenic dysfunction and the other had venous leakage syndrome. Patients administered formulation 7 had results comparable to those who received formulation 5 with erectile angles of 45° to 90° with rigidity grades of 1 to 3. This finding suggests that the 2 formulations are similar in their ability to deliver PGE₁ transurethrally.

The clinical efficacy of transurethral delivery of