Electromotive drug administration (EMDA) is a method of increasing the transport of drugs across barriers by means of an electric current. In patients with Peyronie’s disease, EMDA of verapamil into the tunica albuginea provides measurable drug levels in plaque tissue. Four clinical studies using different methods showed that EMDA of verapamil and dexamethasone is a safe and effective treatment for Peyronie’s disease, reducing plaque volume, penile deviation, and pain, and can contribute to the improvement in erectile capacity and sexual function.

Key Words: Electromotive drug administration; iontophoresis; Peyronie’s disease.

INTRODUCTION

Induratio penis plastica (IPP), commonly known as Peyronie’s disease, is a wound-healing disorder characterized by areas of inflammation followed by fibrosis (scarring) along the shaft of the penis (1). The lesions may be single or multiple; they are situated within the tunica albuginea and have the appearance of hardened plaques.

Although Peyronie’s disease does not cause major health problems and is certainly not life-threatening, for many individuals it significantly impairs quality of life as a source of major distress. In fact, there is frequently pain, angulation (bending) of the penis, and erectile dysfunction (ED) with further psychosexual and psychorelational problems.

The natural history of the disease is not encouraging. In a small proportion (<10%) of patients, plaques become smaller in size and occasionally disappear completely. However, in the majority of subjects there is a “roller coaster” course with intermittent flare-up in which frequently the plaques become calcified/hardened to a chalky, bonelike consistency that becomes a permanent feature of the penile landscape.
Occasionally, IPP is associated with some other diseases, notably the fibrous scarring of Dupuytren of the palm. More frequently, IPP follows some type of penile trauma such as sexual accidents, surgery, or repeated intrapenile injections. But, in many cases, the etiology of IPP cannot be related to any known cause. The presence of many different therapeutic approaches to IPP demonstrates that it is a field vital and crucial in urology and the therapies are often ineffective (2). Surgery is aimed to correct the deformity, but it is not a minor procedure, and full disclosure of side effects causes a substantial proportion of patients to decline treatment. There is also the problem of either an ongoing or a recurrent disease process that leads to failure. Systemic drug administration frequently results in a negative benefits–risks ratio in which side effects exceed the therapeutic benefit.

A classical strategy is to localize drug administration directly into and around the plaque. This provides high concentrations at the site of disease with minimal systemic effects. In a large, uncontrolled clinical study, Levine et al. demonstrated significant improvement in patients following intralesional injection of verapamil (3). However, multiple intralesional injections may be uncomfortable and, although rare, may be harmful.

Another approach is transdermal diffusive drug delivery. A report described that, if verapamil cream is directly applied on the penis skin, no detectable levels of the drug can be found in the underlying tunica (4). On the basis of anecdotal reports suggesting that iontophoretic delivery of steroids is beneficial in some patients with IPP (5–7), transdermal electromotive administration of verapamil has been studied, resulting in detectable drug levels in approx 70% of tunica specimens tested (8). Furthermore, four clinical studies with different drug and treatment regimens using electromotive delivery of verapamil in combination with dexamethasone demonstrated objective improvement in patients with Peyronie’s disease (9–12).

**ELECTROMOTIVE DRUG ADMINISTRATION**

**Basic Principles**

Various electrokinetic phenomena can be recruited to accelerate drug administration across biological membranes and into the underlying tissues: iontophoresis, electroosmosis/electrophoresis, and electroporation.

Iontophoresis describes the accelerated transport of ions (into tissue) by means of an electric current passed through a solution containing the ions \( i \) to be administered (13) at a rate defined by Faraday’s law:

\[
J_i = I(tr)/z F \text{ mol/s}
\]

where \( I \) is the current (amperes), \( tr \) is the proportion of applied current carried by \( I \), and \( z \) is the valency; \( F \) is the Faraday constant (14). Usually, iontophoresis is associated with increased transport of water that will carry any nonionized solutes present, a phenomenon often termed electroosmosis, a form of “solvent drag.” Drug transport rate \( Dd/dt \) is the algebraic sum of that induced by passive diffusion (PD) and by electromotive drug administration (EMDA) \( (Dd/dt = PD + EMDA) \), but when dealing with a membrane of low permeability such as the skin, EMDA is so dominant that, for all practical purposes, it may be considered the sole force manipulating drug transport. Thus, administration rates not only are markedly increased but also are controllable simply by varying the current intensity.