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Optimizing delivery of therapeutics: percutaneous technologies.

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Abstract

The purpose of this communications is to 1) demonstrate the potential of percutaneous drug-delivery on the example of female reproductive steroids, 2) point out the differences between transdermal and conventional drug dosing, and 3) outline new technologies and innovations that are looming on the horizon, specifically in the area of pain control. Transdermal delivery systems are of two basic types. The first ones employ principles of passive diffusion, and they are used for hormonal replacement therapy (HRT) and contraception. Patches for HRT, designed to release estradiol (E2) only, require a simultaneous dosing with oral progestogens. Patches employing both E2 and a progestogen release the combination either continuously or sequentially. In the latter method, estrogen-only patches are applied for 14 days, followed by a 14-day application of patches releasing both hormones. Both methods successfully cope with symptoms and signs of menopause, including bone loss. Contraceptive transdermal patches deliver ethinylestradiol in combination with the progestogen norelgestromin. This system provides high contraceptive protection with predictable withdrawal bleeding and without major adverse events and weight changes. Hormones delivered by the skin avoid first-pass liver metabolism. Other advantages include rapid onset and termination of action, self-administration, and attainment of therapeutic hormone levels with low daily doses. A disadvantage is the variable intra- and inter-individual percutaneous absorption. In some patients, patches can cause skin irritation. Active systems deliver therapeutics across intact skin non-invasively by means of an electric potential (electrotransport). A system consisting of tooth-like titanium microprojections that penetrate only the keratinized epidermis facilitates painless and needle-free transport of complex molecules to the capillaries of the dermis. Other devices use low frequency ultrasound. These systems enable precise dosage, delivery of large molecules, such as growth hormone and vaccines, and dosing of analgesics "on demand". Novel transdermal technologies are profoundly changing the current methods of pain management. (Fig. 6, Ref. 47.).

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