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Customized Medications for Podiatry

Topical 5-Fluorouracil Cream in the Treatment of Plantar Warts

Topical 5-fluorouracil (5-FU) is an antineoplastic antimetabolite that inhibits DNA and RNA synthesis, thereby preventing cell replication and proliferation. This mechanism of action may allow topical 5-FU to be utilized in the treatment of human papilloma virus (HPV). Salk et al. of the Northern California Foot and Ankle Center, San Francisco and Santa Rosa, CA, conducted a study comparing 5% 5-FU cream under tape occlusion versus tape occlusion alone in 40 patients presenting with plantar warts. Nineteen out of 20 patients (95%) randomized to 5% 5-FU with tape occlusion had complete eradication of all plantar warts within 12 weeks of treatment. The average time to cure occurred at 9 weeks of treatment. Three patients (15%) had a recurrence at the 6-month follow-up visit; i.e., an 85% sustained cure rate was observed. It was concluded that use of topical 5% 5-fluorouracil cream for plantar warts is safe, efficacious, and accepted by the patient.¹

A medical record review was conducted by the Podiatry Division, Department of Orthopedics, Cabrini Medical Center, New York, NY to determine the clinical outcome and average time to resolution of verruca plantaris (plantar warts) in 20 patients treated with twice-daily applications of either 0.5% or 5.0% topical fluorouracil (5-FU) combined with topical 17% and 40% salicylic acid. Seven patients used 0.5% fluorouracil, and 13 used 5.0% fluorouracil. All of the lesions were sharply debrided at regular 1- or 2-week intervals. All 20 patients achieved full clinical resolution in a mean +/- SD of 82.5 +/- 56.6 days. Three patients (15%) had recurrent lesions, which subsequently resolved with repeated treatment. Two patients (10%) developed local dermatitis, which resolved with temporary discontinuation of the medication and the addition of a topical corticosteroid. It was observed that the twice-daily application of topical fluorouracil and salicylic acid is a safe and effective treatment for verruca plantaris.²

¹ J Drugs Dermatol. 2006 May;5(5):418-24.

² J Am Podiatr Med Assoc. 2005 Jul-Aug;95(4):366-9.

As it is a caustic agent, 5FU can be compounded in a base that adheres as well as possible to the wart and reduces exposure to normal skin.

Transdermal L-Arginine Improves Circulation and Temperature in Diabetic Feet

Patients with diabetes have abnormally low levels of L-arginine and elevated levels of endothelial nitric oxide synthase (eNOS). Normally, nitric oxide is generated in the endothelium through the oxidation of L-arginine by eNOS. Nitric oxide then causes smooth muscle to relax, resulting in increased blood flow.

To determine if transdermal administration of L-arginine would improve vascular circulation and temperature of the feet of diabetic patients, 16 subjects with diabetes and impaired foot circulation were enrolled and 13 completed a double-blind, vehicle-controlled, two period crossover protocol with washout periods of one week. The active cream contained L-arginine in a proprietary transdermal cream base. Due to the long-lasting effect of the L-arginine cream, the analysis was altered to determine the effect from cumulative exposure to L-arginine throughout the protocol. In feet which received an application of L-arginine cream twice daily for two weeks, average Doppler flow increased 33% at the metatarsal and 35% at the Achilles tendon, and average temperature increased 5 degrees Fahrenheit at the metatarsal and 8 degrees Fahrenheit at the great toe.

Impaired circulation is a major cause of such diabetes-related complications as cold, painful feet and foot ulcers. Restoration of blood flow in the feet of people with diabetes may prevent ulcers and amputations. Additional research is needed to determine if L-arginine cream has any clinical benefit in preventing or reducing amputations or other foot complications.

Diabetes Care. January 2004; 27(1):284-5

Topical Tricyclic Antidepressants for Neuropathic Pain

Phillips and Al-Muhairi of Boston University School of Medicine, recently reported the case of a 66-year-old woman who presented with severe burning sensations in both soles of her feet, which worsened at night and disturbed her sleep. The patient has insulin-dependent diabetes. Skin on both feet was hypersensitive to touch and pressure, peripheral pulses were intact, and capillary refilling time was normal. The patient was diagnosed as having diabetic neuropathy. The soles of her feet were treated with topical doxepin twice daily for four weeks. The patient responded dramatically with loss of the severe burning sensation and no side effects.

Tricyclic antidepressants (TCAs) are important drugs in the treatment of painful neuropathy. Their analgesic effect is independent of their antidepressant activity and generally occurs at low doses with onset of pain relief in one to two weeks. For example, the analgesic effect of topically applied doxepin hydrochloride in chronic human neuropathic pain has been described in a randomized, double-blind, placebo-controlled study of 200 adult patients. Fewer side effects were reported compared with oral administration (the most prominent being a transient somnolence). Minimal percutaneous absorption of topical doxepin occurred with plasma levels of topical doxepin ranging from 0 to 47ng/mL compared to 30 to 150ng/mL reported for orally administered doxepin. Contact sensitization and dermatitis has been reported. Rational use of doxepin cream will minimize side effects. Thin films of doxepin cream should be applied to no more than 10 percent of body surface area, and under no circumstances should occlusive dressings be used.

Other studies have shown that topically applied amitriptyline is effective as an analgesic in humans.

Wounds 2003;15(8):272-276

Br J Clin Pharmacol 2000;49:574-9

Pain Clin 2000;12(1):47-50.

Reg Anesth Pain Med 2003 Jul-Aug;28(4):289-93

Doxepin HCL topical. www.medscape.com.

Topical Zinc for Wound Healing

When zinc is applied on wounds it not only corrects a local zinc deficit but also acts pharmacologically. In a double-blind trial involving 37 leg ulcer patients with low serum zinc levels, topical zinc promoted cleansing and re-epithelialization. Infections and deterioration of ulcers were less common in zinc-treated patients. Zinc also has an anti-bacterial mechanism which appears to be more indirect and to be mediated via local defense systems rather than being directly toxic to the bacteria. A German study found that topical zinc aided in the healing process: in comparison to controls, the granulation tissue was constructed more systematically, the formation of collagen was more advanced, and the amount of collagen increased. Another randomized, double-blind, placebo-controlled study was conducted to determine the safety and efficacy of dual topical therapy with zinc chloride spray and magnesium hydroxide ointment in healing incisional wounds of the abdominal and perineal areas. 85 of 100 ob/gyn patients completed the treatment regimen. A more marked decrease in the size of the wound, a shorter healing time, a better control of infection, less dehiscence, and more effective pain control were observed in patients in the treatment group as compared with those in the placebo group. No side effects were noted.

Acta Derm Venereol Suppl (Stockh) 1990;154:1-36

Clin Ther 1989 Mar-Apr;11(2):258-63

Therapy for Onychomycosis (Fungal Nail) in Special Patient Populations

Diabetes mellitus may be associated with serious sequelae, such as renal disease, retinopathy, and diabetic foot. A recent large prospective study has shown that onychomycosis is among the most significant predictors of foot ulcer. As the severity of onychomycosis may be associated with the length of time the individual has had the infection, early intervention is advisable owing to the progressive nature of the fungal infection. If left untreated, toenails can become thick, causing pressure and irritation, and thus act as a trigger for more severe complications. In the treatment of onychomycosis, compliance and drug interactions are important considerations, as diabetic patients frequently take concomitant medications.

Studies have shown that antifungal agents can be of benefit in treating onychomycosis in patient populations that include the elderly, children, and immunocompromised individuals (e.g., transplant patients, Down's patients, HIV patients, and diabetics). The treatment modality in special patient populations should take into account the clinical presentation of onychomycosis, causative organism, patient and physician preference, concomitant medications that the patient is taking, and the potential for adverse events associated with antifungal therapy. Topical treatment of onychomycosis offers a distinct advantage to oral therapy as topical preparations can be applied directly to the affected area, thus decreasing the potential for serious adverse events associated with oral antifungal therapy, such as drug toxicity and drug interactions.

At the Nail Disease Centre, Cannes, France, 13 patients with onychomycosis, aged 25-78 years, most with involvement of the matrix region, were treated with a solution of 1% fluconazole and 20% urea in a mixture of ethanol and water, applied once daily at bedtime. In four patients there was complete resolution of the condition; four patients who had involvement of one nail only demonstrated a 90% improvement. Of the four patients who had presented with involvement of both big toenails, two showed 50% improvement bilaterally and in the remaining two patients there was a 90% improvement in one nail and a 50% improvement in the other.

Most antifungal medications are not used topically and are not commercially available as topical preparations due to a concerns about lack of penetration. However, we can solve this problem by dissolving the preferred antifungal agent in pharmaceutical grade DMSO (a penetrant enhancer).

Trimming, filing or grinding the nail, in addition to these drug treatments, is likely to be beneficial, but these measures have not been evaluated. Chemical nail destruction with a combination of urea and bifonazole, followed by treatment with an antifungal ointment, can be used when the nail is markedly thickened. Non-comparative trials have shown cure rates close to 70% at three months when the matrix is not involved, and 40% with matrix involvement.

Am J Clin Dermatol. 2009;10(4):211-20.

J Dermatolog Treat. 2005 Feb;16(1):52-5

J Cutan Med Surg. 2004 Jan-Feb;8(1):25-30.

J Cutan Med Surg. 2004 Jan-Feb;8(1):25-30.

Prescrire Int. 2009 Feb;18(99):26-30.