a simple one and may allow diuretic use to be targeted, both reducing potentially burdensome trials in patients unlikely to respond and allowing confident titration in those with central ascites where the benefits may be significant. Further formal work within the malignant ascites population would allow the development of protocol guidance.

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A New Combination Cream for the Treatment of Severe Neuropathic Pain

To the Editor:

Neuropathic pain may be quite resistant to drug treatment. In the case of intractable pain, rational polypharmacy is now well established.[1] The treatment of patients suffering from neuropathic pain with rational polytherapy seems to have the highest likelihood of success.[2] A variety of treatment modalities, such as percutaneous electrical nerve stimulation (PENS) or transcutaneous electrical nerve stimulation (TENS), can be administered together with drugs, potentially allowing use of lower and better-tolerated doses. The same outcome may be possible with the use of topical therapies. The following case did not respond well to our rational polytherapy until a novel combination topical cream, consisting of isosorbide dinitrate (ISDN) 0.4%, capsaicin 0.075%, and lidocaine 3%, was added.

Case

A 62-year-old man suffered from intractable neuropathic pains in both feet and hands since 2003. The diagnosis was painful diabetic polyneuropathy. Glucose levels were within range as a result of treatment with glimepiride 4 mg daily and metformin 500 mg three times a day. Because of the pain, his function was severely compromised. He scored 6 on the Douleur Neuropathique 4 questionnaire (total score 10), which corresponds to severe neuropathic pain. The patient described his pain as burning and excruciating. On the dorsal side of his right foot, he experienced a painful feeling as if a clamp was squeezing his foot (a "clamp pain"). Walking barefoot and sitting increased the pain. The symptoms worsened as the day progressed. Total score on the short-form McGill Pain Questionnaire was 26 (total score 45), the score on the visual analogue scale (VAS; 0–100 mm) was 98, and on the 11-point Brief Pain Inventory scale, the score for pain in the last 24 hours was 10 (0–10).

The treatment consisted of pregabalin 75 mg daily and topical capsaicin 0.075%. Neither of these medications had any effect on the pain

scores. Because of severe flatulence, a known side effect of pregabalin, the patient stopped using this drug. PENS once a week provided only a little pain relief. TENS twice daily, cannabis in the evening, amitriptyline 20 mg daily, alpha lipoic acid 600 mg daily, and acetyl-L-carnitine 1000 mg daily slightly relieved his symptoms but without adequate analgesia.

After adding a novel cream developed in our institute, the pain reduced markedly, starting after three days. The cream was applied in amounts of about 1 g, three times daily, as a thin layer on both soles. After every application, he was instructed to wash his hands because of the burning effect of capsaicin on touching the eyes or mucous membranes.

During the first two weeks, the VAS pain scores decreased to 30 or 40, and the clamp pain of his right foot disappeared. The analgesic effect started a few minutes till half an hour after application. During the next four weeks, he used the cream four to five times daily, applying it whenever the pain started to worsen, usually three to four hours after the previous application. When the application was delayed, the cream seemed to become less effective. The immediate analgesic effect returned after the next two to three applications. After three months of continuous cream application, his VAS pain scores fluctuated between 30 and 70, depending on how much stress he experienced. The clamp pain never returned. None of the possible side effects, including burning because of capsaicin, or pounding headache and orthostatic hypotension because of ISDN, occurred. Most of these side effects are mild and will diminish rather quickly in days.

Comment

We developed this cream, consisting of three different drugs, based on three different mechanisms of action. ISDN has a vasodilatory action and releases nitric oxide (NO). In diabetes, neuropathic pain is partly because of diminished NO release and vasoconstriction.[3,4] In a double-blind, crossover trial, ISDN clearly reduced neuropathic pain.[5] Lidocaine 3% is added because of positive results in recent studies of neuropathic pain.[6] The primary mechanism of action is the inhibition of voltage-gated Na^+ channels in damaged peripheral nerves.[7] The third ingredient is capsaicin 0.075%, which causes desensitization of the sensory C-fibers by depleting substance P from the nerve terminals.[8]

In conclusion, until we added the newly developed cream to the polytherapy, this patient with intractable neuropathic pain did not respond to various treatment modalities. Based on this cream-enriched polytherapy, we were able to reduce his pain considerably: the VAS score decreased by more than 50% for most of the day. Consequently, the patient dares now to go on holidays again, and he resumed activities, such as mowing the lawn.

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