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Successful Treatment of Sacral Pressure Injury With ACU-D1

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ABSTRACT

Pressure injuries, previously known as pressure ulcers, commonly affect elderly patients in the sacral area, resulting in a sacral pressure injury. The mainstay of treatment is supportive care, including avoiding further pressure on the wounded area. In our case report, we encountered a patient with a stage 2 pressure injury that was resistant to a month of supportive treatment, with no improvement. After a trial of 10% ACU-D1, a proteasome inhibitor cream, the patient experienced relief in symptoms and complete re-epithelialization of the injury site within one month. With emerging research suggesting a role of inflammation and neutrophil activation in pressure injuries, we propose that further investigation into ACU-D1 for pressure injuries and other chronic wounds could benefit patients.

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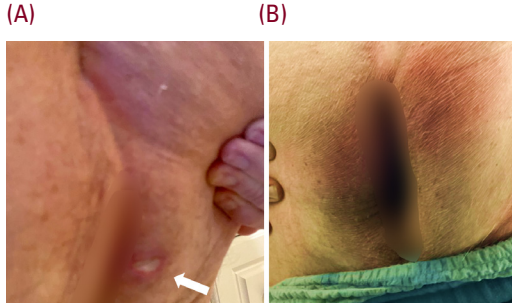
INTRODUCTION

Pressure injuries are exceedingly common lesions which cause a great deal of morbidity, especially in the elderly.[1] Treatment is mostly supportive, with avoidance of pressure on the injury being the mainstay of therapy. Other measures, such as topical ointments and oral antibiotics to treat bacterial colonization are sometimes used.[2] Nevertheless, no adequate therapies exist, and pressure injuries remain a great unmet need. We previously developed a topical proteasome inhibitor, ACU-D1 (Pentaerythritol tetrakis (3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate)), which was tested in a phase 2A clinical trial in rosacea (NCT03064438).[3] In this case report, we demonstrate the efficacy of ACU-D1 in an elderly patient who did not respond to other supportive therapies. This proof of principle case report suggests the need for larger studies to evaluate the efficacy of ACU-D1 in pressure injuries.

CASE REPORT

The patient is an 80-year-old male with a history of type 2 diabetes (treated with Dulaglutide, Levemir U-100 insulin, and metformin), and hypertension (treated with amlodipine and metoprolol succinate). His past dermatologic history is notable for tinea pedis and squamous cell carcinoma. He presented with a stage II pressure injury (partial thickness loss of dermis) on his right gluteal region (Figure 1A). The wound was cleaned initially with hydrogen peroxide. Supportive therapy was then initiated with mupirocin ointment, moist dressing with pressure-offloading bandages, as well as further instructions to avoid pressure on the site. After one month, there was no improvement with pain or healing. The patient elected to try topical 10% ACU-D1 cream on the pressure injury, applied once daily, which led to rapid reduction of pain and re-epithelialization of the injury (Figure 1B).

FIGURE 1. (A) Image of sacral pressure injury on right gluteal region at initial presentation. (B) Resolution of sacral pressure injury after trial of topical 10% ACU-D1 for one month.



DISCUSSION

Pressure injuries are common causes of morbidity in the elderly. The exact etiology is unknown, but is hypothesized to result from compromised small vessels that vascularize the buttocks. In addition, an inflammatory component has been noted, and lesions are commonly colonized by polymicrobial flora, which leads to fibrin lysis and inhibition of re-epithelialization.[4,5] Conservative measures (especially decreased pressure on the wound area), debridement, and both topical and oral antibiotic therapy, are the cornerstones of current pressure injury

therapy.[1,2,6] Pressure injuries are difficult to heal with current therapies. Corticosteroids inhibit inflammation but also inhibit wound healing.[7] Pads and patches are often used, but allergy to adhesives and occlusion of colonized skin may prevent optimal wound healing. For this patient particularly, the pressure injury seemed resistant to supportive treatment, as the expected healing time for a stage 2 pressure injury is under 1 month.[8]

It has been hypothesized that ischemia alone does not fully explain pressure injuries. Chronic inflammation, which may be mediated by several factors, including diabetes and polymicrobial colonization, may prevent wound healing. An emerging role of neutrophil activation has been observed in pressure injuries.[9] These neutrophils may be highly pro-inflammatory and produce cytokines such as interleukin 1 beta but may not be effective in clearing polymicrobial flora.

In our previous clinical trial of ACU-D1 in papulopustular rosacea, we found that there were only minor adverse side effects, primarily skin drying. In addition, ACU-D1 reduced erythema in rosacea patients without causing vasoconstriction. Finally, FDA approval of ACU-D1 for the treatment of rosacea was obtained, based upon IND-enabling studies performed by Accuitis LLC (NCT03064438).[3] Due to its properties in preventing abnormal blood vessel growth and decreasing inflammation, ACU-D1 is also currently being trialed in patients with HPV associated vulvar and perianal lesions who have HIV (NCT06233331). ACU-D1 is an inhibitor of the 26S proteasome, which inhibits NFkB signaling by preventing the degradation of IkB. In addition,The SHP-2 enzyme is required for wound healing and downregulates the 26S proteasome. Thus, inhibition of the 26S proteasome by ACU-D1 might be beneficial in wound healing, including for pressure injuries. Furthermore, topical ACU-D1 was well tolerated on the face and did not exacerbate bacterial infections in patients with rosacea, circumventing the issue of traditional pressure injury pads and patches occluding colonized skin and preventing optimal wound healing.[10]

Additional studies are warranted to determine whether ACU-D1 will be beneficial for chronic wounds, including pressure injuries.

DISCLOSURES

JLA is the inventor of ACU-D1 and a founder of Accuitis LLC, which has conducted a phase 2A clinical trial on ACU-D1.

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