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Well-tolerated topical capsaicin formulation reduces knee OA pain

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By Jeff Craven

REPORTING FROM ACR 2019

ATLANTA – Use of high-concentration topical capsaicin was associated with reduced pain, a longer duration of clinical response, and was well tolerated in patients with knee osteoarthritis, compared with lower concentrations of capsaicin and placebo, according to recent research presented at the annual meeting of the American College of Rheumatology.

Jeff Craven/MDedge News
Tim Warneke

While the ACR has recommended topical capsaicin for the relief of hand and knee OA pain, there are issues with using low-dose capsaicin, including the need for multiple applications and burning, stinging sensations at applications sites. As repeat exposure to capsaicin results in depletion of pain neurotransmitters and a reduction in nerve fibers in a dose-dependent fashion, higher doses of topical capsaicin are a potential topical treatment for OA pain relief, but their tolerability is low, Tim Warneke <http://vizuriusa.com/about/people/> , vice president of clinical operations at Vizuri Health Sciences in Columbia, Md., said in his presentation.

"[P]oor tolerability has limited the ability to maximize the analgesic effect of capsaicin," Mr. Warneke said. "While [over-the-counter] preparations of capsaicin provide some pain relief, poor tolerability with higher doses has really left us wondering if we haven't maximized capsaicin's ability to provide pain relief."

Mr. Warneke and colleagues conducted a phase 2, multicenter, double-blind, parallel-group, vehicle-controlled trial <https://clinicaltrials.gov/ct2/show/NCT03528369> where 120 patients with knee OA were randomized in a 1:1:1 ratio to receive 5% capsaicin topical liquid (CGS-200-5), 1% capsaicin topical liquid (CGS-200-1), or vehicle (CGS-200-0) and then followed up to 90 days. "The CGS-200 vehicle was developed to mitigate the burning, stinging pain of capsaicin," Mr. Warneke said. "It allows the 5% concentration to be well tolerated, which opens the door for increased efficacy, including durability of response."

Inclusion criteria were radiographically confirmed knee OA using 1986 ACR classification criteria, a Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score of 250 mm or greater, and more than 3 months of chronic knee pain. While patients were excluded for use of topical, oral, or injectable corticosteroids in the month prior to enrollment, they were allowed to continue using analgesics such as NSAIDs if they maintained their daily dose throughout the trial. Mr. Warneke noted the study population was typical of an OA population with a mostly female, mostly Caucasian cohort who had a median age of 60 years and a body mass index of 30 kg/m^2. Patients had moderate to severe OA and were refractory to previous pain treatments.

The interventions consisted of a single 60-minute application of capsaicin or vehicle to both knees once per day for 4 consecutive days, and patients performed the applications in the clinic. The investigators compared change in WOMAC pain scores between the groups at

31 days, 60 days, and 90 days post dose.

The results at 31 days showed a 46.2% reduction in WOMAC pain scores from baseline for patients using CGS-200-5, compared with a 28.3% reduction in the vehicle group (P = .02). At 60 days, there was a 49.1% reduction in WOMAC pain scores in the CGS-200-5 group, compared with 21.5% in patients using vehicle (P = .0001), and a 42.8% reduction for patients in the CGS-200-5 group at 90 days, compared with 22.8% in the vehicle group (P = .01). The CGS-200-1 group did not reach the primary efficacy WOMAC pain endpoint, compared with vehicle.

A post hoc analysis showed that there was a significantly greater mean reduction in WOMAC total score for patients using CGS-200-5, compared with vehicle at 31 days (P = .02), 60 days (P = .0005), and 90 days post dose (P = .005). “This durability of clinical response for single applications seems to be a promising feature of CGS-200-5,” Mr. Warneke said.

Concerning safety and tolerability, there were no serious adverse events, and one patient discontinued treatment in the CGS-200-5 group. When assessing tolerability at predose, 15-minute, 30-minute, 60-minute, and 90-minute postdose time intervals, the investigators found patients experienced mild or moderate adverse events such as erythema, edema, scaling, and pruritus, with symptoms decreasing by the fourth consecutive day of application.

Mr. Warneke acknowledged the “robust placebo response” in the trial and noted it is not unusual to see in pain studies. “It’s something that is a challenge for all of us who are in this space to overcome, but we still have significant differences here and they are statistically significant as well,” he said. “You have to be pretty good these days to beat the wonder drug placebo, it appears.”

Four authors in addition to Mr. Warneke reported being employees of Vizuri Health Sciences, the company developing CGS-200-5. One author reported being a former consultant for Vizuri. Three authors reported they were current or former employees of CT Clinical Trial & Consulting, a contract research organization employed by Vizuri to execute and manage the study, perform data analysis, and create reports.

SOURCE: Warneke T et al. Arthritis Rheumatol. 2019;71(suppl 10), Abstract 2760 <https://acrabstracts.org/abstract/a-phase-2-double-blind-clinical-trial-to-examine-the-comparative-effects-on-osteoarthritic-knee-pain-of-cgs-200-1-1-capsaicin-topical-liquid-cgs-200-5-5-capsaicin-topical-liquid-and-cgs-200-0-v/> .