Nabiximols: A New Way to Help Manage Cancer Pain

When a cancer patient's pain doesn't respond to opioids, the simplest answer may be to use an adjuvant analgesic to boost the effect of the opioids, say researchers from Beth Israel Hospital (New York, New York), sf. Ioan cel Nou (Suceava, Romania), the National Cancer Institute of Mexico (San Fernando), Hazel Hawkins Hospital (Hollister, California), Metropolitan Hospital Center (New York, New York), and the Huntsman Cancer Institute (Salt Lake City, Utah).

But maybe that answer isn't so simple. The researchers add that the "paucity of studies in cancer pain," particularly with respect to adjuvant analgesics, can complicate therapeutic decision making. The availability of a novel agent for which there is high-quality evidence of efficacy and safety, they say, "would be an advance."

That drug, the researchers propose, is nabiximols, a cannabinoid being investigated as add-on therapy for cancer pain. In previous studies, nabiximols was shown to have an analgesic effect for peripheral neuropathic pain, for both pain and spasticity resulting from multiple sclerosis, as well as a benefit in a small study in cancer pain. The current study was designed in part to assess the optimal dose range for nabiximols.

Nabiximols is a spray with doses delivered to the oral mucosa. In this study, each actuation of the pump delivered 100 µL of fluid to the oral mucosa. Patients were randomly assigned to receive placebo or nabiximols at 1 of 3 doses: low dose (1-4 sprays/d), medium dose (6-10 sprays/d), or high dose (11-16 sprays/d). The study included a 5- to 14-day baseline period, a 5-week titration and treatment period, and a poststudy visit after 2 weeks. The maximum duration was 9 weeks.

The patients continued their scheduled opioid dose without change and could use their breakthrough opioid analgesic as required. On each day of the study, patients were asked to rate their pain, sleep, use of other medications, and quality of life (QOL) (including the burden of constipation on everyday functioning and well-being).

The primary endpoint (30% response) was not significant for nabiximols vs placebo. However, in the secondary analysis of average daily pain from baseline to end of study, nabiximols showed a greater treatment effect than did placebo. The effect was significant only in the 2 lower dose groups, though. When those 2 groups were combined, the estimated median difference between treatment groups was 10.5% in favor of nabiximols.

The low dose of nabiximols produced a 26% improvement in pain compared with baseline. In the low-dose group, the mean change in pain score was the greatest at week 5: 1.4 points less than the mean baseline score of 5.8 points compared with 0.8 points from the baseline score of 5.7 points in the placebo group.

Overall, sleep disturbance scores also showed a slight benefit with nabiximols, again predominantly because of higher scores in the low-dose group.

Nabiximols had no positive effects on pain-related functional interference, constipation, impression of global change, and QOL. The lack of improvement, the researchers say, may be related to the severity of the disease, the relatively short duration of the study, or limited sensitivity of 1 or more of the questionnaires. Most patients, they note, had advanced illness and multiple problems; "the most likely explanation is that pain relief could not address the array of factors causing functional impairment and suffering."

Adverse events (AEs) were dose related. Of the 90 patients receiving high-dose nabiximols, only 59 continued at that dose until the end of the study. More high-dose patients (28%) withdrew from treatment compared with 17% of the medium-dose, 14% of the low-dose, and 18% of the placebo patients. However, serious AEs were more common among the low-dose patients compared with the placebo patients (30% vs 24%). Moreover, more patients in the low-dose group died (21% of all patients receiving nabiximols compared with 18% of placebo patients) in what the researchers call an "unanticipated finding." The researchers say none of the deaths seemed to be related to nabiximols. Post hoc and independent analyses concluded that most deaths were due to disease progression.

Source: Portenoy RK, Ganae-Motan ED, Allende S, et al. *J Pain.* 2012;13(5):438-449. doi: 10.1016/j.pain.2012.01.003.