Letters to the Editor

Effects of Ultra-Low-Dose Buprenorphine on Suicidal Ideation Confounded by Physical Pain Relief?

TO THE EDITOR: The article by Yovell and colleagues (1) is both interesting and informative. The authors reason that suicidality is linked to mental pain, which is modulated through endogenous opioids. In a randomized controlled trial, the authors tested the efficacy and safety of very low dosages of sublingual buprenorphine. They found patients receiving buprenorphine had a greater reduction in Beck Suicide Ideation Scale scores than patients who received placebo. They conclude that the use of sublingual buprenorphine at very low dosages was associated with decreased suicidal ideation (1).

We wonder if the observed efficacy of low-dosage buprenorphine for reducing suicide ideation could actually result from its analgesic effect for relieving physical pain.

A number of studies suggest that the buprenorphine dosage needed for treatment of pain is much lower compared with dosages for treatment of opioid addiction. The typical analgesic dosage of buprenorphine is 0.3–0.6 mg i.m. or i.v., and its analgesic effects last approximately 6 hours (2). In this regard, transdermal patches that provide buprenorphine at lower dosages (5, 10, and 20 μg/hour) are approved for the management of moderate chronic nonmalignant pain (3). The dosage range of the buprenorphine formation noted above is 120–480 μg/day or 0.12–0.48 mg/day, comparable to sublingual buprenorphine lozenges, with an initial dosage of 0.1 or 0.2 mg/day, with increases of 0.1–0.2 mg increments weekly, to a maximum daily dosage of 0.8 mg in the investigation by Yovell et al.

Calati et al. (4) recently performed a meta-analysis comparing rates of suicidal thoughts and behaviors in individuals with and without physical pain. They found that individuals with physical pain are more likely to report lifetime death wish, current and lifetime suicidal ideation, suicide plan, and suicide attempt. Moreover, these individuals were also more likely to die by suicide.

Suicide rates in the United States have risen sharply for both men and women in all age groups younger than age 75, according to a report from the U.S. National Center for Health Statistics (5).

Szymanski and colleagues (6) recently conducted a study to assess drug type and current risk factors in suicide deaths. They found that of 342 suicide overdose cases, psychiatric illness was present in 72% of cases, while chronic pain was seen in 27.2% of cases. Therefore, without controlling for physical pain, the findings of Yovell et al. could be considered confounded.

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Ultra-Low-Dose Buprenorphine for Mental Pain: Response to Ruan et al.

TO THE EDITOR: Ruan et al. raise the possibility that ultra-low-dose buprenorphine reduces suicidal ideation, as it did in our double-blind, placebo-controlled trial (1), by alleviating physical pain. We agree with them that there is ample evidence to suggest that patients who suffer from physical pain are at high risk for suicidal ideation and suicidal acts (2). Adequate pain control may therefore decrease suicidality in such patients. However, most patients in our study did not suffer from physical pain.

All potential subjects in our trial underwent a workup that included a detailed medical history and a complete physical examination. Of the 88 patients in our intent-to-treat group, three were found to have fibromyalgia, and the rest were free of significant physical pain. Several other potential subjects were also found to have physical pain but were screened out because of medical illnesses or a history of heavy analgesic use.

Thus, while our findings do not prove that ultra-low-dose buprenorphine reduces suicidal ideation by decreasing mental pain, they do suggest that ultra-low-dose buprenorphine may serve as a quick-acting treatment for suicidal individuals, including those who are free of physical pain.