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OXFORD

LETTER TO THE EDITOR

Low-Dose Aripiprazole Augmentation in Amitriptyline-Resistant Burning Mouth Syndrome: Results from Two Cases

Dear Editor,

Despite the efficacy of antidepressants such as amitriptyline for alleviating burning mouth syndrome (BMS) [1,2], BMS may persist after antidepressant monotherapy. However, recent case reports have shown that aripiprazole (APZ) augmentation can reduce chronic pain resistant to other treatments [3]. Herein, we present two cases in which patients with BMS responded well to a very low dose of APZ in combination with amitriptyline; pain reduction was achieved within two weeks of APZ initiation and was substantial at the two-year follow-up.

Case 1. A 69-year-old housewife who lived with her husband was referred to our clinic by her family doctor, complaining of tingling pain on the left edge and tip of her tongue. She had no past medical or psychiatric history, excepting hyperlipidemia, nor did her family. Her symptoms began a year earlier in the absence of any precipitating events. Although she underwent various treatments at dental, otorhinolaryngology, and oral surgery clinics, her oral symptoms persisted.

The results of the laboratory tests provided by the patient's family doctor were normal, as were those of the extra- and intraoral examinations performed at our clinic. No obvious symptoms of depression were observed at the first visit. After administering 10 mg per day of amitriptyline for pain reduction, which was largely ineffective, we increased the dose to 30 mg; however, the patient experienced severe thirst, and the dose was reduced to 20 mg. In addition to amitriptyline, we also prescribed 1 mg per day of APZ, and the patient's oral symptoms rapidly improved. Within two weeks of APZ initiation, the patient reported, "My pain was relieved about 30% at once." Six months after the initial visit, she stated, "I have almost forgotten about the pain." One year after the initial visit, she reported that her pain-related despair was gone and her symptoms had abated. Her visual analogue scale (VAS) score decreased progressively from 22 (initial visit) to 18 (after amitriptyline treatment), 10 (within two weeks after APZ initiation), and 4 (two-year follow-up). Her Patients' Global Impression of Change (PGIC) [4] score at the end of treatment was 7.

Case 2. A 64-year-old woman who ran a business with her husband was referred to our clinic by her family doctor, complaining of constant tingling pain on her tongue and a bitter taste in her mouth after eating. She had no past medical or psychiatric history excepting rosacea, although her daughter had a history of panic disorder. Her symptoms began after dental procedures performed four years earlier. She underwent various treatments at, among others, a dental clinic and the oral surgery department of a university hospital, but her oral symptoms persisted.

The results of the laboratory tests provided by the patient's family doctor were normal, as were those of the extra- and intraoral examinations performed at our clinic. No obvious symptoms of depression were observed at the first visit. Initial treatment with 10 mg per day of amitriptyline only slightly reduced the pain, and the dose was increased to 20 mg. However, the patient felt that her tongue was swollen and continued to experience a bitter taste after eating. Rather than further increasing the dose of amitriptyline, which was unacceptable to the patient because of its side effects (e.g., sleepiness), we also prescribed 0.5 mg per day of APZ, and her symptoms began to lessen 10 days thereafter. After this administration, we gradually increased the dose of APZ to 1 mg and amitriptyline to 30 mg for further pain reduction. Six months after the initial visit, she said, "My tongue has become smooth, and there is no bitter taste in my mouth." One and half years after the initial visit, she said, "I sometimes feel pain slightly, but do not care about it." Her VAS score decreased progressively from 78 (initial visit) to 57 (after amitriptyline treatment), 40 (within two weeks after APZ initiation), and 16 (two-year follow-up). The PGIC [4] score at the end of the treatment was 6.

The two cases presented show that a very low dose of APZ in addition to amitriptyline drastically alleviates pain. APZ has a unique drug profile [5]; it acts by partially antagonizing the actions of dopamine-2 and serotonin-1A receptors. It causes fewer adverse reactions, such as hyperprolactinemia, than do other antipsychotics and is useful for treating many psychiatric and pain-related disorders [3].

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [6]. In particular, in cases of chronic pain, it is not the pain itself but rather the suffering from the persistent pain that elicits the biological and psychological responses that result in complicated, hard-to-treat symptoms [7]. According to the "pain catastrophizing" model [8], pain is amplified by three major elements—magnification, rumination, and helplessness—that implicate various neural circuits in pain exacerbation. Thus, BMS

involves not only a sensory aspect, but also a considerably complex psychological aspect [9].

Interestingly, the administration of low-dose APZ and amitriptyline in our two cases resembles the treatment strategy for obsessive-compulsive disorder (OCD) [10,11], an illness quite different from BMS. BMS patients not only complain of tongue pain but constantly ruminate about the pain—its etiology, relief, and cause—analogous to the way in which OCD patients obsess about their anxieties. Furthermore, delayed diagnosis and treatment [12] of BMS may exacerbate the "suffering" rather than the pain sensation itself. Therefore, an obsessive, anxiety-based thinking process might be a clinical attribute shared by patients with BMS and those with OCD, and the neural circuits of the two diseases might at least partially overlap. In case 2, the patient said that she felt slight pain but did not care about it, indicating that the augmentation treatment might have resolved her obsession with pain, in addition to reducing the pain. In conclusion, low-dose APZ augmentation can be an effective treatment for BMS when an adequate response is not achieved via amitriptyline monotherapy.

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LETTER TO THE EDITOR

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Efficacy and Safety of Long-Term Administration of Tapentadol in Relieving Chronic Pancreatitis Pain

Dear Editor,

Chronic pancreatitis (CP) is a condition associated with severe pain frequently refractory to common analgesics, leading to multiple hospital admissions [1–3]. A novel, centrally acting analgesic has been recently commercialized for the treatment of chronic pain, and several studies demonstrated promising results in the management