*Pain Medicine*, 21(9), 2020, 2009–2010
doi: 10.1093/pm/pnz324
Advance Access Publication Date: 16 December 2019
**Letter to the Editor**

# Real-world Discontinuation of Antidepressant Treatment in Patients with Burning Mouth Syndrome: A Chart Review

**Motoko Watanabe, DDS, PhD,*,† Miho Takenoshita, DDS, PhD,† Trang T. H. Tu , DDS,† and Akira Toyofuku, DDS, PhD†**

*Oral and Maxillofacial Radiology, Tokyo Dental College, Tokyo, Japan; †Psychosomatic Dentistry, Tokyo Medical and Dental University, Tokyo, Japan

Funding sources: JSPS KAKENHI Grant Numbers 19K10328, 19K19211, and the MEXT-Supported Program for the Strategic Research Foundation at Private Universities S1511018.

Dear Editor,

Burning mouth syndrome (BMS) is characterized by a persistent intraoral burning or dysesthetic sensation without clinically evident causative lesions [1]. Amitriptyline is an effective agent for the treatment of BMS [2, 3]. However, there are concerns about associated adverse events, which often result in discontinuation. In contrast, the efficacy of aripiprazole, a partial dopamine agonist, was reported in patients with BMS; moreover, it did not result in severe adverse events [4]. The real-world rates of discontinuation of amitriptyline and aripiprazole have not yet been studied. Here, we present our clinical data for these prescriptions obtained from a clinical chart review.

Of the 466 patients with BMS who were treated with psychopharmacotherapy at our outpatient clinic between April 2013 and March 2015, amitriptyline was prescribed as an initial medication to 151 patients, and aripiprazole was prescribed as an initial medication to 47 patients. Discontinuation of amitriptyline occurred in 50% of patients within 63 days, and discontinuation of aripiprazole occurred in 50% of patients within 53 days (Figure 1). The persistence of both medications reached a plateau at five to six months. No significant difference was observed between amitriptyline and aripiprazole in time to discontinuation of treatment in patients with BMS ($P = 0.443$, Kaplan-Meier, log-rank test).

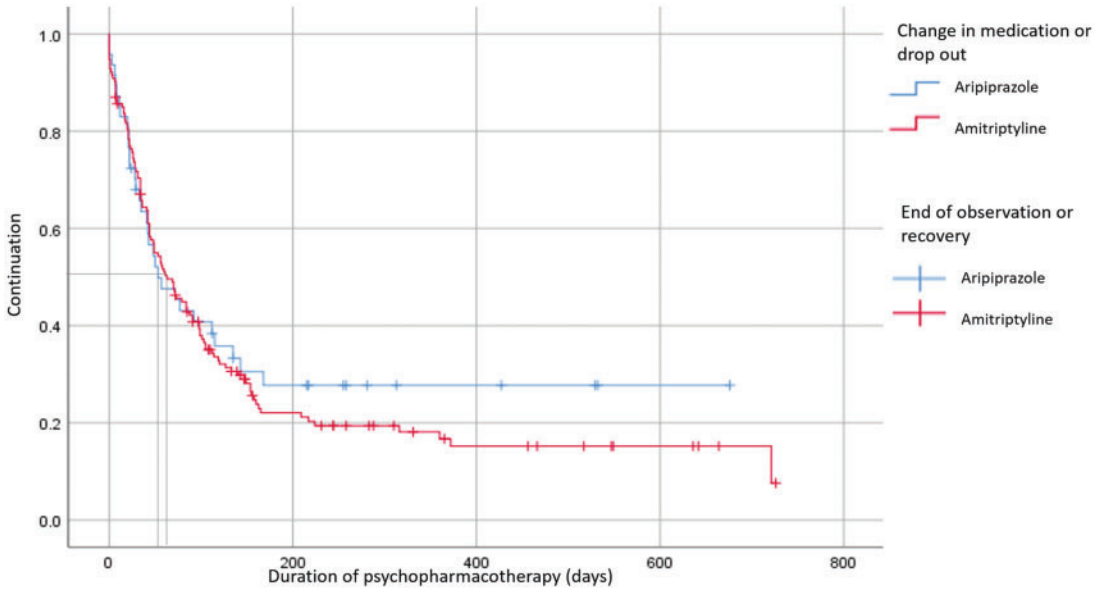


**Figure 1.** No significant difference was observed between discontinuation of amitriptyline and aripiprazole.

**Table 1.** The details of discontinuation

| | Amitriptyline (N = 151) | Aripiprazole (N = 47) |
|---|---|---|
| Continued, No. (%) | 32 (21.2) | 16 (34.0) |
| Discontinued, No. (%) | 119 (78.8) | 31 (66.0) |
| Lost to follow-up | 20 | 7 |
| Switched to other medication | 26 | 5 |
| Added another medication | 73 | 19 |
| Reasons for discontinuation | | |
| Adverse events | 13 | 5 |
| Lack of efficacy | 88 | 21 |
| Average maximum dose, mean ± SD, mg | 1.17 ± 0.53 | 23.12 ± 12.19 |

Of the 119 patients who discontinued amitriptyline, 20 patients were lost to follow-up, 26 patients switched to another medication, and 73 patients added another medication (Table 1). Of the 31 patients who discontinued aripiprazole, seven patients were lost to follow-up, five patients switched to another medication, and 19 patients added another medication. The most common reason for discontinuation was adverse events (13 patients, 10.9%, for amitriptyline; five patients, 16.1%, for aripiprazole). Discontinuation due to lack of efficacy was observed in 88 patients (73.9%) for amitriptyline and 21 patients (67.7%) for aripiprazole. The proportion of patients continuing the same medication until the end of observation was 21.2% (32/151) for amitriptyline and 34.0% (16/47) for aripiprazole, with no significance ($P = 0.073$, chi-square test).

These results may be attributable to the dose of amitriptyline prescribed for BMS treatment. The lower incidence of adverse events occurring at a low- dose use (average maximum dose = 23.12 ± 12.19 mg) may have resulted in a similarly low discontinuation of amitriptyline compared with aripiprazole. In addition, the limitations of monotherapy were also revealed. Besides the burning sensation, BMS results in complex intraoral discomfort, such as oral dryness, a sticky feeling, and a bitter or metal taste. The differences in these mixed symptoms may prevent a single medication from being successful. We have already reported the efficacy of low-dose aripiprazole augmentation in amitriptyline-resistant BMS [5]. Further investigations are needed to examine the efficacy of each treatment with a single medication and with augmentation for BMS with regard to the clinical characteristics.

Moreover, the population of elderly patients with BMS has recently increased, in parallel with an increasingly aging society [2]. It is necessary to be particularly cautious when prescribing amitriptyline to elderly patients. Further, as elderly patients generally have lower tolerance for antidepressants, discontinuation rates may increase, resulting in poorer treatment outcomes. Our findings indicate the importance of enhancing clinicians' ability to handle manageable adverse events and identify more effective medication strategies, including "skillful polypharmacy," in order to minimize discontinuation.

## References

1. The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia 2013;33(9):629–808.
2. Tu TTH, Takenoshita M, Matsuoka H, et al. Current management strategies for the pain of elderly patients with burning mouth syndrome: A critical review. Biopsychosoc Med 2019;13:1.
3. Jaaskelainen SK, Woda A. Burning mouth syndrome. Cephalalgia 2017;37(7):627–47.
4. Umezaki Y, Takenoshita M, Toyofuku A. Low-dose aripiprazole for refractory burning mouth syndrome. Neuropsychiatr Dis Treat 2016;12:1–3.
5. Takenoshita M, Motomura H, Toyofuku A. Low-dose aripiprazole augmentation in amitriptyline-resistant burning mouth syndrome: Results from two cases. Pain Med 2017;18(4):814–5.