

Development of oral candidiasis following initiation and rechallenge of extended-release bupropion in a geriatric patient

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Abstract

Objective: To report a case of oral candidiasis that developed in a 70-year-old white female both upon initiation and rechallenge of extended-release bupropion therapy.

Case Summary: A 70-year-old female with a past medical history of osteoarthritis, degenerative joint disease, and polycythemia vera developed oral candidiasis on 2 occasions following initiation of extended-release bupropion for the treatment of recurrent depression. During both instances, the reaction occurred with an increased dose of the medication, suggesting the adverse event may have been dose-related. The patient had no risk factors for oral candidiasis aside from dry mouth at baseline that reportedly worsened on bupropion.

Discussion: Though there are no other reports to our knowledge describing the development of oral candidiasis with bupropion, the likelihood of this having been an adverse reaction in this patient is probable as indicated by a calculated score of 8 from the Naranjo Algorithm. The adverse event appeared following bupropion administration and improved over time following its discontinuation. The adverse event reappeared following readministration of the agent, and no alternative causes were able to be identified. Additionally, the reaction occurred following an increase in the dose on both occasions, with the lower dose having only resulted in worsening dry mouth.

Conclusion: This case demonstrates that an additional adverse event to screen for with bupropion treatment is the development of oral candidiasis. This adverse event may be more likely to occur in the older adult population.

Keywords: bupropion, candidiasis, thrush, geriatric

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Background

Candidiasis, also known as “thrush,” is caused by an imbalance in normal flora leading to an overgrowth of *Candida albicans*. Risk factors for the development of oral candidiasis include impaired salivary gland function, wearing dentures, oral cancer/leukoplakia, smoking, infection, nutritional deficiencies, and immunosuppressive conditions.¹ Certain drugs have been implicated as well, including immunosuppressive drugs and certain broad spectrum antibiotics.¹

Bupropion is an antidepressant with a distinct side effect profile.² Initial studies^{3,4} comparing bupropion sustained release to placebo-treated patients reported that the most common adverse events were dry mouth, nausea, and insomnia, respectively. Though dry mouth is a commonly reported side effect,⁵⁻⁸ and this is a risk factor of oral candidiasis, we are unaware of any case reports describing this adverse event following bupropion use. We report a case of suspected bupropion-induced oral candidiasis in an older adult.

Case Summary

A 70-year-old white female with past medical history of osteoarthritis, osteoporosis, degenerative joint disease, and polycythemia vera, sought care in our clinic for unresolved depression. She had been referred to us by her nurse practitioner, who had initiated bupropion as an augmentation strategy with sertraline that the patient had previously been taking for 20 years. She was initiated on bupropion XL 150 mg daily, and 2 weeks later her dose was increased to 300 mg. One week following the dose increase, she developed oral candidiasis (thrush), for which her nurse practitioner prescribed nystatin suspension. The patient eventually self-discontinued the bupropion 1 week prior to presenting to our clinic due to the thrush worsening despite nystatin treatment.

When presenting to our clinic for psychiatric evaluation, she expressed dissatisfaction with sertraline monotherapy, stating she preferred bupropion but believed it had caused the thrush to develop. At this time, she was taking sertraline 100 mg daily, aspirin delayed-release 81 mg daily, ibandronate 150 mg once a month, and the nystatin suspension 4 times daily (which she had been taking for 2 weeks). She denied wearing any mechanical dentation and stated a possible history of oral thrush following a course of antibiotics. At this time, it was decided to switch her to escitalopram.

She was seen 1 month after escitalopram initiation and reported the thrush had resolved. She remained on escitalopram for 3 months but had minimal improvement in her depressive symptoms. It was then decided to retry the bupropion with the hope that the thrush was unrelated to the previous trial. The patient was counselled on preventative measures for dry mouth and instructed to follow up with her ears, nose, and throat physician to further discuss preventative options.

After a month of reinitiation on bupropion XL 150 mg daily, she reported no side effects aside from “slight worsening” of dry mouth. Two months later, she reportedly self-increased her dose to 300 mg daily in the context of worsening depression and shortly afterwards

the thrush returned. She was instructed to decrease the dose to 150 mg daily, reinitiate escitalopram 5 mg, and schedule a follow-up appointment. Unfortunately, the patient did not return to clinic for follow-up.

Discussion

To our knowledge, this is the first report describing the development of oral candidiasis associated with bupropion. While there are no known published case reports describing this adverse event with bupropion use, there are case reports^{9,10} discussing the development of aphthous ulcers. These reports however described the cases of a female adolescent and a 23-year-old, while ours describes the case of an elderly female. This is understandable given rates of *C albicans* carriage increases with older age,¹ which is the underlying etiology of oral candidiasis development but not of aphthous ulcer development.¹¹

In our case, other than advanced age, there were no additional risk factors identified. Given the elderly are more vulnerable to accumulation of bupropion and its adverse effects,^{12,13} it is possible that her age may have put her at greater risk for dry mouth,¹⁴ which may have then led to subsequent oral candidiasis development. It should also be considered however that alterations in saliva production can occur in affective disorders during periods of stress/acute anxiety irrespective of the antidepressant.¹⁵ The patient did complain of dry mouth on the lower bupropion dose, which could be considered impaired salivary gland function (a stated risk factor of oral candidiasis). Given this finding, and that the oral candidiasis developed upon rechallenge at the same dose each time, it appears likely that this was in fact an adverse event from the bupropion. According to the Naranjo Adverse Drug Reaction Probability Scale, the likelihood of this having been an adverse drug reaction is “probable,” as indicated by a score of 8 (the adverse event appeared after bupropion administration +2; the adverse event improved upon bupropion discontinuation +1; the adverse event reappeared upon readministration +2; there were no alternative causes identified to have independently have caused the reaction +2; the reaction was more severe when the dose was increased +1).¹⁶

It is important to consider alternative potential risk factors. This patient did have a diagnosis of polycythemia vera, an autoimmune condition that causes erythrocytosis.¹⁷ While a risk factor for development of oral candidiasis is having an autoimmune condition, specific complications of polycythemia vera do not include disrupting the normal oral flora. She was diagnosed with polycythemia vera about a year before initiating bupropion, also suggesting this was not the underlying cause. If

this had been an additional risk factor, it does not decrease the likelihood that the dose increase to bupropion 300 mg led to the oral candidiasis developing, given the clinical timeline of symptoms in relation to her dose increase. Per the package insert, dry mouth occurrence may be dose related, and the risk of development may be reduced by lowering the dose.¹⁸ This is supported by studies identifying the incidence of dry mouth being directly related to bupropion plasma concentrations.¹⁹ It is unfortunate that the patient was lost to follow-up following the dose decrease of bupropion to determine whether this may have been a dose-related adverse event.

The mechanism of dry mouth occurrence with bupropion is unknown, although a previous study evaluating side effects from bupropion, moclobemide, paroxetine, sertraline, and venlafaxine had dry mouth reported as a side effect in 35% or more patients across all 5 groups.²⁰ These agents vary widely in receptor affinities, making it difficult to determine the underlying mechanism. Bupropion specifically lacks appreciable affinity for histamine or muscarinic acetylcholine receptors,² which have been linked to xerostomia.¹³ It's suggested that antidepressants interfere with acinar and duct functions, which lead to alterations in blood flow of the salivary glands²¹; however, no literature was identified reporting the development of oral candidiasis with antidepressants.

Conclusion

This case demonstrates that oral candidiasis is a potential adverse event to screen for with bupropion. This adverse event may be more likely to occur in older adults, especially in those who report experiencing dry mouth. Clinicians should monitor older patients on bupropion for side effects such as dry mouth and be prepared to manage this side effect to reduce the risk of oral candidiasis development.

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