



## BUPROPION INDUCED DELAYED ONSET URTICARIA: A CASE REPORT

**Dr Sriparna  
Bhattacharyya**

MD, Psychiatry, Registrar, Department Of Psychiatry, Gauhati Medical College And Hospital, Guwahati

**Dr Suresh  
Chakravarty**

MD, Psychiatry, Professor, Department Of Psychiatry, Gauhati Medical College And Hospital, Guwahati

**ABSTRACT** Bupropion is an oral antidepressant which acts by inhibiting the reuptake of dopamine and noradrenaline from synapse. Apart from treatment of depressive disorders, it is used off-label for smoking cessation, treatment of attention-deficit hyperactivity disorder and obesity. Bupropion is generally well-tolerated and has a favorable safety profile. Till date there have only been few case reports of allergic skin reactions associated with bupropion. Apart from being a rare adverse reaction, the unique feature of delayed onset of allergic reaction may lead to underreporting of the phenomenon. Here we present a case report of a 30 years old male who presented with generalized urticaria after twenty-three days of bupropion initiation. This report serves to promote awareness among the clinicians about the association of delayed-onset allergic phenomenon with use of Bupropion.

**KEYWORDS :** Bupropion, Depression, Urticaria, Delayed Hypersensitivity Reaction, Pruritus, Skin

### INTRODUCTION

Bupropion (amfebutamone) is an aminoketone which acts as noradrenaline dopamine reuptake inhibitor (NDRI) and is approved by US-FDA for treatment of major depressive disorder, seasonal affective disorder and smoking cessation. The off-label uses include attention deficit/hyperactivity disorder, antidepressant-induced sexual dysfunction, depression-associated with bipolar disorder and obesity. The usual therapeutic dose range is 150-300mg/ day with maximum dose being 450mg/day in divided doses. Bupropion is generally well-tolerated and has a favorable safety profile. Till date there have only been few case reports of allergic skin reactions associated with bupropion. Here we present a case of delayed onset urticaria with use of Bupropion in an otherwise healthy adult male, recently diagnosed with major depressive disorder.

### Case Report

A 30 years old healthy male without any previous history of allergies or skin disorder had presented with a severely pruritic, erythematous rash all over his body which had started 4 days prior to presentation. The rash started from flexor aspect of his bilateral forearms and extended to his trunk and both lower limbs and excluded the face and neck. He was recently diagnosed with major depressive disorder and prescribed Tab Bupropion hydrochloride 150mg (sustained-release formulation) once daily in morning, which he had been taking for past 23 days. There was no history of use of another drug or herbal remedy concurrently with Bupropion. He also denied recent change in dietary habits, hygiene products (soaps, shampoo, detergents) or cosmetics. His condition did not improve with Tab Levocetirizine 5mg (at bedtime) and topical calamine lotion prescribed to him by a general practitioner 3 days ago. Initial physical examination revealed no abnormality in vital signs (pulse, blood pressure, respiratory rate and axillary temperature), cardiopulmonary, neurological, gastrointestinal and musculoskeletal systems. Apart from anxious mood, there was no abnormal finding in mental state examination. Cutaneous examination revealed multiple erythematous urticarial wheals over trunk and upper and lower extremities bilaterally. The findings of the routine blood investigations were within normal limit. Based on the history and clinical examination, the urticarial reaction was suspected to occur as a drug reaction to Bupropion. Bupropion was discontinued and the patient was asked to continue Tab Levocetirizine 5mg orally at bedtime and topical application of lotion consisting of diphenhydramine and calamine thrice daily after consultation with dermatologist. The urticaria subsided within 7 days and the antihistamine medications were discontinued after 10 days. The patient refused re-challenge with Bupropion and so for his mood symptoms, he was started on Tab Escitalopram 10mg once in morning and advised to follow-up periodically. The score on Naranjo Adverse Drug Reaction Probability Scale was 7 suggesting that Bupropion is a 'Probable' cause of urticaria in his case.

### DISCUSSION

Adverse effects of Bupropion range from mild (dry mouth, insomnia,

excess sweating, headache, rhinitis, gastrointestinal disturbances like nausea and vomiting) to severe (seizure, anaphylaxis, suicidality).<sup>[1]</sup> The prevalence of serious adverse reactions in bupropion users is 0.06%, of which 31.2% are cutaneous or allergic reactions, which include anaphylaxis, angioedema, erythema multiforme, Steven-Johnson's syndrome, generalized exanthematous pustulosis, serum sickness-like reaction.<sup>[2,3,4,5,6,7,8,9,10]</sup> The incidence of mild dermatologic reactions after bupropion use is between 1% to 10%.<sup>[11]</sup> These reactions are idiosyncratic and commonly subside after discontinuation of the drug.<sup>[11]</sup>

Bupropion-induced urticaria is an uncommon adverse reaction with an incidence of 1% to 2%, occurring more commonly in males less than 40 years of age.<sup>[12]</sup> While the exact mechanism is not known, the urticarial reaction is attributed to the structural similarity of Bupropion with amfepramone (a selective norepinephrine releasing agent) which is associated with stress-induced adrenergic urticaria. Alternatively, the patient might have had an allergic reaction to any of the other components involved in the tablet formulation.<sup>[3,4]</sup>

In contrast to other antidepressants which caused allergic reactions between day 1-14, allergic reactions in Bupropion users occur most frequently after day 15.<sup>[3]</sup> Bupropion lowers the level of anti-inflammatory factors, tumour necrosis factor  $\alpha$  (TNF  $\alpha$ ) and interferon gamma (IFN- $\gamma$ ) which may explain the delayed onset of urticaria in our patient.<sup>[13]</sup>

Drug re-challenge may be tried at a lower dose after the resolution of the allergic reaction with close monitoring and careful weighing of the clinical benefit and risk. In our patient, drug re-challenge was not tried as firstly, he had refused it and secondly, he had no previous history of any other antidepressant trial.

### CONCLUSION

To date there have been few case reports and only one large-scale study assessing the occurrence of urticaria associated with bupropion use. Further, the clinicians may miss the link between Bupropion and urticaria due to the delayed onset of the allergic phenomenon. This case report serves to sensitize the clinicians about the delayed allergic phenomenon associated with bupropion and highlights the importance of having a cautious and vigilant mind while looking for the causative agent. It also opens the scope of future research focusing on factors causing increased risk of allergic reactions in a Bupropion user.

### Key Message

The delayed onset of urticaria is an adverse reaction which is unique to Bupropion among all the antidepressants and is hypothesized to be due to the additional anti-inflammatory action of Bupropion. This case report serves to sensitize the clinicians about the delayed allergic phenomenon associated with bupropion and highlights the importance of having a cautious and vigilant mind while looking for the causative agent.

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