

Development of an incipient Stevens–Johnson reaction while on a stable dose of lamotrigine

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Abstract

Objective: To describe a case of a possible incipient Stevens–Johnson reaction while a patient had been on a stable dose of lamotrigine for several months and to consider the likely cause.

Methods: The history is recounted.

Results: One likely cause implicates differing effective doses of lamotrigine across differing brands and raises quality control issues.

Conclusion: The patient's severe reaction may reflect changing to a brand of lamotrigine that precipitously generated a higher serum level of lamotrigine.

Keywords: lamotrigine, bipolar disorder, skin reactions

History

A woman in her mid-thirties was diagnosed with a prototypic bipolar II disorder marked by oscillating melancholic depressive and hypomanic episodes for nearly two decades. She had been previously trialled by her general practitioner on two antidepressants, two antipsychotic drugs and one mood stabiliser without distinctive benefit.

After reducing and ceasing her medications I commenced her on lamotrigine according to a common 'slow titration' schedule (an initial dose of 25 mg nocte for a week and then increased by 25 mg a week to a maximum of 200 mg). At a two-month review, she reported that her mood swings had ceased when she reached a dose of 175 mg. She remained euthymic on the maintenance dose of lamotrigine 200 mg for a further three months before developing a severe rash.

A lamotrigine rash generally occurs on starting the medication, on escalating the dose too rapidly or on taking an excessive amount. None of these factors were operative, while both she and her partner were firm in rejecting any possibility of her having forgotten to take her medication and to have risked subsequent exposure to a high dose on recommencing it again. She was not taking any other medication at that time, so arguing against any drug interaction effect.

When asked about any brand changing, she stated that she had been unable to obtain her initially prescribed brand. After one week of taking the new brand of lamotrigine, a minimally itchy rash had developed on her right rib cage. A week later she developed swollen glands in her neck, headaches and sensitivity to artificial light. The rash then spread to almost her entire trunk, with some blistering symptoms indicative of an emerging Stevens–Johnson syndrome, toxic epidermal necrolysis or hypersensitivity syndrome, all potentially fatal conditions. She then ceased the lamotrigine and the rash completely disappeared over the next week, although she did have some withdrawal symptoms (i.e. headache, excessive thirst, metallic taste in mouth, nausea and feeling generally unwell). She did not present to me for another two weeks and thus I did not judge that a serum lamotrigine level would be informative, nor would a skin biopsy have been appropriate as the blistering had disappeared.

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Discussion

Lamotrigine-induced rashes are usually divided into 'benign' and 'serious', with representative data provided by Calabrese et al.¹ quantifying rates of 8.3% and 0% respectively in one sample and 13.1% and 0.1% in another. While there have been case reports² of late onset of side-effects, they have more been in the nature of neurological symptoms rather than rashes. I am not aware of any previous journal report of such a late-onset serious side-effect, although there are anecdotal reports on the internet. I have previously had patients report a loss of benefit when changing brands of lamotrigine and return of benefit when recommencing the brand initially established as beneficial. In this instance, it would appear that the second brand trialled by her may have effectively exposed her to a very high level of lamotrigine or, less likely, to a brand-specific excipient and induced the serious reaction.

The Therapeutic Goods Administration (TGA) requires generic medications to meet the same quality criteria and manufacturing standards – including equivalent drug plasma concentration profiles – but such data are provided by the manufacturer rather than being tested under the authority of the TGA prior to PBS listing and subsequently.

Conclusion

This case report and observations raise the issue of quality control of lamotrigine (for which there are some one dozen brands in Australia) to ensure its safety. If differing brands generate variable serum doses, there is the risk of some brands being 'ineffective' in clinical practice if the dose is low or risking serious and fatal side-effects if the dose is effectively high. Such a hypothesis would appear worthy of clarification by the TGA and by individual practitioners testing serum lamotrigine levels in any similar disquieting circumstances.

Disclosure

The author has received remuneration from one manufacturer of lamotrigine to give lectures on bipolar II disorder and the role of lamotrigine as a mood stabiliser.

References

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