Further Experience using Clarithromycin in Patients with Kleine-Levin Syndrome

Comment on Rezvanian and Watson. Kleine-Levin syndrome treated with clarithromycin.
J Clin Sleep Med 2013;9:1211-2.

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LETTER TO THE EDITOR

We read with interest Drs. Rezvanian and Watson's report of Kleine-Levin Syndrome (KLS) treatment with clarithromycin.¹ We appreciate their expansion upon our work using GABA-A receptor antagonists, including flumazenil and clarithromycin, for hypersomnia disorders.²⁻⁴ Our experience treating four KLS patients with clarithromycin follows.

In patient 1, clarithromycin 500 mg bid was added to chronic bupropion at spell onset. His next three episodes were truncated. After stopping clarithromycin, he experienced 3 typical episodes. Resuming clarithromycin at his next spell again decreased symptoms, and he remains on intermittent clarithromycin.

Patient 2 was treated unsuccessfully with oxcarbazepine, amphetamine/dextroamphetamine, modafinil, and theophylline. Clarithromycin 250 mg bid during a spell resulted in immediate improvement, which was sustained over one week. One week after then discontinuing clarithromycin, KLS symptoms returned.

Patient 3 experienced 3 KLS episodes/ year despite modafinil, amantadine, and bromocriptine. Clarithromycin was titrated to 500 mg tid for daily use. His only KLS episode during the next 10 months coincided with discontinuation of clarithromycin. However, he then developed a KLS episode while taking clarithromycin and decided to discontinue treatment, citing side effects.

Patient 4 experienced mild improvement from modafinil during an episode, while clarithromycin resulted in marked improvement. Despite accompanying nausea, she plans to take clarithromycin (500 mg bid) with subsequent episodes.

All four KLS patients responded at least partially to clarithromycin, and benefit was sometimes sustained. Thus, in some KLS patients there might be a role for clarithromycin use, although optimal timing of treatment (e.g., chronic or only during a spell) remains to

be determined. Given KLS's medication-refractory nature, a medication effective in even a subgroup of patients may have clinical importance.

We agree that essential questions remain about mechanisms of KLS and clarithromycin. The activity of clarithromycin on GABA-A receptors⁵ is a parsimonious explanation for a benefit in sleepiness. However, the failure of flumazenil during a KLS episode, reported in two prior cases⁶ and in patients #1 and #2 above, suggests an alternate mechanism may be at work. Clarithromycin's anti-inflammatory actions might affect sleepiness via a reduction in soporific cytokines, or its antibiotic properties might result in a beneficial alteration in gut flora. Further treatment and mechanistic evaluations of clarithromycin are warranted.

CITATION

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DISCLOSURE STATEMENT

Dr. Trotti reports no conflicts of interest. Dr. Bliwise has served as a consultant for Ferring, New England Research Institute, Vantia, and Morehouse School of Medicine. Dr. Rye has received honoraria from or has consultancies with Jazz Pharmaceuticals, UCB Pharm, and Xenoport, and has US20110028418A1 patent pending for use of flumazenil in treating hypersomnia.