

*The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column is a composite with characteristics of several real patients.*

### Topiramate augmentation in a patient with obsessive-compulsive disorder

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A 31-year-old woman presented to an anxiety disorders clinic with a history of intrusive thoughts, including concerns about illness and contamination, and being responsible for bad things happening to loved ones. Her primary concern involved intrusive images of harming her 2-year-old son and she was fearful of being alone with him, particularly at bedtime. This patient was extremely distressed by these symptoms. In addition, she reported experiencing intrusive images of accident scenes and had a number of checking rituals that she completed each day, lasting about 30–40 minutes in total. She also reported comorbid symptoms of social and performance anxiety, excessive worrying, panic attacks and agoraphobic avoidance. She had had previous treatment trials of the selective serotonin reuptake inhibitors (SSRIs) sertraline and paroxetine, and her current treatment consisted of lorazepam 0.5 mg once daily when necessary and an oral contraceptive. Treatment was initiated with citalopram, titrated from 5 mg to 40 mg over a 12-week period. By week 16, the patient reported substantial improvement in her checking compulsions such that at times she was able to resist checking completely; when she did check, she went through her ritual only once. In addition, she reported substantial improvement in her social and performance anxiety, had had no panic attacks and was able to dismiss many of her worries about day to day issues. Unfortunately, the intrusive images of harming her son had not improved and continued to be very distressing and interfering.

First-line pharmacological treatments for obsessive-compulsive disorder (OCD) are SSRIs with effect sizes ranging from 0.37 to 1.09.<sup>1</sup> About 25%–60% of patients with OCD do not respond to initial SSRI treatment,<sup>2–4</sup> making treatment-refractory OCD the norm rather than the exception. In cases of treatment resistance, clinicians generally adopt one of several strategies, including continuing with the chosen SSRI for an extended period of time, raising the dose to the highest tolerated level, switching to another first-line treatment agent (usually another SSRI), or augmenting the SSRI with an agent from a different drug class.<sup>2,5–7</sup>

The patient's dose of citalopram was subsequently increased to 60 mg/d; however, she experienced excessive daytime somnolence and recurrent awakenings through the night. We reviewed potential augmentation strategies, including clomipramine, antipsychotics and anticonvulsants. The tricyclic antidepressant clomipramine has demonstrated efficacy as monotherapy for OCD;<sup>3,8</sup> however, there is limited evidence to support clomipramine augmentation with an SSRI.

Although the strongest evidence for SSRI augmentation in OCD is for antipsychotics,<sup>3</sup> the patient refused to take these agents for fear of metabolic syndrome. Over the past decade, the role of the neurotransmitter glutamate in OCD has attracted closer examination.<sup>9</sup> Glutamate is the main excitatory neurotransmitter in the adult brain.<sup>10</sup> Its primary function is on postsynaptic cells (Group I metabotropic and N-methyl-D-aspartate receptors); however, it also appears to have presynaptic action in the form of autoreceptor inhibitory feedback.<sup>11</sup> Literature on glutamatergic pharmacological agents in OCD is limited but emerging. The glutamate-modulating agent riluzole has demonstrated positive effects as an augmentation agent to an SSRI in case reports and open-label studies of treat-

ment-refractory comorbid OCD and major depressive disorder.<sup>12–14</sup> However, there has been a negative randomized controlled trial (RCT) in children with OCD using riluzole.<sup>15</sup> Lamotrigine has been reported to be beneficial in some case reports,<sup>16</sup> but not in others.<sup>17</sup> Topiramate is an anti-convulsant with a novel chemical structure. It has been used off label in clinical practice as an augmentation agent and as an alternative mood stabilizer in treating bipolar disorder, refractory depression, and binge-eating disorder. Augmentation with topiramate has shown some promise in the OCD literature in 1 RCT<sup>18</sup> as well as case reports and 2 open-label studies;<sup>19,20</sup> however, another RCT of adjunctive topiramate reported significantly improved compulsions, but not obsessions.<sup>21</sup> Nevertheless, we elected to start a trial of topiramate, which was initiated at 25 mg/d for 1 week and was titrated by 25 mg/d/week until she had reached a dose of 50 mg twice daily. Following 8 weeks of adjunctive topiramate treatment, this patient reported improvement in her intrusive thoughts and was able to put her son to bed on her own. After 12 weeks, she had achieved a full response. She was no longer worried about harming her child and denied any impairment in her day to day functioning. Although adverse events with topiramate are not uncommon, (particularly difficulties with parosmia, word-finding problems and short-term memory), this patient tolerated the treatment well and has been maintained on this treatment combination for more than 1 year without recurrence of OCD symptoms.

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