

Cyclic Vomiting Syndrome Association USA/Canada

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cyclic vomiting
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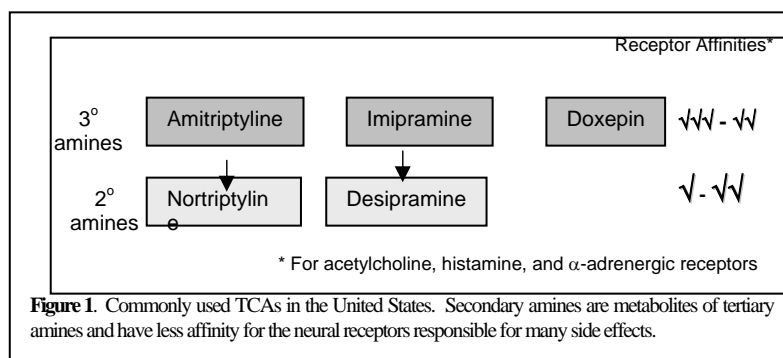
ANTIDEPRESSANTS FOR CYCLIC VOMITING SYNDROME

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Antidepressants are used to manage a variety of symptoms and syndromes other than psychiatric disorders. They are particularly useful in controlling functional symptoms, i.e., those with no definable pathological explanation.^{1, 2} Examples include irritable bowel syndrome, functional dyspepsia, and fibromyalgia. Antidepressants also are used to manage chronic pain syndromes, whether the pain is of unexplained origin or related to a defined medical condition. These agents have an important role in migraine prophylaxis and also have been used to suppress unexplained nausea and vomiting associated with functional gastrointestinal conditions.³ Consequently, it is not surprising that antidepressants have been offered to patients with Cyclic Vomiting Syndrome (CVS), and fortunately they have proven useful for both children and adults.

Two important observations are nearly uniform when antidepressants are used for management of somatic (non-psychiatric) symptoms, observations that hold true for CVS.⁴ The first is that benefits on the physical symptoms can be independent of the drugs' psychiatric effects. Although ratings on anxiety and depression scales may improve during antidepressant therapy, the benefits on pain, nausea, and vomiting, for example, typically are unrelated to these changes. Active psychiatric symptoms are not required for drug efficacy, and, in fact, may interfere with a positive response. The second observation is that not all antidepressants are equivalent in their ability to reduce somatic complaints.^{4, 5} The tricyclic antidepressants (TCAs), such as amitriptyline, nortriptyline, or desipramine, appear particularly useful, even in low daily dosages that would be considered subtherapeutic from the psychiatric standpoint. Onset of action with TCAs often is rapid, corroborating an action independent of usual anti-depressant effect and a characteristic not typically seen with more contemporary antidepressants, such as the selective serotonin reuptake inhibitors (SSRIs).

In CVS, clinical experience has been restricted almost exclusively to the TCAs.^{6, 7} No single TCA has surfaced as superior to the other for the syndrome, although amitriptyline is most often utilized. At least some attenuation of episode severity or frequency is observed in 80% of patients treated with these agents. Tricyclic antidepressants are used for maintenance therapy – not acutely to abort episodes. This high success rate with open-label use of TCAs only can be attained through careful dosage and drug adjustments depending on individual patient response. My experience in using these medications is restricted to older children and adults, but many of the treatment principles apply across all ages. One of the most common errors in clinical practice is failure to maximize the use of TCAs, possibly the most beneficial maintenance medication available for CVS. Failures are too often declared and treatment abandoned for unsatisfactory response at a suboptimal dose or when side effects interfere with therapy yet rational adjustment in drug or dosage has not occurred. The first error relates to dosage. CVS typically responds to TCAs at a low daily dosage, the average adult dosage being 50 mg per day for drugs in this class.⁶ However, the dosage range needed for response is large. What is a suitable "low dosage" for one patient may not necessarily be the correct dosage for another.



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Continued increment may be necessary, as long as side effects are not interfering with therapy, and failure should not be declared unless the patient remains unchanged on a full psychiatric dosage of the tested medication. One of the best predictors of eventual sustained response to TCAs for functional gastrointestinal syndromes is a prompt initial response.⁸

When the patient breaks through, the dose should be incremented until symptoms no longer occur. Finding the most effective maintenance dosage is sometimes difficult with CVS, because symptoms are sporadic. Nevertheless, treatment should not be abandoned without a fully escalated trial; at times TCA blood levels may be necessary to confirm that a maximal dose has been reached.

The second error relates to premature treatment discontinuation for side effects. Side effects are common with TCAs.⁹ As many as 30-40% of adult patients treated for functional gastrointestinal complaints will have interfering side effects, most typically sedation, other CNS alterations, and anticholinergic side effects (dry mouth, urinary retention, tachycardia).^{3,10} Initial sedation can be minimized by starting at a very low dose (10-25 mg per day for the adult-sized patient) and incrementing slowly, at 5 to 7 day intervals. Side effects also can be reduced by using secondary rather than tertiary amines within the TCA class (Figure 1). Although amitriptyline has received the most attention in CVS, many patients may better tolerate nortriptyline or desipramine.⁶ Weight gain and symptoms of orthostatic hypotension also are less pronounced with the secondary amines. Side effects that are less conspicuously related to the receptor affinities shown in the figure, such as nightmares or "zombie-like" feelings, may be eliminated simply by switching agents.

Patients often can appreciate beneficial effects while discriminating them from side effects, helping with their adherence in reaching a successful maintenance regimen. Educating the patient and family regarding potential side effects and methods used to manage or attenuate them is an important part of successful treatment. Other encouraging observations are that tachyphylaxis (an increasing need for medications because of loss of effect) is not observed, and retreatment following discontinuation of an initially successful agent is uniformly effective with the same medication. Breakthrough symptoms can be managed with transient dosage escalations. The potential exists for serious side effects, including syncope, seizure, and cardiac dysrhythmias. Serious side effects are seen in less than 5% of patients who use tricyclic antidepressants for chronic pain conditions, and they have not been reported in large series of adult patients given TCAs for functional gastrointestinal syndromes, the most common gastroenterological indications.

CVS is heterogenous in its pathogenesis, and no single therapy can have expected benefits for all patients. TCAs have no impact on vomiting episodes in some patients, but fortunately this is a minority. The successful therapeutic window for dosing may be narrow, however, and careful manipulation of drug and dose is necessary to achieve optimal outcomes for the majority that does respond. Further clinical observation will be required to determine whether contemporary antidepressants with better side effect profiles have an important role in CVS management. At present, we reserve these agents for the subset that fails to respond or is intolerant to TCAs, and full psychiatric dosages typically are employed. Despite the fact that some contemporary antidepressants, particularly the SSRIs initially can provoke nausea and vomiting from their effects on serotonergic neurons, such physiologic effects typically are transient and do not necessarily prohibit a therapeutic trial .

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Cyclic Vomiting Syndrome Association-USA/Canada, founded in 1993 actively pursues the following mission:

"CVSA USA/Canada will raise awareness, provide education and support to those affected by CVS and advocate for research about nausea and vomiting."