

## President's Page

# Cardiogenic Syncope and Serotonin Reuptake Inhibitors

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**T**he conventional pathophysiological view of the mechanism of neurocardiogenic syncope involves the activation of peripheral baroreceptors, as occurs in the Bezold-Jarisch reflex, in which there is a reflex withdrawal of sympathetic tone and an increase in parasympathetic tone. The result of these changes is a dramatic fall in blood pressure with or without excessive bradycardia, leading to a reduction in cerebral oxygenation and the manifestation of syncope.

However, this classical pathophysiological mechanism cannot fully explain all the aspects of the syndrome. Specifically, it cannot explain neurocardiogenic syncope in the case of a transplanted heart, which is known to be completely denervated. In this case it is not possible for nerve impulses from the inferior left ventricular wall (Bezold-Jarisch reflex receptors) to be conducted to the central nervous system.

Apart from peripheral mechanisms, the central nervous system appears to play an important role, and in particular the serotonin (sympathetic) system, given that the nuclei of the central nervous system that control blood pressure have a high content of serotonin neurons.<sup>1,2</sup>

Studying the responsiveness of the central serotonergic system, as estimated from the increase in plasma levels of cortisol and prolactin after the intravenous administration of clomipramine,<sup>3</sup> we observed that patients with neurocardiogenic syncope have an elevated central serotonergic response to clomipramine challenge.<sup>4</sup> Clomipramine is known to increase central serotonergic activity via the inhibition of serotonin reuptake by the neurons of the central

nervous system,<sup>5</sup> a fact that demonstrates the great importance of central serotonergic activity in the pathogenesis of syncope.

Furthermore, we have shown in other studies that the use of clomipramine during tilt testing significantly increases the diagnostic value of the test.<sup>6,7</sup> In addition, the administration of fluoxetine, a substance that acts on the central nervous system and inhibits serotonin reuptake, appears – via a reduction in central serotonergic activity caused during its long-term administration – to reduce the number of syncopal and presyncopal episodes of neurocardiogenic aetiology.<sup>8</sup>

Based mainly on the above studies, the guidelines for the diagnostic and therapeutic approach to neurocardiogenic syncope were recently updated.<sup>9,10</sup> Thus, they now recommend the use of clomipramine as a drug challenge for syncope during tilt testing, and fluoxetine in the therapeutic approach to patients with persistent neurocardiogenic syncope.

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