LETTERS TO EDITOR

VENLAFAXINE - INDUCED ORTHOSTATIC HYPOTENSION

Sir,

Venlafaxine is a selective serotonin-noradrenaline reuptake inhibitor available in the Indian market in immediate and extended release (XR) preparations. Although dose-related hypertension is the commonly reported adverse effect of this drug with an incidence ranging from 3 to 13% depending on the dose (Beauclair et al., 2000), we describe a patient who developed unexpected orthostatic hypotension and had no underlying cardiac compromise.

P.T., a 46-year-old male diagnosed with treatment-resistant bipolar depression was started on venlafaxine-XR at a dose of 37.5 mg/day. Then next dose hike was by 37.5 mg/day after four days with subsequent increase by 75 mg/day after a
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week's interval till a dose of 225 mg/day. His baseline blood pressure before commencing venlafaxine was 110/70 mmHg. At a dose of 225 mg/day, the patient started experiencing episodes of severe dizziness on getting up and even had a fall on two occasions. Blood pressure record showed a significant postural drop from 100/70 mmHg in the supine position to 50 mmHg systolic blood pressure with the diastolic component not recordable in the standing position. On reducing the dose of venlafaxine to 150 mg/day, there was a significant improvement in both the postural drop and the patient’s subjective condition with the former remitting completely after a week of reducing venlafaxine. There was no dysfunction of other autonomic functions or cardiac abnormality or any other evidence to suggest any central nervous system pathology. A previous cranial CT scan showed mild cerebral atrophy but revealed no discernible cause for this postural drop. As he was on two drugs, venlafaxine-XR (225 mg/day) and valproate (600 mg/day) we speculated that either of these two or an interaction between these might have lead to the orthostatic hypotension. However, there was no evidence in literature to implicate valproate alone or in combination with venlafaxine for this presentation. As reduction in the dose of venlafaxine paralleled the improvement in orthostatic hypotension, it was tempting to speculate that venlafaxine may have caused this picture. Indeed, some evidence did emanate to support this contention.

An EMBASE Psychiatry CD-ROM search using the key words 'orthostatic hypotension' and 'venlafaxine' along with a manual search yielded few reports citing the existence of this adverse effect with venlafaxine. According to one source book on drugs, postural hypotension occurred in 1% out of 1033 subjects on venlafaxine as compared to nil out of 609 subjects on placebo (Facts and Comparison, 1998). Another study demonstrated unexpected orthostatic hypotension in 13 out of 18 patients who incidentally had some cardiac decompensation as well (Wiese & Alderman, 1999). In the same study, the orthostatic hypotension was more severe at the initiation of treatment and when the dose was increased, a finding concurring with ours in this patient. The rate of orthostatic hypotension with venlafaxine is comparable with rates seen with selective serotonin reuptake inhibitors (Feighner et al., 1994). The underlying mechanism for this adverse reaction of venlafaxine is speculative. Blocking of post-synaptic a1-adrenergic receptors, which is responsible for orthostatic hypotension, is minimal for venlafaxine in view of its considerably lower affinity than tricyclic antidepressants for binding with this receptor site (Holliday & Benfield, 1995). However, some binding with these receptors still occurs which may be idiosyncratically high in some patients resulting in a postural drop.

Thus to conclude a clinician needs to bear in mind that venlafaxine, besides causing the usually known adverse effect of hypertension, can also lead to a significant orthostatic hypotension especially at higher doses. Whether this adverse effect is related to an underlying cardiac compromise or occurs idiosyncratically or is a harbinger of incipient dysautonomia needs to be addressed.

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HARPREET S. DUGGAL, DPM, Resident, K. JAGADHEesan, MD, Senior Resident, S. HAQUE NIZAMIE*, MD, DPM, Director and Professor of Psychiatry, C.I.P. Kanke, Ranchi - 834006.
*Correspondence