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LETTER TO THE EDITOR

Elevation of blood pressure induced by high-dose milnacipran

Dear Editor

Milnacipran is a novel serotonin and noradrenaline reuptake inhibitor (SNRI). Spencer and Wilde (1998) reported that milnacipran produced no more adverse events than placebo and SSRIs, and fewer adverse events than tricyclic antidepressants. There has been little information about the elevating effect on blood pressure of milnacipran (Caron *et al.*, 1993) and there have been no case reports of hypertension induced by high-dose milnacipran. We present a patient with major depressive disorder whose blood pressure elevated during the treatment of high-dose milnacipran.

The case was a 53-year-old man. He had no previous history of hypertension or other cardiovascular diseases. He came to our hospital because he suffered from sadness, insomnia, reduced appetite, concentration difficulties and lassitude. He had lost 4 kg of weight in the past 2 months. Physical examination and laboratory studies, including thyroid-stimulating hormone and free thyroxin, were normal. His blood pressure was 120/80 mmHg. He was diagnosed with major depressive disorder and administered milnacipran of 50 mg/day (bid). Brotizolam 0.25 mg was given at bedtime. The dosage of milnacipran was increased to 100 mg/day (bid) after a week. Six weeks after beginning on milnacipran, his sadness, insomnia and reduced appetite ameliorated completely. His lassitude and concentration difficulties partially remained and he could not work efficiently. We prescribed 150 mg/day (tid) of milnacipran to improve the remaining depressive symptoms. Two weeks after increasing milnacipran, his blood pressure went up to 150/100 mmHg without any subjective symptoms. His lassitude and concentration difficulties remained unchanged. We reduced the dose of milnacipran every 2 weeks, 125 mg/day (tid) to 100 mg/day (bid). His blood pressure went down from 140/95 mmHg to 135/85 mmHg following the reduction of milnacipran.

The optimal dosage of milnacipran is 100 mg/day (bid) based on clinical trials, but the efficacy of higher dosages of milnacipran is suggested (von Frenckell *et al.*, 1990). Venlafaxine is one of the SNRIs. The ordinary dosage of venlafaxine is up to 275 mg/day, but higher dosage (approximately 350 mg/day) was reported to be effective in hospitalized patients with major depression and melancholia (Guelfi *et al.*, 1995). Thase (1998) reported that venlafaxine elevated supine diastolic blood pressure at high dosages of more than 300 mg/day in a meta-analysis of original data from 3744 depressed patients. High dosage of milnacipran may cause elevation of blood pressure as does venlafaxine, possibly through potentiating the noradrenergic neurotransmission. Thase (1998) stated that careful serial monitoring of blood pressure was clearly indicated for patients taking venlafaxine in a dose of more than 300 mg/day. When milnacipran is prescribed in a dosage of more than 100 mg/day, careful observation of blood pressure is needed.

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