HUMAN PSYCHOPHARMACOLOGY
Hum Psychopharmacol Clin Exp 2002; **17**: 195–196.

LETTER TO THE EDITOR

Remarkable effect of milnacipran in the treatment of Japanese major depressive patients†

Dear Editor

Milnacipran is a new specific serotonin and noradrenaline reuptake inhibitor (SNRI) that has been shown to be equally as effective as tricyclic antidepressants (TCAs) in the treatment of depression (Kasper *et al.*, 1996). Milnacipran has been recently marketed in Japan. We first investigated the antidepressant effect of milnacipran in Japanese patients with major depression in a fixed-dose regimen. We also investigated the relationship between the clinical effects and the plasma levels of milnacipran, because there has been no report on the relationship between the antidepressant response and the plasma levels of milnacipran, except for a preliminary report dealing with 17 patients only (Retz *et al.*, 1995).

Thirty-two patients meeting the DSM-IV diagnosis of major depressive disorder without psychotic features, whose score on the Montgomery and Åsberg (1979) depression rating scale (MADRS) was more than 20 points, were included in this study. One case was excluded from the analysis of this study because of his poor compliance. The patients were free from psychotropic drugs for at least 14 days before their entry into the present study. The mean age of 31 patients (8 males, 23 females) was 51.5 ± 13.2 years. The mean entry MADRS score was 29.6 ± 5.4. All patients provided informed consent. Milnacipran was administered two times daily (after dinner and at bedtime in the same dose) for 6 weeks. The daily dose was 50 mg/day for the first week, and up to 100 mg/day thereafter. No other psychotropic drugs were given except for occasional brotizolam (0.25 or 0.5 mg) as a hypnotic. Depressive symptoms were evaluated by the MADRS just before and at 1, 2, 4 and 6 weeks after the beginning of this study. A clinical response was defined as a 50% or greater decrease in the baseline MADRS score. Blood samples were collected almost 12 h after the last dose at 4 weeks after beginning this study, and were analysed using the high-performance liquid chromatography (with fluorescent detector) method by Asahi Kasei Corporation (Japan).

Twenty-three patients (74%) were responders according to the definition mentioned above. This response rate for milnacipran was considerably higher than that in the Caucasian major depressive patients reported by Kasper *et al.* (1996). Figure 1 shows the change of MADRS scores during treatment in responders and non-responders. Significant differences were seen from one week after the beginning of this study ($p = 0.005$, unpaired t-test) between responders and non-responders. This rapid response to milnacipran in the treatment of Japanese major depressive patients is worthy of note. It is necessary to confirm these results in a large number of patients in the future.

The plasma milnacipran levels of the 31 patients ranged between 44.3 and 156.8 ng/ml. The mean plasma milnacipran level of the responders, 87.5 ± 30.8 ng/ml, was similar to that of the non-responders, 86.9 ± 25.6 ng/ml; there was no significant difference between responders and non-responders. In the present study, no significant correlation was found between the plasma levels of milnacipran and the antidepressant response. This result was similar to the findings of a preliminary report (Retz *et al.*, 1995). However, there are several reports suggesting a significant relationship between plasma levels and the clinical effect of TCAs in endogenous depression or major depression with melancholia. Therefore, it is necessary to investigate the relationship between plasma levels and the antidepressant response of milnacipran in major depressive patients with melancholia in the future.

†This study was presented at the 2nd International Forum on Mood and Anxiety Disorders (28 November–1 December, 2001, Monte-Carlo).

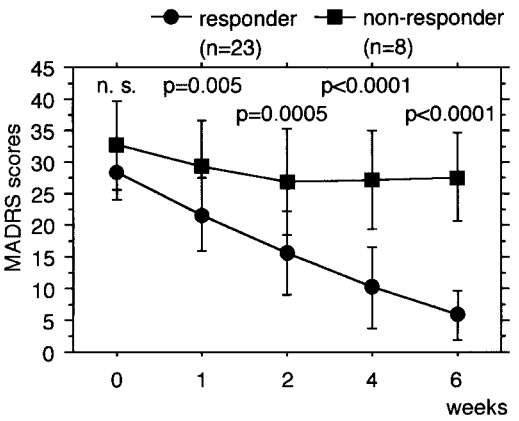

Figure 1. Change of MADRS scores during treatment in responders and non-responders. Each point represents the mean ± SD scores

REFERENCES

Kasper S, Pletan Y, Solles A, Tournoux A. 1996. Comparative studies with milnacipran and tricyclic antidepressants in the treatment of patients with major depression: a summary of clinical trial results. *Int Clin Psychopharmacol* **11**(Suppl. 4): 35–39.

Retz W, Becker T, Schmidtke A, Riedener P, Beckmann H. 1995. Multiple and single dose pharmacokinetics of milnacipran in major depressive patients (abstract). *Eur Neuropsychopharmacol* Sep; 5 Spec. Issue: 296–297.

Montgomery, Åsberg. 1979.

HISASHI HIGUCHI[1], KEIZO YOSHIDA[2]
HITOSHI TAKAHASHI[2], SHINGO NAITO[2]
KEI TSUKAMOTO[2], MITSUHIRO KAMATA[2]
KENICHI ITO[2], KAZUHIRO SATO[2]
TETSUO SHIMIZU[2]
[1]*Omagari City Hospital, 210 Aza Sekihigashi Iida, Omagari, Akita 014-0067, Japan*
[2]*Department of Psychiatry Akita University School of Medicine 1-1-1 Hondo Akita 010-8543, Japan*
DOI: 10.1002/hup.392

