Letters to the Editor

Dr Portella and Colleagues Reply

To the Editor: In his letter to the editor, Prof Terao doubts whether pindolol can enhance, apart from accelerate, the antidepressant effect of selective serotonin reuptake inhibitors (SSRIs). As correctly stated by Prof Terao, a number needed to treat (NNT) higher than 10 is not clinically meaningful, and therefore an NNT of 13 regarding late clinical response is not relevant. The results of our meta-analysis show that pindolol accelerates antidepressant effects within the first 4 weeks, but not for any longer, as previously reported by Ballesteros and Callado1 and Whale et al.2

It should be emphasized that our conclusion regarding enhancement of antidepressant effect by pindolol is based on the results of a clinical trial3 in which pindolol treatment clearly increased the likelihood of sustaining remission until the end of the 6-week trial when using a binomial regression model to account for the number of remissions experienced throughout the trial. Indeed, animal studies using pindolol suggest that it occupies a significant proportion of presynaptic 5-HT1A autoreceptors,4 thus preventing acute self-inhibitory mechanisms on serotonergic neurons. In the letter by Terao, it is argued that once 5-HT1A autoreceptors are desensitized, pindolol cannot further block the 5-HT1A autoreceptor-mediated negative feedback on serotonergic activity.

Nevertheless, 2 aspects may contribute to the observed remission rates in our clinical trial. First, the degree of 5-HT1A autoreceptor desensitization evoked by antidepressant drugs in patients is unknown and may presumably be lower than 100%. This would leave room for pindolol to further prevent 5-HT–mediated self-inhibitory actions. Second, in addition to augmenting the effects of SSRIs on 5-HT release, pindolol also elevates cortical catecholamine release by complex and still poorly understood mechanisms.5 In light of the apparent benefits of achieving an early response and maintaining remission from the beginning of treatment, we believe that it is not too much of a speculation to conclude that there is an improvement of antidepressant effects with coadministration of pindolol in the first weeks.

References


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