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 Callado[1] 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 trial[3] 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-HT_{1A} autoreceptors,[4] thus preventing acute self-inhibitory mechanisms on serotonergic neurons. In the letter by Terao, it is argued that once 5-HT_{1A} autoreceptors are desensitized, pindolol cannot further block the 5-HT_{1A} 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-HT_{1A} 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.

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