Relation between the remission of depression and quality of life perceibed by the patient

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Dear Editor,

Mental disorders, especially depression, are an important health problem whose growing prevalence is observed in the Primary Care and Mental Health Medical Offices.[1] A comprehensive approach for depressive disorders in which primary care professionals and mental health professionals work in a coordinated and complementary way is important.[2] There is evidence available that the chronic care models aimed at depressed patients seen in primary care are effective to improve the care process and clinical results.[3]

Our group has designed a care model to improve the approach to depression in primary care: the INDI model - Interventions for Depression Improvement -. This is a structured program based on the chronic care model[4] that includes different components having a clinical, training and organizational character. The INDI program has been evaluated by means of a clinical trial in which its effectiveness was measured against the usual care during a one-year follow-up period.[5] As outcome variables, we calculated depression-free days (DFD) based on the symptomatic severity scores of depression measured with the Patient Health Questionnaire (PHQ-9)[6] and we also measured the health-related quality of life with the SF-12 questionnaire. Based on this, we could calculate the quality adjusted life years (QALF),[7] even though there is a debate about whether the generic instruments of quality of life are appropriate for the evaluation of psychological interventions.[8]

We determined that the INDI model gives rise to better health results than the usual treatment.[9] However, it has caught our attention that both outcome variables, a measurement with clinical meaning based on depressive symptoms, the DFD, and another based on perception and evaluation by the patient per se on his/her health (the "utility" of the quality adjusted life days) differ relevantly. With the INDI model, an incremental clinical efficacy was obtained (versus the usual treatment and during one year of follow-up) of 40.09 DFD and incremental utility of 0.045 additional QALF (corresponding to 365 x 0.045=16.4 days lived with full quality).8 Thus, we observe a ratio of 1:0.41 between the DFD - reflection of the clinical perspective - and the quality adjusted days - that would represent the perspective of the patient on his/her own improvement. This information seems to indicate that the subjective improvement perceived by the patient is significantly less than the clinical improvement observed.

This observation quite accurately reflects that found in the scientific literature. A study by Reviki[10] determined that the transition from a depression state to remission is associated to an improvement in the "utility" perceived of 0.35, while Lave,[11] after reviewing the literature, proposes that a gain of 0.41 quality-adjusted days for each depression free day achieved can be assumed. In a recent clinical trial on a *collaborative care* intervention conducted in primary care sites in Germany, the disproportion is even greater and we can calculate that there is only an improvement of 0.12 quality-adjusted days for each depression free day gained.[12]

Evaluating only the clinical symptoms for judging the evolution of the depression or effectiveness of the treatment may be insufficient if we do not also consider the patient's perspective on his/her own health, functionality and quality of life perceived. And for the same reason, the therapeutic approach (pharmacological or non-pharmacological) of the depression should not be limited to orientation towards achieving relevant symptomatic responses or remission - understood as the absence of depressive symptoms. It should also adopt a wider perspective that would make it possible to include dimensions of subjective improvement perceived and evaluated by the patients (wellbeing, functionality, social relations, physician health, etc.) going beyond the strict depressive symptoms as treatment objectives and as part of the definition itself of depression.[13]

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Combined use of desvenlafaxine and electroconvulsive therapy

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Dear Editor,

Electroconvulsive therapy (ECT) remains a reference treatment in severe depression, especially in those cases resistant to pharmacotherapy[1,2]. However, in the last decades, new antidepressant drugs that look promising in terms of efficacy have emerged. One might think that the combination of ECT and serotonin-norepinephrine reuptake inhibitors (SNRIs) could bring benefits, or even synergism, in the treatment of some depressive states. Yet, clinical guidelines address this issue superficially[3]. Somehow, the current situation is not so different from that described in 1993 by Pritchett et al., who, in their review about combined ECT and antidepressants, warned of the lack of studies[4].

Desvenlafaxine is a novel antidepressant approved for the treatment of major depressive disorder. Its mechanism of action resides in the inhibition of serotonin and norepinephrine reuptake, with a weaker dopaminergic action and no significant affinity for other neurotransmission routes[5]. It has proven efficacy in depression at doses from 50 mg/day[6].

We present two cases of depression in which ECT and desvenlafaxine were administered concurrently.

Clinical Cases

In both cases, patients and their closest relative signed an informed consent. Prior to the start of ECT, patients were evaluated by an anaesthesiologist. Physical examinations and additional tests showed strictly normal results.

The employed ECT machine was *THYMATRON™ DGx*. This device generates a bidirectional pulse at width between 0.5 and 1.5 msec. In both cases, stimulus electrodes were placed at the standard bitemporal position. Initial output was determined by titration. The presence of ictal response was observed by EEG recording following the stimulus. EKG and blood pressure were monitored throughout the entire procedure. In both patients, sedation was performed with etomidate and succinylcholine.

Case 1

A 56-year-old woman suffering from a major depressive episode with psychotic features[7] was admitted to our psychiatric ward and proposed for ECT. As psychiatric background, she presented a depressive episode ten years before with complete remission with pharmacological treatment. She had remained asymptomatic until six months prior to admission, when she showed depressive symptoms again, with lack of response to pharmacotherapy. At admission, she presented an inexpressive face, downcast with limited and hypophonic speech and showing hypochondriacal delusions. She still presented significant apathy, demotivation, anhedonia and a subjective feeling of affective anesthesia. She verbalized wishes of death. HDRS score of 42 was observed.[8] Upon admission to our clinic, she was having imipramine 300 mg/day, quetiapine 400 mg/day, clorazepate dipotassium 75 mg/day, lormetazepam 2 mg/day, atorvastatin 20 mg/day and levothyroxine 50 mcg/day. Her responsible psychiatrist decided to withdraw imipramine and instead start a 50 mg/day treatment with desvenlafaxine in parallel to ECT. The dosage of desvenlafaxine was progressively increased up to 200 mg/day with satisfactory tolerance. The patient received twelve sessions of ECT. The observed secondary effects were primarily cognitive: mild anterograde amnesia and spatial and temporal disorientation of short duration. Physically, she complained of headaches and also presented a recurring shoulder dislocation that required transient immobilization (which had already been

diagnosed). The rest of clinical parameters (haemodynamic, etc.) were in the normal ranges. After clinical improvement she was discharged to continue her follow-up at an outpatient clinic.

Case 2

A 76-year-old woman was admitted for ECT due to a severe and resistant depressive episode, without psychotic features[7]. She had been previously treated for bipolar disorder for more than twenty years, with a predominance of depressive phases throughout her illness. She had not previously received ECT. For several months, she showed a depressive mood with slow motor skills, apathy and anhedonia as well as other melancholic features, having experienced no improvement after several pharmacological combinations, including treatment with lithium. She scored 37 at HDRS[8].

At admission, her pharmacological therapy consisted of a 100 mg/day of desvenlafaxine and 30 mg/day of mirtazapine, which were adequately tolerated. During admission, she received a course of five ECT sessions, which took place without incidents. 100 mg/day of quetiapine were added to her previous pharmacological regimen, showing a complete remission of her depressive symptoms. Observed secondary effects were mainly cognitive, suffering from transient temporal disorientation with recent memory alterations. No other adverse symptoms were found.

Discussion

In both cases, although from different approaches (a replacement strategy in the first one while maintaining previous antidepressant in the second one), the responsible psychiatrist decided to add desvenlafaxine in an attempt to enhance the effect of ECT. However, not much literature confirms the efficacy of this approach, especially concerning SNRIs[9]. For example, in a published clinical trial, concomitant use of venlafaxine increased ECT short-term antidepressant efficacy, though it showed a weaker degree of improvement than nortriptyline[10].

Another issue of importance is the one concerning the safety of the ECT-antidepressant combination. Antidepressants can directly influence the outcome of ECT (e. g. modulating seizure threshold) but may also interact with other drugs used during the whole procedure, such as anaesthetics. For a detailed review of these interactions, particularly in regard to classic drugs, we refer to the work of Naguib et al.[11]

Some clinical series and trials have been published, studying the safety of the concomitant use of venlafaxine with ECT. In a study of 21 bipolar and depressed patients undergoing ECT and venlafaxine (daily doses from 150 to 225 mg), no serious complications appeared. Concentration problems and headaches were observed in more than half of patients[12]. Similarly, no cardiovascular complications or prolonged seizures were detected when venlafaxine was compared to nortriptyline (although in this case venlafaxine tended to worsen cognitive adverse effects)[10].

As for duloxetine, the available evidence for its safety in combination with ECT is much lower. In two published reports (3 patients in total), concomitant use was safe, without cardiovascular complications or other serious events[13,14]; while in a fourth patient, a post-ictal ventricular tachycardia appeared. To explain it, the authors took into account the role of lithium, which the patient was also taking, and a possible interaction with succinylcholine[15].

With respect to the combination of ECT with other SNRIs, a search of the published literature failed to identify any relevant references. While this is a first report on desvenlafaxine and ECT, investigations with minalcipran or levominalcipran along with ECT are still to be published.

In our two cases, the combined use of desvenlafaxine and ECT was safe and well tolerated (though it is worth mentioning post-ECT symptoms of headache and mild confusion). Considering the pharmacokinetics of desvenlafaxine, with very low metabolism via hepatic cytochrome P450, some authors have suggested that its tolerance profile might be beneficial compared to other antidepressants (such as venlafaxine). Desvenlafaxine would have a more predictable pharmacokinetic behaviour, leading to fewer interactions and side effects[16,17]. However, some of those, such as the risk of seizure induction, are not well established in the literature. For our part, awaiting further evidence, we simply intend to point out that desvenlafaxine might have a role as adjunctive therapy to ECT, especially in severe or resistant depression.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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