Pro and Contra

Selective Serotonin Reuptake Inhibitors for the treatment of major depression in patients with heart failure

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Pro

Major depression is the most severe mental health problem worldwide, in Europe and in Germany (12). Psychiatric treatment guidelines for severe major depression strongly recommend treatment with antidepressant drugs as in severe major depression they have consistently been shown to be superior to other interventions. These recommendations are in general based on studies in somatically healthy patients (6).

In recent years, particular focus has been given to comorbid situations such as the comorbidity of depression with heart disease in general and heart failure in particular. The relationship is bidirectional. Life time major depression increases the risk to develop coronary disease and heart failure later in life by the factor 2 to 3. Vice versa, comorbid major depression significantly and markedly increases mortality risk in coronary disease and heart failure. Given the strength of this reciprocal relationship, specific treatment of major depression aside of the therapy of heart failure signs and symptoms may thus contribute not only to improved quality of life, but also to reduced mortality (7, 11, 13, 16).

The use of antidepressant drugs in cardiovascular patients, however, is problematic given typical adverse effects such as prolongation of QTc intervals (17). Given their relative benign profile of adverse effects and their relative superiority compared with other antidepressant drugs as regards adverse effects in patients with heart disease (5), studies in cardiovascular patients have focused on selective serotonin reuptake inhibitors. Although study results were inconsistent, some positive treatment effects of selective serotonin inhibitors on depression outcomes and/or cardiovascular status including mortality risk were observed in patients with coronary heart disease and myocardial infarction (10, 15, 16, 20).

Based on these considerations and data and extending observations from comorbid major depression and coronary heart disease to comorbid major depression and heart failure, the drugs considered safest and recommended for the pharmacological treatment of major depression associated with heart disease in general are selective serotonin reuptake inhibitors (1, 11, 16).

Contra

Studies in patients with heart failure clearly demonstrate the relevance of major depression for the prognosis of this condition. The need for intervention thus is consensus between psychiatrists and cardiologists (3, 13, 19). The question is what is the treatment of choice?

There is a considerable lack of data on the safety and efficacy of antidepressants such as selective serotonin uptake inhibitors in major depression with heart failure. Until now the only randomized controlled study in a heart failure population demonstrated the safety of sertraline, but no positive effect on depression and cardiovascular status after 12 weeks (14). On the other hand QTc prolongation was observed also with selective serotonin reuptake inhibitors (e.g. 18), and in 2011/2012 so-called red hand letters were issued warning against the use of (es)citalopram particularly in elderly patients with heart disease.

In general the question arises whether the extrapolation of treatment studies and practice from major depression without comorbidity (6) or with coronary disease (10, 20) on major depression with heart failure is justified. There is considerable evidence that symptomatology (3) as well as etiology of major depression in heart failure may differ from that of primary major depression. In fact, using the 9-item Patient Health Questionnaire to assess depressive symptoms and the Kansas City Cardiomyopathy Questionnaire to evaluate patient-reported functional status in over 800 patients, Faller et al recently reported that depressive symptoms were no longer significant predictors of mortality risk after adjustment for heart failure severity and co-

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morbidities as well as patient-reported functional status, which by itself proved predictive of mortality risk (8).

As alternatives to selective serotonin reuptake inhibitors, there is good evidence that in addition to optimized cardiovascular treatment both exercise (4) and psychosocial and medical interventions implicating optimization of heart failure therapy (9) are safe and effective measures with proven survival benefits in populations suffering from both heart failure and depression, which recommends them as treatments of first choice.

However, there are no data yet analyzing the additional effect of selective serotonin inhibitors on top of optimized cardiovascular treatment, comparing their effects with that of a psychosocial intervention or studying their longterm effects over a period of at least 6 months, which is generally considered the minimum medication time for the treatment of major depression (6). To answer these open questions, the MOOD-HF Study was designed. All patients received optimized heart failure treatment plus a standardized psychosocial intervention for up to 24 months. 376 patients were randomized either to treatment with the selective serotonin reuptake inhibitor escitalopram or one with placebo (2). Results of this study will be published in 2015.

Conclusions and perspectives

The complex reciprocal effects of heart disease and negative emotional states have so far obscured better understanding of pathophysiological pathways and impeded the development of evidence-based treatment strategies for subjects suffering from both heart failure and depression. Optimized cardiac treatment, exercise and psychosocial interventions appear to be effective and safe interventions. In heart failure, the only published randomized study on efficacy and safety of treatment of major depression with selective serotonin reuptake inhibitors failed to demonstrate beneficial effects. Further prospective research is needed to ascertain the benefits of tailored interventions and to establish more precisely the effects of their specific components.

References


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