Placebo treatment in mild to moderate depression

Most patients with depression seen in primary care have mild to moderate depression. In trials these patients respond equally well to placebo as to pharmacologically active treatment. We discuss the role of placebo treatment in this situation.

An estimated 3 million people in the UK are currently depressed, with winter and the economic situation likely to increase this number. Even without screening for depression in primary care it is likely that more patients with sub-threshold to moderate depressive symptoms will require care.

A recent paper by Fournier and colleagues showed that the pharmacological management of mild and moderate depression is based on poor evidence. They, and others, found that for mild to moderate depression placebo is as effective as antidepressant treatment. Fournier and colleagues concluded that ‘there is little evidence to suggest that they produce specific pharmacological benefit for the majority of patients with fewer severe acute depressions.’

Furthermore, in clinical care, patients with mild to moderate depression can be expected to have a better placebo than in clinical trials and the placebo response has been shown to persist over time.

Current NICE guidance recommends sleep hygiene, active monitoring, and low-intensity psychosocial interventions but advises against antidepressants routinely to treat persistent subthreshold depressive symptoms or mild depression because of a poor risk–benefit ratio.

Where to from here: sleep hygiene, active monitoring, and low-intensity psychosocial interventions are first-line treatment but access to psychological therapies remains a problem.

We believe that it should be possible to augment (not replace) these options with a drug that does not carry the risks of antidepressants, is significantly cheaper, and is equally effective for mild to moderate depression — a placebo.

Folic acid is essential for the synthesis of monoamines and may well be the most suitable placebo. It may even have intrinsic activity and is currently the subject of a randomised controlled trial as an augmenting treatment in moderate to severe depression.

We recently recommended an approach to the safe use of placebo treatment and believe that for patients with mild to moderate depression who cannot access psychological therapies immediately, such an approach would be more honest, ethical, evidence-based, safer, and cheaper than the use of selective-serotonin reuptake inhibitors. The period when a patient is receiving sleep hygiene, active monitoring, and low-intensity psychosocial interventions should also be used for placebo treatment.

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References


Depression management

We feel the need to raise two key issues regarding the management of depression at a primary care level. First, the importance of recognising occult bipolar II disorder (depression with episodes of hypomania) in a primary care setting. Such patients often present with episodes of major depression and thus screening for symptoms of hypomania may be overlooked. Moreover, there may be a lack of recognition by the patient of their, often quite brief, hypomanic episodes particularly in their depressed state. The treatment for bipolar II disorder, however, differs significantly from that of patients with major depression: mood stabilisers versus antidepressants. Besides, treating bipolar II patients with the standard cocktail of antidepressants runs the risk of driving such individuals into rapid cycling and mixed affective states. Notably, these states are associated with a high risk of suicidality and hence the importance of not missing bipolar II disorder.

Second, there is a growing body of evidence suggesting the adoption of a collaborative (shared care) model in depression management. This involves the introduction of case managers (mental health workers who are responsible for regularly following up patients, offering psychotherapy, and medication management) working with GPs. From our own experience in Luton, we found the deployment of community mental health nurses in both the primary and secondary care settings acting as both case managers and as a liaison between both teams produced high levels of patient satisfaction, and GPs felt a reduced need for referral to specialist services. Such an approach to care would help to better manage potential occult bipolar II patients as well as the risk of patients running into mixed affective or rapid cycling states. Furthermore, there is strong evidence indicating the clinical effectiveness of collaborative care, with regard to short and long-term depression outcomes as well as cost savings for major episodes of depression. However, further randomised controlled trials in a UK setting would be