Randomised controlled trial of Antiglucocorticoid augmentation (metyrapone) of antiDepressants in Depression (ADD Study)

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Plain English summary

The ADD Study

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Plain English summary

Depression is common and can have a terrible impact on patients and their families. Guidelines recommend talking therapies for patients with milder depression and adding antidepressants for moderate and severe depression. However, antidepressants work in only about 70% of sufferers. Why this happens is not known. One possibility is that increases in the stress hormone cortisol may reduce the effectiveness of antidepressants. Cortisol rises when people are stressed and may stay high in depression. Raised cortisol reduces the effect of antidepressants on the chemicals in the brain, which are thought to be important in how they work. Small studies have suggested that reducing the level of cortisol produces better outcomes for depression. We have tested the drug metyrapone, which blocks the production of cortisol, in a group of 165 people who remained depressed after previous treatment with at least two antidepressants. Metyrapone was given for 3 weeks. We investigated whether or not it led to benefits over the next 6 months compared with a group of similar people who received dummy tablets. Both groups of depressed people improved but there was no difference between them. There was also no difference in anxiety scores or quality of life with metyrapone treatment. Changes in memory, processing emotions and brain function were found in the depressed patients but no effects of metyrapone were found. It appears that this particular drug does not produce benefits for such patients. Further research is needed to find a treatment that reduces the effects of cortisol and improves the outcome for depression.

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