

35 - Maintenance treatment

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Depression and anxiety disorders CHAPTER 3 Ketamine formulations Many of the more recent studies include ketamine and esketamine, which are increasingly used to treat MDD and bipolar affective disorder,¹⁶ and are possibly efficacious for psychotic depression.¹⁷ Evidence is limited because people with psychotic depression are usually excluded from clinical trials owing to the concern that these drugs may worsen psychotic symptoms, albeit transiently.^{17,18} Le et al.¹⁷ reviewed the evidence for the use of ketamine in the treatment of psychotic depression. This comprised two case series, three case reports (n = 1), one retrospective chart review (n = 12) and one secondary analysis of a randomised controlled trial (n = 10). Most patients received ketamine 0.5mg/kg IV (fewer received SC), infused over 40 minutes. The number of treatments was very varied, ranging from one to seven over a number of weeks (approximately 3-8 weeks). The patients in the retrospective chart review were given 30-120mg intranasally at intervals of 3-7 days. A 2023 study¹⁶ examined the effects of add-on ketamine (0.5mg/kg IV twice a week) in 36 patients and found improvements in all domains. Overall, these lines of evidence indicated that ketamine reduces depressive symptoms and, in a few cases, psychotic symptoms as well. The review did not describe any patients experiencing a worsening of psychotic symptoms. However, all these studies had very small sample sizes. A case series including four patients also provides some limited evidence for the safety and efficacy of esketamine (0.5mg/kg IV or SC) for the treatment of TRD with psychotic features.¹⁹ ECT There is a role for ECT in the treatment of psychotic depression, especially where a rapid response is required. Pooled analysis of the two largest sham-controlled ECT trials found a significant improvement in depressive scores with real ECT compared with simulated ECT in patients with depression and delusional features at 4 weeks. However, there was no significant difference between these groups at 6 months.²⁰ ECT is effective in MDD (see section on ECT and psychotropic drugs in this chapter) and a few studies indicate that ECT may be more efficacious in people with depression with psychotic features.²¹⁻²³ ECT may also be more protective against relapse in psychotic depression than in non-psychotic depression.^{24,25} One small RCT demonstrated superiority of maintenance ECT plus nortriptyline over nortriptyline alone at 2 years.²⁶ Maintenance treatment Generally, acute treatment should be continued. Evidence from the STOP-PD II (Study of the Pharmacotherapy of Psychotic Depression II) trial suggested that withdrawal of olanzapine from sertraline co-therapy worsens outcomes in the medium term.^{27,28} Relapse was more than twice as likely in the sertraline placebo group than in the combination group (55% vs 20%) and almost all the excess risk of relapse occurred in the first 2 months. However, one in five patients in the combined group relapsed over 36 weeks from randomisation into the single drug phase of the study (people were on the combination for much longer than this as all patients in the study started on the combination therapy prior to the 8-week remission phase needed prior to randomisation to monotherapy).⁴ The evidence from this study

suggests that combined treatment

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