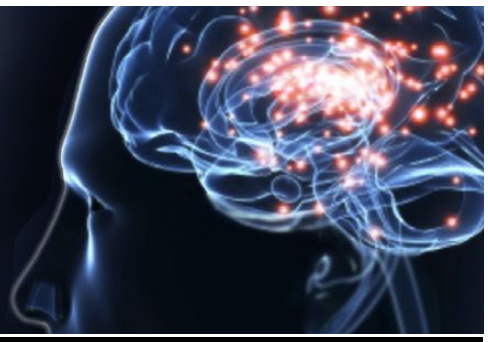
Psychiatry Research Review™



Making Education Easy

Issue 65 - 2021

In this issue:

Abbreviations used in this issue:

BPD = borderline personality disorder; **CGI-S** = Clinical Global Impressions-Severity of Illness Scale; **CI** = confidence interval; **COVID-19** = coronavirus disease 2019; **ECT** = electroconvulsive therapy; **GAD-7** = 7-item Generalized Anxiety Disorder; **MADRS** = Montgomery–Åsberg Depression Rating Scale; **NAC** = N-acetylcysteine; **PANSS** = Positive and Negative Syndrome Scale; **PHQ-9** = 9-item Patient Health Questionnaire; **QIDS-SR-16** = 16-item Quick Inventory of Depressive Symptomatology–Self-Report; **TD** = tardive dyskinesia.

Welcome to the latest issue of Psychiatry Research Review.

A highlight of this review is results from the most rigorous trial of a psychedelic medicine to-date by a team from the Centre for Psychedelic Research, Imperial College London in the UK published in the *New England Journal of Medicine*. The phase 2 trial assessed the antidepressant efficacy of psilocybin in comparison to escitalopram. While the primary outcome measure of improvement in a depression rating scale failed to show a statistical superiority for psilocybin, multiple secondary outcome measures favoured psilocybin and in terms of response rate and remission rates psilocybin outperformed the antidepressant. Whilst the issue of potential long-term addiction remains to be addressed, hopefully further trials can more clearly elucidate the benefits and risks of psilocybin treatment for depression. Results from the phase 3 ENLIGHTEN-1 trial published in *Journal of Clinical Psychiatry* demonstrate a clinically meaningful antipsychotic efficacy for olanzapine when administered in conjunction with the opioid receptor antagonist samidorphan, comparable to olanzapine monotherapy, in patients with acutely exacerbated schizophrenia. Together with results from the ENLIGHTEN-2 trial that revealed the combination therapy mitigated olanzapine-associated weight gain these results have led to the approval of a once daily oral formulation of olanzapine/samidorphan, named LYBALVI, for schizophrenia in the US either as a maintenance therapy or as an adjunct to lithium or valproate. Hopefully the combination drug will soon make its way to Australia as it will be a distinctly welcome addition to options for the treatment of psychoses. We also look at a cross-sectional study of the New Zealand population that reports an adverse impact of the coronavirus disease 2019 (COVID-19) pandemic and associated containment measures early in the pandemic with significantly higher depression and anxiety compared to published population normative data and the evidence to support psychiatric telehealth continues to accumulate with a Rhode Island study finding no mitigation of treatment efficacy in a partial hospital setting compared to in-person treatment.

We hope you find these and the other selected studies interesting, and look forward to receiving any feedback you may have.

Kind Regards,

Professor Nick Keks

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N-acetylcysteine as an adjunctive treatment for bipolar depression

Authors: Nery F et al.

Summary: This systematic review and meta-analysis of randomized controlled trials aimed to elucidate the efficacy of N-acetylcysteine (NAC) adjunctive therapy for the treatment of bipolar depression. A search of the PubMed online database identified six trials with 248 participants published between 1966 and 2020. A moderate effect size was found for NAC supplementation over placebo (d=0.45; 95% confidence interval [CI], 0.06-0.84) although there was a high degree of heterogeneity (I^2=49%). Baseline depressive scores, mean NAC dose and duration of study did not moderate the treatment effect.

Comment: NAC is a medicine with important applications for paracetamol overdose and in respiratory disorders. However, it has also been classified as a nutraceutical and trialled in multiple neuropsychiatric disorders with mixed results. In psychiatry, some studies identified NAC as useful adjunctive therapy in treatment-resistant depression, particularly bipolar depression. Persuasive evidence was published by Professor Michael Berk and colleagues, leading many clinicians to advise their patients to use NAC in addition to standard treatments. The experience of many clinicians however, is that some patients appear to benefit, and others do not. There have now been two meta-analyses, and both first appeared in 2020. Kishi T et al. (N-acetylcysteine as an adjunctive treatment for bipolar depression and major depressive disorder: a systematic review and meta-analysis of double-blind, randomized placebo-controlled trials. Psychopharmacology 2020; 237:3481–87) found no difference between NAC and placebo in depression ratings, but identified an advantage to NAC in Clinical Global Impression severity score. The meta-analysis here by Nery et al. demonstrates NAC to be superior to placebo but with a large confidence interval (possibly due to the inclusion of an outlying study). Both meta-analyses have been criticised methodologically. At this point it remains unclear whether NAC is effective in treatment-resistant bipolar depression as an adjunctive therapy. A major possibility is that NAC is useful in only some, as yet uncharacterised, patients. Further studies are required.

Reference: Bipolar Disord 2020; Dec 22 [Epub ahead of print]
Abstract

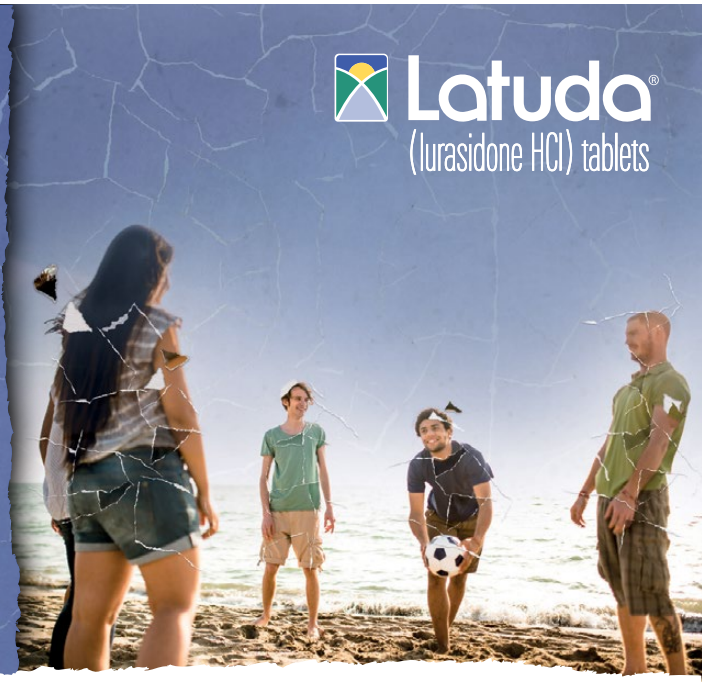
Efficacy and safety of a combination of olanzapine and samidorphan in adult patients with an acute exacerbation of schizophrenia

Authors: Potkin S et al.

Summary: Outcomes from the randomized, phase 3 ENLIGHTEN-1 (ClinicalTrials.gov Identifier: NCT02634346) study published in *Journal of Clinical Psychiatry* demonstrate a superior antipsychotic efficacy for the combination of olanzapine and the opioid antagonist samidorphan to placebo, similar to olanzapine monotherapy, with clinically significant improvements in patients with acutely exacerbated schizophrenia. The Alkermes sponsored phase 3 trial accrued a total of 401 adult patients (mean age 41.4 years) with a clinical diagnosis of schizophrenia from sites across the USA, Bulgaria, Serbia and the Ukraine. Trial inclusion criteria specified a baseline Positive and Negative Syndrome Scale (PANSS) total score of >80 plus a score ≥ 4 on at least three of the following items from the PANSS: delusions, conceptual disorganization, hallucinatory behaviour or suspiciousness/persecution. Following a 10-day screening period and discontinuation of all prior antipsychotic medications, patients were randomised to four weeks of therapy, the first two as inpatients, in one of the three trial arms: olanzapine/samidorphan (20 mg and 10 mg once daily, respectively; n=134), olanzapine monotherapy (20 mg once daily; n=134) or placebo (n=135). Olanzapine/samidorphan elicited significantly improved reductions from baseline in the PANSS total score at week 4, the primary outcome measure, compared to placebo (mean change, -23.7 vs -19.4; least squares difference versus placebo, -6.4; $p<0.001$). Olanzapine monotherapy also conferred a significantly improved PANSS score from baseline compared to placebo (mean change, -22.4 vs -19.4; least squares difference versus placebo, -5.3; $p=0.004$). At week four, both olanzapine/samidorphan and olanzapine monotherapy also significantly reduced Clinical Global Impressions-Severity of Illness Scale (CGI-S) from baseline compared to placebo (least squares mean difference to placebo, -0.38, $p=0.002$ and -0.44, $p<0.001$, respectively). Subgroup analysis confirmed the similar antipsychotic efficacy of olanzapine/samidorphan and olanzapine monotherapy across key patient groups including ages, genders and races. The main adverse events in the treatment groups were weight gain, somnolence, dry mouth and headache.

Comment: Psychiatry Research Review has previously reported research findings with a new compound drug which consists of olanzapine and samidorphan, a new opioid receptor antagonist. Although olanzapine is very effective as an antipsychotic and mood stabiliser, and well-tolerated in short-term use, the majority of patients taking it are likely to gain weight. Olanzapine has been found to have the highest propensity for weight gain risk among antipsychotics (see Huhn M et al. Comparative efficacy and tolerability of 32 oral antipsychotics for the acute treatment of adults with multi-episode schizophrenia: a systematic review and network meta-analysis. The Lancet. 2019; 394:939–51). The study here supports pre-existing evidence that olanzapine-samidorphan has equivalent efficacy to olanzapine alone in the treatment of acute schizophrenia. Efficacy has also been established in maintenance treatment of schizophrenia and in bipolar mood disorder, while significant weight gain with the combination drug is about 50% less than that with olanzapine alone. The US Food and Drug Administration has just approved combined olanzapine-samidorphan (trade name Lybilvi) for the treatment of adults with schizophrenia and bipolar I disorder, as a maintenance monotherapy or for the acute treatment of manic or mixed episodes, as monotherapy or an adjunct to lithium or valproate. Hopefully the combination drug will soon make its way to Australia as it will be a distinctly welcome addition to options for the treatment of psychoses.

Reference: J Clin Psychiatry 2020;81(2):19m12769
Abstract



Cost-effectiveness of routine screening for autoimmune encephalitis in patients with first-episode psychosis in the United States

Authors: Ross E et al.

Summary: Results from decision-analytic modelling with a five-year horizon from the US health care sector and societal perspective support routine screening for autoimmune encephalitis in patients with first-episode psychosis as a cost-effective option. The model was based on a cost of US$291 for serum autoantibody panel testing and used published data to approximate the prevalence of neuronal autoantibodies in first-episode psychosis at 4.5%, remission probability with antipsychotics at 0.58 and remission probability with immunotherapy for patients diagnosed with autoimmune encephalitis at 0.85. The mean gain in quality-adjusted life-years was 0.008 overall and 0.174 in patients with neuronal autoantibodies with incremental cost-effectiveness ratios of $99,330 and $147,460 per quality-adjusted life-years. Both of these were below the incremental cost-effectiveness ratio thresholds to qualify as cost effective. More definitive cost effectiveness analyses for screening will be enabled by immunotherapy efficacy data.

Comment: It is estimated that about 4.5% of patients with first-episode psychosis suffer from autoimmune encephalitis. Although patients with autoimmune encephalitis usually eventually develop neurological symptoms, psychosis can be an early presentation. In autoimmune encephalitis, antibodies against neuronal proteins cause inflammation underlying the encephalitis. The most established form of autoimmune encephalitis is anti-NMDA receptor encephalitis (NMDA receptors mediate effects of the excitatory amino acid glutamate which is linked to the pathogenesis of psychosis). The prevalence of about 5% of autoimmune encephalitis in first-episode psychosis is substantial, and immunosuppressive therapy is an effective treatment for these patients. It is an interesting reflection on healthcare in the United States that this paper examines the cost effectiveness of routine screening for autoimmune encephalitis in first-episode psychosis patients. Luckily the answer is in the affirmative. There is now even less argument against routine screening for autoimmune encephalitis in acute first-episode psychosis patients.

Reference: J Clin Psychiatry 2020;82(1):19m13168
Abstract

Treatment outcomes of electroconvulsive therapy for depressed patients with and without borderline personality disorder

Authors: Yip A et al.

Summary: This retrospective study by Yip et al examined if borderline personality disorder (BPD) impacts the efficacy of electroconvulsive therapy (ECT) for depression. Analysis was based on 693 patients with depression of at least moderate severity treated with an acute course of ECT at the McLean psychiatric hospital in Massachusetts, USA, between 2011 and 2016. The researchers reported a BPD prevalence rate of 20.9% (based on The McLean Screening Instrument for Borderline Personality Disorder without a follow-up diagnostic interview). ECT elicited significant improvement in symptoms of depression as assessed using the Quick Inventory of Depressive Symptomatology-Self Report including overall depression severity, suicidality, core emotional, sleep and atypical symptoms. No difference in efficacy was found between patients without BPD and those who screened positive for BPD. Post-hoc analysis showed a slightly reduced robustness of ECT efficacy in the cohort with BPD by the 15th treatment.

Comment: Many patients with BPD will suffer episodes of severe and dangerous major depression. The presence of BPD in a severely depressed patient has frequently been regarded as a poor prognostic factor for ECT. However, empirical evidence for the efficacy of ECT in borderlines with severe major depression has not been particularly extensive. Many clinicians would be reluctant to utilise ECT in patients with BPD, especially as there is a clinical impression that such patients are more likely to suffer from adverse effects from treatment. The retrospective study of Yip et al here indicates that major depression in patients with BPD does respond to ECT though possibly not quite as well as other patients. However, adverse effects such as cognitive dysfunction were not evaluated. A methodologically rigorous study is clearly needed.

Reference: J Clin Psychiatry 2021;82(2):19m13202
Abstract

The prevalence and national burden of treatment-resistant depression and major depressive disorder in the United States

Authors: Zhdanava M et al.

Summary: This study was conducted by Janssen Scientific Affairs in conjunction with the Canadian Analysis Group to estimate the burden of treatment-resistant depression and major depressive disorder in the US. Antidepressant prescription data were extracted from four insurance databases - Medicare, Medicaid, commercial plans and the US Veterans Health Administration – and data from the 2017 Kantar National Health and Wellness Survey used to estimate unemployment burden. Results revealed a 12-month prevalence of medication-treated major depressive disorder of 8.9 million adults, 30.9% (2.8 million) of whom had treatment-resistant depression. Estimates for the financial burden of depression found that despite treatment-resistant depression accounting for less than one-third of cases of depression it was responsible for more than half of the health care costs (56.6%; US$425.8 billion), almost half of the unemployment financial burden (47.7%; US$8.7 billion) and almost half of the total annual financial burden (47.2$; US$43.8 billion). The total cost per year of medication-treated major depressive disorder was US$92.7 billion.

Comment: In contrast to usual epidemiological studies of depression in population samples, Zhdanava et al. rely on comprehensive insurance data concerning medicated major depressive disorder in the United States. The numbers will probably be underestimates, but interesting because of this. According to this study, about 3% of the current US population is being treated with antidepressants. All insurers defined treatment-resistant depression as present when a third antidepressant (with augmentation) is commenced following use of two previous antidepressants at an adequate dose and duration, which is a strict definition. About a third of patients taking antidepressants meet the criteria for treatment-resistant depression. The costs are predictably massive with respect to healthcare and productivity. The findings clearly point to the economic benefits which could be derived from more effective treatment. The problem is how to achieve improved treatment efficacy.

Reference: J Clin Psychiatry 2021;82(2):20m13699
Abstract

Telehealth treatment of patients in an intensive acute care psychiatric setting during the COVID-19 pandemic

Authors: Zimmerman M et al.

Summary: Comparative safety and effectiveness to in-person treatment is achieved by psychiatric telehealth treatment in an acute partial hospital setting according to a study from the Rhode Island Hospital in the US published in *Journal of Clinical Psychiatry*. Self-reported outcomes were compared between psychiatric patients who underwent therapy through a partial hospital program delivered in-person in 2019 (n=207) or virtually in 2020 due to the COVID-19 pandemic (n=207). Partial hospital level of care delivered in-person or via telehealth significantly improved symptoms, functioning, coping ability, suicidal ideation, positive mental health and general well-being with a large treatment effect (Cohen $d>0.8$; assessed using the modified Remission from Depression Questionnaire; all $p<0.01$). Benefits over traditional in-person therapy were found in the virtually-treated group including a greater likelihood of completing treatment (72.9% vs 62.3%; $X^2=5.34$; $p<0.05$). Virtual therapy also offered a method of therapy that was acceptable to patients that would not have considered in-person treatment and the authors recommended that telehealth continue after resolution of the COVID-19 pandemic.

Comment: There is now considerable evidence that telehealth services in psychiatry are as effective and safe as face-to-face treatment in a range of disorders. In my opinion telepsychiatry via video is a substantial advantage in mood disorders if face-to-face treatment involves masks. However, the evidence concerning telepsychiatry relates almost exclusively to outpatient treatment. In Australia Medicare supports outpatient telehealth. However, telehealth is not supported by either Medicare or private hospital insurance for inpatients or day programs. The study by Zimmerman et al demonstrates the effectiveness of intensive acute care psychiatric treatment, which involved day-long interventions consistent with acceptance and commitment therapy daily until patients improved. This is not strictly inpatient care, but does approximate inpatient therapy programs in private psychiatry settings. It constitutes strong support for telehealth in private psychiatry day programs which hopefully the government will consider. Telehealth in psychiatry is here to stay beyond the pandemic.

Reference: J Clin Psychiatry 2021;82(2):20m13815
Abstract

Trial of psilocybin versus escitalopram for depression

Authors: Carhart-Harris R et al.

Summary: Carhart-Harris and colleagues from the Centre for Psychedelic Research, Imperial College London in the UK have reported results from their head-to-head comparison of psilocybin, the primary psychoactive substance in 'magic mushrooms', and the selective serotonin receptor inhibitor escitalopram for moderate to severe depression. The phase 2 trial enrolled a total of 59 adult patients (mean age 41 years; 34% female) with a diagnosis of major depressive disorder of at least moderate severity (score ≥ 17 on the Hamilton Depression Rating Scale) and randomised them to six weeks of treatment with either psilocybin (two doses of 25 mg three weeks apart; n=30) or escitalopram (10-20 mg daily plus two doses of 1 mg psilocybin three weeks apart to maintain blinding; n=29). No results were reported for change in blood oxygen level dependent signal during functional magnetic resonance imaging in response to emotional faces, the primary outcome measure as per the US clinical trials registration site (https://clinicaltrials.gov/ct2/show/NCT03429075). An absolute larger improvement in 16-item Quick Inventory of Depressive Symptomatology–Self-Report (QIDS-SR-16) score at week 6 from baseline, stated as the trial's primary outcome measure in the *New England Journal of Medicine* publication, was seen in the psilocybin trial arm compared to the escitalopram arm but this did not result in a statistically significant difference (-8 vs -6; between group difference of 2; 95% CI, -5 to 0.9; p=0.17). Secondary outcome measures of QIDS-SR-16 response and remission rates both favoured the psilocybin arm (70% vs 48%, between group difference of 22 percentage points, 95% CI, -3 to 48 and 57% vs 28%, between group difference of 28 percentage points, 95% CI, 2 to 54, respectively). Other secondary outcome measures reported in the supplementary appendix including well-being, work and social functioning, anxiety, avoidance, feeling pleasure, suicidality and other depression rating scales also favoured psilocybin with the caveat that analyses were not corrected for multiple comparisons. Adverse events were reported as similar between arms. It has not been disclosed whether psilocybin will progress to phase 3 testing.

Comment: Psilocybin was isolated from the mushroom Psilocybe mexicana by the Swiss chemist Albert Hoffman from Sandoz laboratories in 1959 (Hoffman had also synthesised lysergic acid diethylamide or LSD in 1938). The use of psychedelics in psychiatry (particularly LSD) went through a period of intense popularity in the 1960s but ended badly with abuse, addiction and serious complications such as psychoses. As well as psilocybin and LSD, psychedelics include mescaline, dimethyltryptamine (DMT), methylenedioxymethamphetamine (MDMA or ecstasy), phencyclidine (angel dust), ketamine and tetrahydrocannabinol (THC, the psychedelic component of cannabis). The study of Carhart-Harris et al has been published by the prestigious *New England Journal of Medicine*. The methodology is technically sophisticated but patient numbers are small. The findings are "suggestive" of efficacy but not statistically different from escitalopram. A larger sample and possibly less self-selected patients (who were recruited by advertisements) are needed. As with all psychedelics, the most difficult unanswered question concerns long-term potential for addiction.

Reference: N Engl J Med 2021;384(15):1402-11
Abstract

Depression, anxiety and stress during the COVID-19 pandemic: results from a New Zealand cohort study on mental well-being

Authors: Gasteiger N et al.

Summary: This cross-sectional study of the New Zealand community used an online questionnaire to examine mental health status, especially depression, anxiety and stress during the first ten weeks of the COVID-19 pandemic. A total of 681 adults (mean age 42 years; 89% female; 46% keyworkers) completed an online questionnaire that included questions regarding health behaviours such as exercise, smoking and alcohol consumption. Depression, anxiety and stress were assessed using the 9-item Patient Health Questionnaire (PHQ-9), the 7-item Generalized Anxiety Disorder (GAD-7) Scale and the 4-item Perceived Stress Scale, respectively. A deleterious impact on mental health was found early in the pandemic in New Zealand with significantly higher levels of depression and anxiety compared to published population normative data (mean PHQ-9 7.88 vs normative mean 2.91; mean GAD-7 6.25 vs normative population mean 2.95; both p<0.0001). Greater depression, anxiety and stress were reported in younger adults and people with risk factors for COVID-19. Modifiable factors protective against adverse mental health were lower loneliness, greater exercise and greater positive mood. Lower depression and anxiety were also observed in pet owners. An age- and gender-adjusted comparison of mental health outcomes in New Zealand and the UK revealed comparable depression but significantly lower anxiety and stress in the New Zealand cohort with lower perceived risk (all p<0.01).

Comment: Melbourne has just been in its fourth prolonged lockdown. The effects on so many of my patients have been terrible. Rather than getting used to restrictions, many of my patients experience emotionally traumatic reactions whereby the consequences for anxiety and depression are worse with each repetition, not better. For some, agoraphobia has set in and may be irreversible. There are major effects with respect to alcohol and both licit and illicit drug abuse. This comparatively small and selective study from New Zealand yet again shows negative consequences of stringent lockdowns. As other studies have found, it is younger patients who seem to be most affected. The people I am seeing are mostly older so clearly, they also are not immune. The protective effect of having a pet is notable (though NDIS refuses to support getting a pet for some of my patients).

Reference: BMJ Open 2021;11(5):e045325
Abstract

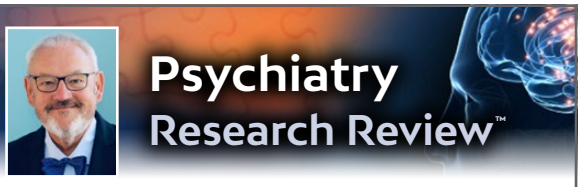
Standard versus reduced dose of antipsychotics for relapse prevention in multi-episode schizophrenia

Authors: Højlund M et al.

Summary: This systematic review and meta-analysis of randomised controlled trials published in *The Lancet Psychiatry* investigated the risks and benefits of dose reduction of antipsychotic medication in schizophrenia. A search of the Embase, Medline, PsycINFO and the Cochrane Library online databases up to June 17, 2020 identified 22 studies that reported on 24 trials with 3,282 total participants (median age 38 years; 34% female). All trials compared ≥ two doses of an antipsychotic in adult patients with schizophrenia or schizoaffective disorder. Trials in first-episode psychosis or treatment-resistant schizophrenia were excluded. Any level of reduction from the standard antipsychotic dose (low-dose and very low-dose defined as within 50-99% and <50% of the lower limit of the standard dose, respectively) was significantly associated with increased risk of both relapse and all-cause discontinuation with greater risk seen for both outcomes with the lowest doses (risk of relapse: low vs standard dose, risk ratio 1.44, 95% CI 1.10-1.87, p=0.0076; very low vs standard dose, risk ratio 1.72, 95% CI 1.29-2.29, p=0.0002). The same pattern was seen in subgroup analyses of first-generation versus second-generation antipsychotics and oral versus long-acting injectable antipsychotics.

Comment: Long-term use of antipsychotic medications is associated with the risk of inducing tardive dyskinesia (TD), metabolic syndrome and less common adverse effects, depending on the drug. Introduction of new-generation antipsychotics has led to substantial but variable reduction in the risk of TD. Patients with TD induced by other antipsychotics who are then treated with clozapine can expect remission in about 50% of cases. Given the risk of TD, many clinicians have attempted to utilise antipsychotic dose minimisation during maintenance therapy. Sometimes the doses used are significantly lower than the therapeutic dose range for acute psychoses. This meta-analysis of maintenance treatment in schizophrenia indicates that, on average, dose reduction is likely to be associated with poorer outcomes. Less clear is how applicable these findings are to individual cases. As usual in the heterogeneous condition of schizophrenia, what applies for most patients may not be what is the best for particular individuals. Some patients do appear to have better outcomes with lower doses than were required for acute treatment. On the other hand, it appears that this is not the case for the majority.

Reference: Lancet Psychiatry 2021;8(6):471-86
Abstract



Independent commentary by Professor Nicholas Keks AM

Nicholas Alexander Keks is Professor of Psychiatry at Monash University, a psychiatrist in private practice at Delmont Private Hospital, Honorary psychiatrist at Monash Health, Executive Director of the Centre of Mental Health Education and Research at Delmont, and Professorial Fellow at the Florey Institute of Neuroscience and Mental Health. He is also a Senior Examiner for the Australian Medical Council, and Honorary Secretary of the Psychiatry Section of the Australian Medical Association Victorian Branch. Prof Keks' qualifications include a Bachelor of Medicine and Bachelor of Surgery from the University of Melbourne, Master of Psychological Medicine from Monash University, Fellow of the Royal Australian and New Zealand College of Psychiatrists, Foundation member of its Faculty of Forensic Psychiatry, and Doctor of Philosophy from Monash University. Prof Keks is the author of over 220 peer-reviewed publications. His major interests are in psycho-pharmacology, mood disorders, anxiety disorders, psychoses and suicide prevention.

Symptomatic and functional outcomes and early prediction of response to escitalopram monotherapy and sequential adjunctive aripiprazole therapy in patients with major depressive disorder: A CAN-BIND-1 report

Authors: Kennedy S et al., for the CAN-BIND Investigator Team

Summary: The Canadian Biomarker Integration Network for Depression (CAN-BIND) trial is an open-label two-phase treatment trial of escitalopram ± aripiprazole aiming to identify biomarkers and clinical predictors of response to treatment in major depressive disorder. A total of 211 patients diagnosed with major depressive disorder undergoing a major depressive episode were accrued from six Canadian outpatient psychiatric facilities between August 2013 and December 2016. In phase one all patients received eight weeks of open-label escitalopram therapy (10-20 mg). In phase two patients who did not achieve a Montgomery–Åsberg Depression Rating Scale (MADRS) response (defined as ≥ 50% reduction from baseline; 53% of patients) were administered eight-weeks of open-label add-on aripiprazole (2-10mg) therapy while responders continued with escitalopram monotherapy. At week 16, 91% of patients on escitalopram monotherapy maintained their response and 61% of patients in the adjunctive cohort achieved a MADRS response. The authors reported that early symptomatic improvement was only a moderately accurate prognostic factor for outcome.

Comment: This study adds to the existing evidence concerning the efficacy of aripiprazole as an augmentation to antidepressant medications where response to antidepressants has been inadequate. Psychiatrists in Australia are becoming increasingly aware of the utility of adjunctive aripiprazole in the treatment of resistant major depressive disorder. Usually, lower doses than those required for treatment of psychosis are needed. As long as dose titration is carried out fairly slowly, most patients will tolerate aripiprazole quite well in the longer-term with few, if any, adverse effects. Unfortunately, Medicare does not support aripiprazole for the treatment of major depressive disorder. However, low dose aripiprazole is affordable on a private script if obtained through discount chemists.

Reference: J Clin Psychiatry 2019;80(2):18m12202
Abstract

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