Professional Practice Guideline 6

Guidance for the use of stimulant medications in adults

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The Royal Australian & New Zealand College of Psychiatrists

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Stimulant medications enhance the presynaptic release of catecholamines, in particular dopamine. The Royal Australian and New Zealand College of Psychiatrists (RANZCP) supports their appropriate use in the treatment of attention deficit hyperactivity disorder (ADHD) and narcolepsy in adults, for which there is a sound evidence base and as one part of a holistic treatment plan.

Although stimulant medications have occasionally been used in other clinical disorders (see below), those indications are supported by a limited evidence base, and generally fall outside prescription regulations.

Key messages

- Prescribing rules and regulations vary across jurisdictions, and it is the responsibility of clinicians to be aware of these prior to prescribing.
- Stimulants are drugs of dependence and care must be taken prior to prescribing psychostimulant medications, especially in complex cases or for high-dosage prescriptions.
- Psychostimulant medication should be carefully monitored, especially for cases with a history of psychosis or substance use disorder.
- Psychostimulant medication should only be prescribed after comprehensive psychiatric assessment.
- Evidence for efficacy of psychostimulants is limited for mental health conditions other than ADHD and narcolepsy
- Further research is needed for the use and risks of psychostimulant medications in non-ADHD populations.

Scope

This Guideline is not intended to provide clinical guidance for the prescription of psychostimulants. This Guideline provides a high-level overview of the considerations that a psychiatrist should be aware of when prescribing psychostimulants for any condition. The decision matrix for the prescription of psychostimulants will vary by condition and on an individualised case-by-case basis.

Stimulant medications are classified by Australian and New Zealand regulations as drugs of dependence or controlled drugs. Stimulant regulations and the legal mechanisms for their prescription vary between jurisdictions and are subject to legislative change. In the absence of uniform regulation for stimulant prescription across jurisdiction, local regulations will determine who should initiate pharmacological therapy. Practitioners should familiarise themselves with regulations in their jurisdiction prior to prescription.

Background

Rates of psychostimulant prescription have been increasing rapidly in both Australia and Aotearoa New Zealand in the past 10 years.[1, 2] Access to psychostimulants, largely for the treatment of ADHD, has become a key area of interest from several stakeholders including consumer and tāngata whaiora groups, governments, health services and peak bodies. There has been an increasing interest in expanding access to psychostimulants by opening prescribing up to a wider group of clinicians.[3-5]

Given the increasing need and authority for prescribing stimulant medications it is important that consideration is given to the relevant issues, including consumer and tāngata whaiora safety and wellbeing.

Primary Considerations for Safe and Effective Stimulant Prescription

Misuse and Diversion

As noted above, stimulants are drugs of dependence. Evidence shows that prescription stimulant medications are subject to misuse and diversion, including amongst people with ADHD.[6] However, the rate of misuse and diversion shown in recent research is inconsistent.[7]

A recent systematic review showed that self-reported rates of non-medical use of stimulants ranges from between 2.1% to 58.7%, with self-reported diversion rates ranging from 0.7% and 80%.[8] Misuse and diversion are linked to particular risk factors such as higher or more frequent dosage levels, short-acting medications, surplus supply of medication, misuse by peers, lack of awareness of the risks of misuse, and complex medical histories.[7, 9] Rates of misuse and diversion appear to be rising based on some studies, especially among young people of university age, however more research is required.[8, 9] There are also growing concerns regarding malingering, especially amongst young people seeking ADHD diagnoses. [10, 11]

However, although studies have shown some increase, evidence about the extent, nature, and prevalence is scant. As such, consumers should not be assumed to be seeking diagnosis for the purpose of obtaining stimulants with the intention to misuse or divert unless other risk factors are clearly shown, or assessments do not support diagnosis. As with the prevalence and nature of misuse and diversion of prescribed stimulants, further research is required to properly assess whether malingering is a current or growing issue.

Misuse and diversion can be mitigated. The primary way to reduce risks is to ensure that diagnosis is only made after comprehensive psychiatric assessment which seeks to identify and address all co-occurring mental health conditions.[9] Reliance on self-report or less rigorous diagnostic processes are insufficient to prevent malingering or incipient misuse or diversion.[10] Ongoing monitoring of dosages and adherence to treatment plans can also help to prevent misuse, both deliberate and accidental, and are part of best practice when prescribing stimulants for any condition.

Substance Use Disorder

Caution is required in the consideration of stimulant prescription to persons who have a history of substance use disorder (SUD). As in all cases where consumers have, or are suspected to have, SUD, clinicians must ensure that universal precautions are applied when prescribing stimulants.[12]

Treatable co-morbid conditions must be managed in such a way as to optimise a consumer's health outcomes.[12] This includes where SUD is co-morbid with psychiatric conditions that are routinely managed with psychostimulants. Co-morbid ADHD and SUD are common, and in such cases psychostimulants are still a mainstay treatment.[13] Prescription stimulant use has been shown to decrease the likelihood of illicit stimulant use in people being evaluated for SUD.[14] However, modifications of standard treatment plans and additional precautions are required. Advice is available for clinicians treating ADHD with stimulant medications where co-morbid SUD is present.[13, 15, 16]

Similar precautions should be developed for all cases where psychostimulant medication is a standard treatment for mental and behavioural disorders which are co-morbid with SUD. Although caution is required clinicians should not rule out treating with psychostimulants provided adequate precautions and monitoring is undertaken. RANZCP acknowledges, however, that there is limited clinical evidence for other psychiatric disorders traditionally treated with stimulants and co-morbid SUD – including narcolepsy.[17] As such individual clinicians should manage such disorders in line with best clinical practice and adapted precautions to ensure the consumer's best health outcomes are maintained.

Side Effects and Comorbidities

Stimulant medications have well recorded side effects that can present at even low dosages. Associated adverse effects include impairment of memory, tics and psychosis, sleep issues, and cognitive control/executive function behaviours as well as physical health issues, especially related to the heart in long-term users.[18] However, when used effectively and well managed - including through regular follow-ups, dosage adjustments, and holistic health monitoring - the benefits for consumers, especially those with ADHD, outweigh the risks.[19]

It is important to note that there is very little evidence for people who have been prescribed dexamphetamines following effective assessment and diagnostic practices developing dependence to prescribed stimulant medications. [20] However, non-prescribed use may lead to addiction, such as with methamphetamine and other illicit stimulants – for more information on the impacts of general stimulant misuse please see Position Statement 82: Recognising and addressing the harmful mental health impacts of methamphetamine use. Further research is required across all cohorts regarding the impact of prescribed stimulants on dependence behaviours.

Stimulant medications also have the propensity to interact with other mental and physical health conditions to produce negative health outcomes. Several mental health conditions are associated with increased risk of adverse effects including eating disorders, depression, Alzheimer's and schizophrenia.[21] There is limited clinical evidence of a causal link between the use of stimulants and the onset of schizophrenia or psychosis in people with ADHD.[19, 22] However, misuse may increase the risk of medication induced psychosis in other individuals.[23] Further research is required to show any definitive link between stimulant prescription and the emergence of schizophrenia or psychosis.

Some psychiatrists have raised concerns that stimulant medication prescribed to individuals with specific comorbidities, such as schizophrenia and bipolar, may increase the risks of instances of mania or psychosis. Some research mirrors these concerns raised by clinical observation – the odds of instances of psychosis and mania were increased when stimulants had been prescribed within the last month.[24] A dose response relationship was also observed with higher doses of amphetamine associated with higher risk of incident mania or psychosis.[24] Risks are more readily associated with amphetamine prescription rather than methylphenidate.[25] However studies have stopped short of establishing causality.[25] There is also no evidence to suggest a specific link between stimulant prescription and increased episodes of mania in individuals with bipolar disorder.[26] More research is required to establish a direct link between stimulant prescription and increased risk of psychosis and mania in individuals with existing conditions such as schizophrenia and bipolar disorder. However, due to the risk of iatrogenic harm, caution should be exercised when prescribing with rigorous follow up and monitoring protocols established to mitigate possible side effects.[27]

Despite the low risk of severe adverse side effects in evidence-based stimulant treatment, it is important that clinicians and consumers are fully aware of the risks. Caution should be taken when prescribing where there is a history of schizophrenia or other psychosis disorder, or when dosages in excess of 30 mg daily of dexamphetamine or 60 mg daily of methylphenidate are contemplated. Specific monitoring of effectiveness and clear endpoints for treatment (where applicable) should be documented.

Prescribing Overview by Condition

ADHD

ADHD is a clinical syndrome of pervasive inattention and/or hyperactivity and impulsivity, which is in excess of that typical for one's developmental age. It adversely affects learning, interpersonal relationships, and occupational and overall functioning, and has a mortality rate above that in the general population.[16, 28]

Pharmacological treatment using stimulants is an evidence informed treatment for ADHD but requires particular considerations before and during the prescription process to ensure the efficacy of treatment and to mitigate associated risks. RANZCP has endorsed the AADPA Evidence-Based Clinical Practice Guideline for ADHD and its recommendations and guidance regarding the prescription of psychostimulants for ADHD. There is further advice available in Position Statement 55: ADHD across the lifespan and RANZCP's submission to the *Senate Standing Committee on Community Affairs' Inquiry into the Barriers to consistent, timely and best practice assessment of attention deficit hyperactivity disorder (ADHD) and support services for people with ADHD*.

Monitoring Treatment

Clinicians should arrange regular and frequent follow-up until medication is optimised and stabilised. Once medication is titrated and stabilised, arrange routine individualised monitoring and encourage the person taking medication to monitor and record adverse effects.[16] Standard symptom and adverse effect rating scales should be used for clinical assessment and throughout the course of treatment.[16]

Before titration, baseline ADHD symptoms and level of functioning should be recorded.[29] During titration, adverse effects should be monitored and recorded at each dose change and progress reviewed regularly during the titration period. Titrate the dose against symptoms, level of functioning and adverse effects until the optimal dose has been identified.[16] Titrate slower and monitor more frequently if other neurodevelopmental disorders, mental health conditions and/or physical health disorders are present.[16]

Adherence to Medication Treatment

Due to its symptomology, people with ADHD may have difficulty adhering to treatment plans. Ensure people are fully informed of the balance of risks and benefits of any medication for ADHD to ameliorate misconceptions and non-adherence.

Narcolepsy

Stimulant medications are a long-established mainstream treatment for narcolepsy. A limited number of controlled trials containing small numbers of patients have been published. These studies, together with the extensive clinical experience provide support for the efficacy of this strategy.[30-32] There is also some evidence that consumers with narcolepsy are less likely to exhibit addictive behaviours.[31] However, this still requires further clinical research and when prescribing stimulants for the treatment of long-term narcolepsy the same precautions should still be taken to ensure that misuse is not evident or suspected.

Other Clinical Conditions

Stimulant medications have also been reported as useful in the management of cognitive and behavioural disturbances after traumatic brain injury, in the treatment and management of binge eating disorders, , and in the adjunctive treatment of major depressive disorder.[32-43] Evidence is limited however, and there may be the risk of interactions with other medications used in these conditions. Further research is required before clinicians should prescribe stimulants for conditions other than ADHD or narcolepsy as a matter of course.

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