

Medication Holidays

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Medications are used by the majority of adult Americans and an increasing number of children and adolescents. One or more medication is used by 7 in 10 adults in the United States (US), with 22.4% using at least 5 medications within a 30-day time period.¹ Many prescribed medications are for chronic conditions that require continued use to manage a disease state, such as hypertension; however, certain medications can be taken as needed or even discontinued for a time period. This temporary or permanent cessation of medication use is referred to as a medication holiday.² This newsletter will explain the purpose of medication holidays and medications that may be considered for a pause in pharmacotherapy.

Medication Holidays

There are several reasons medication holidays have been proposed. Medication holidays can be used for therapeutic assessment, therapeutic benefit, and central nervous system (CNS) resensitization, as described below.²

Therapeutic assessment: verify medication effectiveness or determine if use is related to unwanted adverse reactions.

Therapeutic benefit: initiated to minimize adverse events related to treatments and to enhance long-term medication effectiveness for diseases such as Parkinson's disease.

Central nervous system resensitization: continued pharmacological stimulation may result in psychological changes in neurons and neuronal networks in the CNS. Such adaptations may lead to tolerance and even delay adverse effects to some drug classes (e.g., tardive dyskinesia with antipsychotic drugs and motor dyskinesias with levodopa).

Medication Selection

Certain medications can be considered for a medication holiday based on demonstrated evidence of benefit and patient specific characteristics, such as willingness to navigate interruption in therapy. **Table 1** provides examples of medications or classes of medications in which medication holidays have been suggested.²

Table 1. Treatments that May Qualify for a Medication Holiday^{2,3,4}

Medication	Rationale	Tapering Required*
Methylphenidate	Determine effectiveness, needs assessment and resensitization	None

Guanfacine	Determine effectiveness and needs assessment	Yes
Lisdexamfetamine	Determine needs assessment	Yes
Melatonin	Determine needs assessment	None
Antiestrogenic Drugs	To improve adherence and persistence	None
Levodopa	Potential delay of motor dyskinesias and resensitization	Yes
Dopamine agonists (e.g., ropinirole, pramipexole)	Remission or reduction of symptoms assessment	Yes
Amantadine	To restore efficacy	Yes
Antipsychotics	Reduce tardive dyskinesias and resensitization	Yes
Selective serotonin reuptake inhibitors (SSRIs)	Minimization of sexual adverse effects	Yes
* Medication Tapering Resource: A Practical Guide to Stopping Medications in Older People: https://bpac.org.nz/BPJ/2010/April/docs/bpj_27_stop_guide_page_s_10-23.pdf		

Medication holidays have been suggested for patients who use medications for attention deficit hyperactivity disorder (ADHD). Guidelines recommend considering medication holidays for children and adolescent patients who take medication for ADHD, such as methylphenidate.⁵ The use of methylphenidate can be associated with adverse reactions such as anorexia, decreased appetite, weight loss, sleep disruptions and reduced height gain. Evidence suggestions that longer medication holidays from ADHD medications may enable child growth.⁵ Improvements in insomnia and increased appetite may result with the use of shorter medication holidays.

The Institute for Clinical Symptoms Improvement recommends managing linear growth impairment due to ADHD medications by prioritizing the use of stimulants to high priority situations and discontinuing use during weekends or vacations. The American Academy for Child and Adolescent Psychiatry (AACAP) recommends evaluating the need of ongoing ADHD treatment after one year of being symptom free.⁶ The National Institute for Health and Care Excellence (NICE) recommends patients that use methylphenidate over a long period of time should undergo periodic re-evaluation and trial periods of discontinuation.⁵ However, a 2018 NICE review found low to

moderate quality evidence that withdrawing methylphenidate or atomoxetine in children and young people resulted in an increase in clinical symptoms of ADHD.⁷ In adult patients, there was no difference in symptoms of ADHD or health-related quality of life in patients withdrawing therapy with methylphenidate or amoxetine.⁷ Therefore, benefits and risks of recommending a medication holiday need to be carefully accessed.

There is limited evidence for the use of medication holidays for people who take antiosteoporotic drugs (e.g., antiresorptive and anabolic drugs affecting bone mineral density).⁸ Medication holidays are recommended to avoid severe adverse events, such as osteonecrosis of the jaw and atypical femur fractures, associated with antiosteoporotic therapy.⁸ In patients that are at low-risk for fractures, a medication holiday for up to 5 years may be appropriate. A systematic review and meta-analysis analyzed medication holidays in patients that are high-risk (e.g. history of fragility fracture) and found the incidence of re-fractures was lower in those treated with continuous antiresorptive therapy compared to medication holiday therapy (relative risk [RR] 0.49; 95% confidence interval [CI], 0.25 to 0.98) (low to moderate quality evidence).⁸ Recommendations from guidelines recommend continuous therapy for most patients, especially those at higher risk to reduce the risk of fractures.^{8,9,10}

Additionally, some guidelines recommend against routine cessation of ant-resorptive therapy.¹¹ High quality evidence regarding medication holidays in osteoporosis is limited and a decision should be based on individual patient assessment of benefits and risks.

Medication holidays have been proposed for certain medications, such as for people taking antidepressants or antipsychotics experiencing sexual dysfunction, but there is insufficient evidence demonstrating benefit.^{12,13} Two Cochrane reviews also failed to find high-quality evidence for the use of medication holidays to reduce tardive dyskinesia secondary to antipsychotic use.^{13,14}

Medication Holiday Considerations

There can be disadvantages of medication holidays in some patients. The condition being treated, pharmacology of the drug, length of medication holiday and patient specific factors all need to be taken into account when considering a suspension in medication treatment.² Potential sequelae of medication discontinuation can be destabilization of illness or rebound of symptoms of the disease that was being treated. Additionally, discontinuation effects of withdrawing of the medication and the associated pharmacological effects can also be seen.² Another potential disadvantage of a medication holiday could be worsening of adverse events upon reinstating the medication. Suggesting to patients that it is appropriate to not take prescribed

medications may also be an unwanted consequence of the use of medication holidays.

Barriers to Medication Holidays

There are several barriers to instituting a medication holiday. One study found that only 30% of providers in the US would consider discussing medication holidays with patients.⁵ Studies show that most medication holidays for ADHD medications are requested by parents in contrast to being initiated by providers.

Practitioners cite the following barriers to implementation of medication holidays⁵:

- Lack of skills and training on medication holidays
- Unfamiliarity regarding guideline recommendations regarding medication holidays
- Time constraints
- Parents unwillingness due to concerns around interrupting treatment
- Lack of educational materials on medication holidays
- Reliance on specialists
- Concerns over withdrawal symptoms

Conclusion

There is limited evidence that medication holidays may be beneficial for certain patients; however, some patients may experience more harm and, therefore, benefits and risks of disruption in therapy need to be appropriately assessed. Many medications lack high-quality evidence to recommend for, or against, a medication holiday. Additional studies providing evidence on the most beneficial way to conduct a medication holiday, identifying the most appropriate patients for a medication holiday and medication selection would be beneficial.

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