Adverse Neurologic Effects of Medications Commonly Used in the Intensive Care Unit

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KEYWORDS

• Adverse effects • Neurologic complications • Drug interactions • Critical care • Neurocritical care

KEY POINTS

- A detailed medication history should be performed and maintenance medications which are associated with potential withdrawal or rebound effects should be restarted if the benefit outweighs the risk.
- Numerous medications commonly used in the intensive care unit (ICU) have been associated with seizures.
- Benzodiazepines, opioids, corticosteroids, and histamine receptor antagonists have been associated with neurologic side effects, including delirium.
- Sedative, analgesic, and cardiovascular medications have been associated with increased intracranial pressure in patients in the ICU.
- Drug fever may occur at any time after initiation of the offending agent, but commonly occurs between 7 to 10 days.

INTRODUCTION

Polypharmacy is typical in most critically ill patients, which increases the risk for adverse effects and drug interactions. Furthermore, many patients have multiple comorbidities which require continuation of maintenance medications that may complicate their intensive care unit (ICU) course. Therefore, the pharmacotherapy of each patient must be evaluated to avoid adverse neurologic effects of commonly used ICU medications.

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This article focuses on medications commonly used in critically ill patients that can cause unwanted neurologic effects, and provides clinical pearls to avoid adverse drug events and drug interactions.

NEUROLOGIC COMPLICATIONS FROM MEDICATION DISCONTINUATION

Critically ill patients often require multiple medications for treatment of their acute injury. However, before starting these therapies and evaluating the potential for adverse effects and drug-drug interactions, it should be recognized that several of the patient's home medications may cause complications on abrupt discontinuation. Therefore, a detailed medication history should be performed and maintenance medications which are associated with potential withdrawal or rebound effects should be restarted if the benefit outweighs the risk. The pharmacokinetic characteristics of the individual medication will provide information regarding when withdrawal effects may begin to be observed (ie, approximately 3–5 times the half-life of the medication), and should be used to determine the window for reinitiation of therapy. **Table 1** lists

Table 1
Intensive care unit medications commonly associated with withdrawal symptoms

Drug Category	Withdrawal/Rebound Complications	Recommendations for Reinitiation of Therapy (Time After Last Dose)
Baclofen[8]	Delirium, hallucinations, agitation, muscle rigidity, hyperthermia, tachycardia, seizures	<12–24 h
Benzodiazepines[9–11]	Seizures, restlessness, anxiety, sleep disturbances, tremors, hallucinations, sweating	<48–72 h for short-acting agents; <4–7 d for long-acting agents
β-blockers[12,13]	Hypertension, tachycardia, myocardial ischemia	<24–48 h
Caffeine and Fioricet (40 mg caffeine/dose)[14,15]	Rebound headaches, decreased alertness	<12–24 h
Clonidine[16–19]	Hypertensive crisis, tachycardia, tremor, headache, anxiety, agitation	<18–36 h
Opioids[9–11]	Agitation, diaphoresis, nausea, vomiting, arthralgias, hypertension, tachycardia	<24–72 h
SSRIs[20,21]	Flu-like symptoms (nausea, vomiting, headache, lethargy), dizziness, paresthesias, tremors	<72 h (most common with shorter-acting SSRIs [eg, paroxetine > fluvoxamine > sertraline > fluoxetine])
Statins[4–7,22,23]	Cerebrovascular events, cardiovascular events	<24–48 h
Steroids (dosages ≥20 mg prednisone equivalents per day for ≥5 d or smaller doses for longer durations)[24]	Acute adrenal crisis, hypotension, fatigue, nausea, vomiting, abdominal pain, fever	Variable

Abbreviation: SSRI, selective serotonin reuptake inhibitor.

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