Canterbury District Health Board
Te Poari Hauora ō Waitaha

Clinical Pharmacology Bulletin

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Drug-induced seizures

Unprovoked seizures are estimated to occur at an incidence of <0.1% in the general population. Certain drugs are known to increase the risk e.g. antidepressants are reported to increase the risk in the general population 7-fold. Drug overdose, toxicity or abrupt withdrawal of some drugs (e.g. antiepileptics, benzodiazepines, alcohol and barbiturates) can also provoke seizures. The aim of this bulletin is to highlight drugs commonly implicated in drug-induced seizures and additional factors that put patients at higher risk.

Risk factors

Patients most likely to experience drug-induced seizures are those with additional risk factors. In some patients a combination of factors may lower the seizure threshold, including:

- **Concomitant conditions**: epilepsy, cerebrovascular disease, neurological illness, systemic illness (e.g. infection, cardiac disease), metabolic imbalance (e.g. electrolyte abnormalities, hypoglycaemia).
- **Drugs**: alcohol or drug abuse, drug withdrawal, non-compliance with antiepileptics, rapid dose increases, use or initiation of a drug that either lowers the seizure threshold or interacts with antiepileptic drugs (includes over the counter medication).
- **Other risk factors**: a family history of epilepsy, age related reduction in renal and/or liver function, sleep deprivation, stress.

Mechanism

Drug-induced seizures may be precipitated by either direct or indirect mechanisms:

- **Direct**: These include neurotoxic actions with antipsychotics (e.g. chlorpromazine, clozapine) or penicillins/cephalosporins at high plasma concentrations, pro-convulsant effects with ciprofloxacin and paradoxical neuronal excitation with general anaesthetics. Antiepileptics may paradoxically induce seizures, especially at high concentrations e.g. carbamazepine.
- **Indirect**: Drug interactions may lead to seizures. Enzyme inhibitors may interact with an antiepileptic drug resulting in high concentrations (toxicity), while enzyme inducers may cause sub-therapeutic concentrations (loss of seizure control). The side effects of some drugs may also lead to seizures, such as profound hypoglycaemia from sulphonylureas, or encephalopathy with cisplatin. Other drugs may have additive adverse effects that can result in toxicity and seizures, such as serotonin toxicity from concomitant use of tramadol and a serotonergic antidepressant.

Seizure inducing drugs

The table contains some common drugs associated with drug-induced seizures. It does not include drugs that interact with anticonvulsant medications. This table is not exhaustive.

Drug	Seizure risk
antipsychotics	
chlorpromazine	intermediate to low
clozapine	high
flupenthixol	low
haloperidol	intermediate to low
olanzapine	intermediate to low
risperidone	intermediate to low
antidepressants	
maprotiline	high
MAOIs	intermediate to low
mirtazepine	intermediate to low
SSRIs	intermediate to low
tricyclic antidepressants	intermediate to low
venlafaxine	intermediate to low
antibiotics	
cephalosporins	high to intermediate (with large IV doses)
fluoroquinolones (e.g. ciprofloxacin)	intermediate
imipenem	high to intermediate (with large IV doses)
penicillins	high to intermediate (with large IV doses)
analgesics	
codeine	low
fentanyl	low
morphine	low
NSAIDs	low
pethidine	high
tramadol	intermediate
antihistamines	
pheniramine	low
promethazine	low

Summary

When initiating a new drug in patients with epilepsy or a high risk of seizures consider the risk of provoking drug-induced seizures. In such patients drugs that lower the seizure threshold should be used only if there are no safer alternatives and at the lowest dose possible.