Clinical Pharmacology & Toxicology Pearl of the Week

~ Drug-Induced Seizures ~

Major mechanisms involved in drug induced seizures:

1. Antagonism of inhibitory neurotransmitters like GABA, glycine, adenosine, histamine
2. Agonism of excitatory neurotransmitters like glutamate and acetylcholine
3. Metabolic disturbances (hypo/hypernatremia, hypomagnesemia, hypocalcemia, hypoglycemia)
4. Sodium channel blockade

Table 1: Xenobiotics causing seizure by class (non-exhaustive list)

Analgesics	Mefenamic acid (NSAID), salicylate, opioids (meperidine, propoxyphene, tramadol)
Anticonvulsants	Carbamazepine, topiramate
Cellular asphyxiants	CO, CN, H_2S, azides
Antidepressants	TCA, citalopram/escitalopram (SSRI), venlafaxine/desvenlafaxine (SNRI), bupropion (NDRI)
Antipsychotics	Phenothiazines, butyrophenones, atypical (olanzapine, quetiapine). These lower seizure thresholds but usually not sole cause
Antihistamines	Diphenhydramine, doxylamine
Drugs of abuse	Amphetamine, MDMA, cocaine, phencyclidine, GHB
Hypoglycemics	Insulin, sulfonylureas
Heavy metals	Arsenic, lead, thallium
Sodium channel blockers	Propranolol, local anesthetics, antimalarials (chloroquine, hydroxychloroquine, quinine), antidysrhythmics (flecainide)
Substance withdrawal	Ethanol, benzodiazepines, phenobarbital, baclofen, GHB
Plants, herbs, natural products	Water hemlock, *Gyromitra* mushroom, Ephedra, Nicotine
Miscellaneous	Boric acid, camphor, fluoride, isoniazid, iron, organophosphates, carbamates, organochlorine pesticides, rodenticides (bromethalin, zinc phosphide), methylxanthines (theophylline, caffeine)

Alternatively, the mnemonic OTISCAMPBELL may be used:

O	Organophosphate, oral hypoglycemics, opioid
T	TCA, theophylline
I	Isoniazid, Insulin
S	Salicylates, Sympathomimetics, Strychnine
C	Cocaine, Camphor, CO, CN
A	Amphetamines, anticholinergics, amantadine, antibiotics (beta-lactams)
M	Methylxanthines
P	Pesticides/insecticides, PCP, plants (water hemlock)
B	Benzodiazepine withdrawal
E	Ethanol Withdrawal
L	Lead, lithium, lindane
L	Local anesthetics

Management:

- ABCs, rule out hypoglycemia, consider decontamination and elimination
- GABA agonists: Benzodiazepines (midazolam, diazepam, lorazepam) are indirect GABA agonists and are first line therapy. Phenobarbital and propofol are direct GABA agonists and can terminate seizures when benzodiazepines fail. IV levetiracetam has also been used.
- Avoid phenytoin as it is a neuronal sodium channel blocker which treats seizures with a structural focus. Drug induced seizures are generalized processes for which phenytoin is ineffective.
- Consider pyridoxine (Vit B6) in suspected cases involving pyridoxine deficiency (INH, hydrazine, *Gyromitra* mushroom) overdose. Empiric dose is 5g IV in adult or 70mg/kg in children or give gram per gram amount if ingested dose known.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the Alberta Referral Directory (ARD) by searching "Pharmacology" from the ARD home page. Click HERE for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in Alberta Referral Directory (ARD) by searching "Toxicology" from the ARD home page.

More CPT Pearls of the Week can be found HERE.

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