ANXIOLYTIC AND HYPNOTIC DRUGS

From Lippincott

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DRUG CLASS	DRUG NAMES	MOA	THERAPEUTIC USES	ADVERSE EFFECTS	OTHER POINTS	ANTIDOTE
BENZODIAZEPENES	-Long half life = 1 - 3 days Clorazepate Chlordiazeoxide Diazepam Flurazepam Quazepam -Intermediate half life = 10 - 20 hours Estazolam Lorazepam Temazepam -Short half life = 3-8 hours Alprazolam Midazolam Oxazepam Triazolam	Modulate GABA effects by binding to a specific, high affinity site (distinct from GABA-binding site) located at the interface of alpha and gamma subunit on GABA receptor. Benzodiazepenes increase frequency of chloride channel openings produced by GABA	-Reduction of anxiety (anxiolytic) -sedative/ hypnotic effects (decrease latency to sleep onset and increase stage II of non REM sleep) -premedication for endoscopy, dental procedures, and angioplasty -Midazolam is used to facilitate anterograde amnesia while providing sedation prior to anesthesia -Clonazepam used as adjunctive therapy for certain types of seizures -Lorazepam and diazepam are drugs of choice in terminating status epilepticus - Chlordiazepoxide, Clorazepate, diazepam, lorazepam, oxazepam are useful in acute treatment of alcohol withdrawal-related seizures - Diazepam is useful in treatment of skeletal muscle spasms and in treating spasticity from degenerative disorders, such as multiple sclerosis and cerebral	-Drowsiness - confusion - Ataxia occurs at high doses - Cognitive impairment (decreased recall and retension of new knowledge) can occur - should be used cautiously in patients with liver disease -have the potential for dependence and withdrawal seizures may occur - Withdrawal of triazolam results in re-inbound insomnia	-All cross the placenta and may depress CNS of newborn if given before birth -Nursing infants may be exposed to the drugs in breast milk - They are excreted in urine as glucoronides or oxidized metabolites - Psychological and physical dependence can develop if high doses are given for prolonged period - Abrupt discontinuation result in withdrawal symptoms, including confusion, anxiety, agitation, restlessness, insomnia, tension, and (rarely) seizures. - Lorazepam and Temazepam do not require Phase I metabolism and therefore, show fewer drug interactions and are safer in patients	-Flumazenil (a GABA receptor antagonist) Onset of Flumazenil is rapid but duration is short with a half life of about 1 hour. Dizzines, nausea, vomiting, agitation are most common effects of Flumazenil

			palsy. -Alprazolam is agent of choice for treating panic disorders		with hepatic impairment	
ANTI DEPRESSANT (AS ANXIOLYTICS)	SSRIs Escitalopram Paroxetine SNRIs Venlafaxine Duloxetine		only certain SSRIs or SNRIs have been approved for the treatment of anxiety disorders such as General Anxiety Disorder (GAD)	After 4 to 6 weeks, when the anti depressant begins to produce an anxiolytic effect, benzodiazepene dose can be tapered.		
BUSPIRONE			-chronic treatment of GAD - Useful in long-term therapy for chronic anxiety with symptoms of irritability and hostility.	-headache - dizziness - nervousness - nausea - light headedness	-Buspirone does not potentiate the CNS depresion of alcohol -No muscle relaxation nor anticonvulsant activity.	
BARBITURATES	LONG ACTING (1-2 days) Phenobarbitol SHORT ACTING (3-8 hours) Pentobarbital Secobarbital Amobarbital Butalbital	They potentiate GABA action on chloride entry into the neuron by prolonging the duration of chloride channel openings. In addition, barbiturates can block excitatory glutamate receptors. These molecular actions lead	-At low doses,produce sedation (having a calming effect and reduce excitement) - used to induce anethesia (now replaced by other drugs) - Phenobarbital has specific anti convulsant activity that is distinguished from nonspecific CNS depression. - Phenobarbital can depress cognitive development in children and decrease cognitive performance in adults, and it should be used for seizures only if other therapies have failed - Phenobarbital may be used for treatment of refractory status epilepticus - used as mild sedatives to relieve anxiety, nervous tension, and insomnia When used as hypnotics, they	-drowsiness -impaired concentration -mental and psychomotor impairment -Hypnotic doses of barbiturates produce a drug hangover that may lead to impaired ability to function normally for many hours after waking -occassionally nausea and dizziness occur -Abrupt withdrawal may cause tremors, anxiety, weakness, restlessness, nausea,	-They have been largely replaced by benzodiazepenes, primarily bcz barbiturates induce tolerance and physical dependence, are lethal in overdose, and are assiciated with severe withdrawal symptoms. - Barbiturates do not raise pain threshold and have no analgesic properties -Barbiturates readily cross the placenta and can depress the fetus - metabolized in liver - inactive metabolites excreted in urine	Treatment include supportive care and gastric decontaminatio n for recent ingestions

		to decreased neuronal activity.	suppress REM sleep more than other stages. -commonly used in combination products (with acetaminophen and caffeine or aspirin and caffeine) as a sedative to assist in the management of tension or migraine headaches.	vomiting, seizures, delirium, and cardiac arrest. withdrawal is much more severe that that associated with opioids and can result in death. Death may also result from overdose. -Severe depression of respiration and central cardiovascular depression results in a shock-like condition with shallow, infrequent breathing	-contraindicated in patients with acute intermittent porphyria	

OTHER HYPNOTIC AGENTS

DRUG NAME	MOA	THERAPEUTIC USES	DURATION OF ACTION	ADVERSE EFFECTS	OTHER POINTS
ZOLPIDEM	Binds to GABA receptors with relative selectivity for those with alpha 1 subunit	-A sublingual tablet formulation may be used for middle-of-the-night awakening. -Unlike the benzodiazepines, at usual hypnotic doses, the nonbenzodiazepine drugs, zolpidem, zaleplon, and eszopiclone, do not significantly alter the various sleep stages and, hence, are often the preferred hypnotics	Zolpidem is rapidly absorbed from the gastrointestinal (GI) tract, and it has a rapid onset of action and short elimination half-life (about 2 to 3 hours). It provides a hypnotic effect for approximately 5 hours	-nightmares -agitation -anterograde amnesia -headache - GI upset -dizziness - daytime drowsiness.	-Zolpidem has no anticonvulsant or muscle-relaxing properties. It shows few withdrawal effects, exhibits minimal rebound insomnia, and little tolerance occurs with prolonged use.

ZALEPLON			half-life of approximately 1 hour		zaleplon causes fewer residual effects on psychomotor and cognitive function compared to zolpidem or the benzodiazepines.
ESZOPICLONE	It is an oral nonbenzodiazepine hypnotic that also acts on the BZ1 receptor	-shown to be effective for insomnia for up to 6 months	Eszopiclone is rapidly absorbed (time to peak, 1 hour), extensively metabolized by oxidation and demethylation via the CYP450 system, and mainly excreted in urine. Elimination half-life is approximately 6 hours.	-Anxiety -dry mouth -Headache -peripheral edema -somnolence -unpleasant taste.	
MELATONIN RECEPTOR AGONISTS (Ramelteon, Tasimelteon)	selective agonist at the MT1 and MT2 subtypes of melatonin receptors	-induce and promote sleep - for treatment of insomnia characterized by difficulty falling asleep (increased sleep latency) - Tasimelteon is indicated for non-24-hour sleep-wake disorder, often experienced by patients who are blind.		-dizziness -fatigue -somnolence - Ramelteon may also increase prolactin levels -Common adverse effects of Tasimelteon are headache, abnormal dreams, increase in liver function tests and possible upper respiratory infections	-can be administered long term due to minimal potential for abuse, and no evidence of dependence or withdrawal
ANTI HISTAMINES		Some antihistamines with sedating properties, such as diphenhydramine, hydroxyzine, and doxylamine, are effective in treating mild		anticholinergic effects	

		types of situational insomnia			
ANTI DEPRESSANTS		-Doxepin is approved at low doses for management of insomnia			
SUVOREXANT	An antagonist of orexin receptor. Orexin is a neuropeptide that promotes wakefulness.			-Daytime somnolence - increased suicidal ideation	