

Treatment of anxiety disorders

A- Stress anxiety disorder:	<ol style="list-style-type: none">1- treated by BDZs: for short- term relief; resolve < 1 month.2- Beta blockers can be used
B- Social anxiety and situational anxiety disorder	<ol style="list-style-type: none">1- Beta-adrenergic blockers e.g. propranolol2- Long term benefit from SSRIs
C-Panic attacks	<ol style="list-style-type: none">1- BDZs (alprazolam) for short-term relief2- SSRIs antidepressants e.g. paroxeti or TCAs e.g. clomipramine for long-term control
D- Phobias	<ol style="list-style-type: none">1-Phobias are treated by Behavioral therapy2- drugs like Alprazolam (acute), or SSRIs (long-term).
E-Generalized anxiety disorder	<ol style="list-style-type: none">1-BDZs: for acute symptoms or for chronic use.2- Buspirone : for chronic control esp. in elderly.3- Antidepressants esp. SSRIs are also helpful
F- Obsessive-compulsive disorder (OCD)	<ol style="list-style-type: none">1- Psychotherapy2-Antidepressants e.g Clomipramine or SSRIs.3- BDZs are not helpful in OCD
G- Post-traumatic stress disorder (PTSD):	<ol style="list-style-type: none">1- BDZs: should be used early to promote sleep and minimize mental re-experience of the stress trauma which can lead to its persistence. May be used long- term for 62- SSRIs: paroxetine for long term control .3- Other antidepressants TCAs may also be used.

Miscellaneous sedative hypnotics

	1- Chloral hydrate	2.Chlormethiazole	Alpha 2-Adrenoreceptor Agonists		β -Adrenoreceptor Antagonists	5- Antihistaminic drugs
			1- clonidine	2- 2- Dexmedetomidin		
Note	<p>1- it is metabolized in liver to active metabolite Trichloroethanol (which is also a microsomal hepatic enzyme inducer).</p> <p>2- It displaces warfarin from plasma protein binding sites.</p>	<p>1- It is a thiamine analogue.</p> <p>2- It enhances GABA actions.</p>			e.g., Propranolol)	H1-blockers as diphenhydramine
Use	<p>1-Little used now as hypnotic.</p>	<p>1- It may be used as hypnotic in elderly.</p> <p>2- It may also be used IV for status epilepticu</p>	<p>1- Antihypertensive</p> <p>2- Has been used for the treatment of panic attacks.</p> <p>3- Has been useful in suppressing anxiety during the management of withdrawal from nicotine and opioid analgesics</p>	<p>1- It is used for sedation in mechanically ventilated adults</p> <p>2- it may reduce time needed for extubating patients</p> <p>3- reduce the time of ICU stay.</p>	<p>Used to treat some forms of anxiety, particularly when physical (autonomic) symptoms (sweating, tremor, tachycardia) are severe.</p>	<p>1- can be used as sleep aids for children with insomnia.</p>
•Adverse effects	<p>1- It is a gastric irritant</p>		<p>Withdrawal from clonidine, after long use, may lead to a life-threatening hypertensive crisis.</p>		<p>1- lethargy,</p> <p>2- vivid dreams</p> <p>3- hallucinations</p> <p>4- bronchospasm,</p> <p>5- bradycardia</p> <p>6- hypoglycemia with insulin</p> <p>7- hyperlipidemia.</p>	

Barbiturates

<p>Pharmacokinetics</p>	<ol style="list-style-type: none"> 1-They are weak acidic drugs, absorbed orally. 2- redistribute in the body 3- metabolized in the liver 4- induce P450 microsomal enzymes 5- inactive metabolites are excreted in the urine. 6- Alkalinization of urine helps their excretion (IV sodium bicarbonate is used for management of acute barbiturate toxicity) 7- readily cross the placenta and can depress the respiratory center of the fetus.
<p>Therapeutic uses</p>	<ol style="list-style-type: none"> 1- Anesthesia :(The ultra-short acting barbiturates, such as thiopental, are used intravenously to induce general anesthesia.) 2- Treating anxiety and insomnia (BZD are preferred now): <ol style="list-style-type: none"> a- used as mild sedatives to relieve anxiety, nervous tension, and insomnia (amobarbital). b- Barbiturates suppress REM sleep significantly. 3- Anticonvulsant: (phenobarbital, mephobarbital): <ol style="list-style-type: none"> a- Phenobarbital is used in long-term management of tonic- clonic seizures, status epilepticus, and eclampsia. b- Primidone is also used for seizure disorders and tremors. c- The anticonvulsant doses are less than hypnotic doses and doses used for anaesthesia. 4- Treatment of young children with recurrent febrile seizures: <ol style="list-style-type: none"> a- phenobarbital can depress cognitiveperformance in children b-drug should be used cautiously. 5- Treatment of neonatal jaundice:(Stimulation of microsomal hepatic enzymes by phenobarbital can accelerate bilirubin metabolism. 6- Methohexital <ol style="list-style-type: none"> a-is used for procedural sedation of short duration b-e.g. cardioversion and pediatric outpatient surgery, fracture reduction for elective intubation). 7- Butalbital:(is used for the treatment of headache disorders.)
<p>Adverse effects of barbiturates</p>	<ol style="list-style-type: none"> 1- Dose dependent CNS depression:(Barbiturates cause drowsiness, vertigo, impaired concentration, etc.) 2-Drug hangover: (Hypnotic doses of barbiturates produce a feeling of tiredness well after the patient wakes.) 3- In toxic doses (respiratory depresion, Cardiovascular colapse, and coma. Death occurs due to respiratory failure) 4- induce the P450 system (affect metabolism of many drugs (drug-drug interactions)). 5- increase porphrin synthesis (C.I : in patients with prophyria) 6- behaviour change in children 7- tolerance , dependence, addication (more than BZD) 8- Abrupt withdrawal (anxiety, restlessness, delirium, seizures, weakness, vomting , cardiac arrest)

	Buspirone	Melatonin and Ramelteon	Orexin receptor antagonists
	<p>1-It selectively binds to SHTIA (serotonin) receptor acting as a partial agonist.</p> <p>2- It has no relation to BZD receptor or GABA inhibitory neurotransmitter.</p> <p>3- Ipsapirone:</p> <p>a- one is a selective 5-HTIA receptor partial agonist.</p> <p>b- It has both antidepressant and anxiolytic effects</p>	<p>1- Both melatonin and Ramelteon are agonists at MT 1 and MT 2 melatonin receptors located in the brain.</p> <p>2- The drug has no direct effects on GABAergic neurotransmission in the CNS (Little CNS depression).</p> <p>3- Ramelteon (Synthetic tricyclic analog of melatonin)</p>	<p>1- orexin receptor antagonists), which include Almorexant and suvorexant.</p>
	<p>1- Its anxiolytic effect does not appear before 2-4 weeks of its administration.</p> <p>2- it is highly bound to plasma protein</p> <p>3- metabolized in the liver by CYP 3A4</p> <p>4- Tolerance to its effect does not occur, little potential to abuse and no withdrawal symptoms develop after abrupt withdrawal.</p>	<p>1-Melatonin is used orally or sublingual</p> <p>2- It is safe for children.</p> <p>3- It has no rebound insomnia or significant withdrawal symptoms.</p> <p>4- Ramelteon has minimal potential for abuse, and regular use does not result in dependence</p>	<p>1- Orexin A and B are peptides that are involved in the control of wakefulness and that are silent during sleep.</p> <p>2- Orexin levels increase in the day and decrease at night.</p> <p>3- Loss of orexin neurons is associated with narcolepsy (daytime sleepiness).</p> <p>4- Animal studies show that orexin receptor antagonists have sleep-enabling effects.</p>
	<p>1- suitable for chronic anxiety</p> <p>2- <u>not</u> effective in severe anxiety like panic attacks</p> <p>3- <u>not</u> effective in acute anxiety states.</p> <p>4- It has <u>no</u> hypnotic or anticonvulsant effects.</p>	<p>1- novel hypnotic drug specifically useful for patients who have difficulty in falling asleep.</p>	<p>1- A new class of hypnotics (orexin receptor antagonists)</p> <p>2- Suvorexant was approved for use as hypnotic by FDA.</p>
	<p>1- cns :headache, nausea, drowsiness but sedation is minimal.</p> <p>2- paresthesias may occur.</p> <p>3- tachycardia</p> <p>4- eye: causes a dose-dependent pupillary constriction (miosis).</p> <p>5- Other : palpitations, GI distress</p>	<p>1- dizziness</p> <p>2- fatigue</p> <p>3- endocrine changes (increases prolactin and decreases testosterone).</p>	