Antianxiety drugs

Benzodiazepines (BD) - the most effective antianxiety drugs
Antidepressants
- –Selective serotonin reuptake inhibitors (SSRIs)
- –Tricyclic antidepressants (TCAs)
- –Heterocyclics
  - •Mixed norepinephrine/serotonin reuptake inhibitors
  - •Mixed-action drugs
- –Monoamine oxidase inhibitors (MAOIs)

•Buspirone
•Antipsychotics (neuroleptics)
•Barbiturates
•Antihistamines
•Clonidine
•Beta-blockers
•Meprobamate and derivatives
•Antiepileptic drugs

Benzodiazepines (BD)

Mechanism of action:
•Facilitate neuronal membrane inhibition by actions as specific receptors
•Binds to specific receptors in CNS that are involved in modulation of GABA (γ-aminobutyric acid) transmission (enhancement of affinity of GABA)
•This inhibitory neurotransmitter increses the influx of chloride ions through cell membrane channels, thus inhibiting membrane depolarization
•BD do not substitute for GABA but appear to enhance GABA's effects without directly activating GABA receptors or opening the associated chloride channels
•The enhancement in chloride ion conductance induced by the interaction of BD with GABA takes the form of an increase in the frequency of chanel-opening events
•Receptors for BD – in many brain regions (thalamus, limbic structures, cerebral cortex)

Short-acting BD: •Midazolam •Lorazepam •Oxazepam •Alprazolam •Halazepam
Long-acting BD: •Diazepam •Chlordiazepoxide •Chlorazepate •Prazepam •Clonazepam

Administration
•They are best used only for brief periods (psychological and physiological dependence, tolerance)
•The best results – treating time-limited anxiety (in response to clear-cut stress and when treatment lasts less than 8 weeks)
•Chronic anxiety, limited intrapsychic or external resources, inefficacy of buspirone and antidepressants - may need long-term therapy
•Repeated treatment - often necessary

Addiction
•Is rare in medical patients
•Individuals with a history of alcohol or drug abuse, physician shopping, antisocial behavior – are at risk of abusing BD
•The most frequently abused BD: •diazepam •alprazolam •lorazepam
Adverse effects – sedation, impaired cognitive defects (difficulty focusing attention, memory impairment,confusion), disinhibition, tolerance, abuse potential, withdrawal, may cause or aggravate depression

Abstinence syndromes (withdrawal symptoms)
•May appear up to 10 days after abrupt discontinuation of moderate doses of BD that have been taken for more than 1 month
•Anxiety, insomnia, irritability, at times psychosis, delirium, seizures
•Some patients - withdrawal symptoms lasting up to 1 year
•Withdrawal is more abrupt and severe after discontinuation of short-acting BD•

SSRIs: Fluoxetine •Sertraline •Paroxetine •Fluvoxamine •Citalopram •Escitalopram

TCAs: Amitryptyline, Nortriptyline, Imipramine, Desipramine, Doxepin, Clomipramine

Mixed-action drugs: •Bupropion •Trazodone •Nefazodone •

Buspiron
Mechanism of action:
•Unclear
•May involve alteration of dopaminergic or serotinergic activity in CNS (partial agonist of the serotonin 5-HT1A receptor)
•Nonsedating, doas'nt produce tolerance or dependence, doas'nt interact with BD receptor or alcohol•
•Takes 1 month lag time before clinical response; Requires thrice-daily dosing
Indications: the same as the BD**,** generalized anxiety disorder, social phobias
Adverse effects: minimal sedation, nausea, headache, psychomotor impairment

Barbiturates
Effective sedative-hypnotics; Impairment of motor and intellectual performance; Interact with many drugs; High fatality rate with overdoses; High addiction potential
•Facilitate the actions of GABA at multiple sites in the CNS, but (in cotrast to BD) appear to increase the duration of the GABA-gated chloride channel openings
•At high concentrations may also be GABA-mimetic, directly activating chloride channels
•These effects involve a binding site (sites) distinct from BD binding site
•Also depress the actions of excitatory neurotransmitters (eg glutamic acid)

Antihistamines
•Hydroxizine – limited usefulness as a pre-anesthetic sedative (patients who do not respond to BD), Diphenhydramine
•Usually with effective dosage – sedation, increase muscle tone, lower seizure threshold, affect the peripheral nervous system

Antipsychotics
Not cosistently effective in treating anxiety; Seldom used to treat anxiety

Anticonvulsants
•GABAergic properties (gabapentin, oxcarbazepine, tiagabine, pregabalin, divalproex)

Beta-blokers
Effective in **preventing performance anxiety** by suppressing sympathetic nervous system activity and autonomic symptoms (palpitations, tremor); Ineffective in preventing the emotional symptoms

Clonidine
Acts by decreasing the firing of locus ceruleus. **Side effects:** dry mouth, increased tension, drowsiness, sleep disturbances;

Meprobamate and derivatives
•Muscle relaxant properties, sedative and anticonvulsant activity; Induce liver microsomal enzymes; Tolerance, dependence