Anxiety

- Unpleasant state of tension, apprehension or uneasiness that seems to arise from an unknown source.

- Usually associated with somatic symptoms →tachycardia, sweating, tremor, palpitation, hyper apnea, etc

anxiety

tachycardia

dilated pupils

tremor

sweating

ANXIETY DISORDERS

- Panic Disorder
- Generalized Anxiety Disorder
- Phobic Disorders
- Stress Disorders
- Obsessive-Compulsive Disorder

Anti anxiety drugs

- Mostly mild CNS depressants
- Control the symptoms of anxiety, produce a restful state of mind without interfering with normal mental or physical functions.

Classification

1. Benzodiazepines: Diazepam ,Chlordiazepoxide Oxazepam, Lorazepam, Alprazolam, Flurazepam
2) Azapirones :Buspirone ,Gepirone, Ipsapirone
3) Sedative Antihistaminic: Hydroxyzine
4) Beta blockers :Propranolol
5) Others: SSRIs, TCA, MAO- inhibitors, SNRI (venlafaxine)

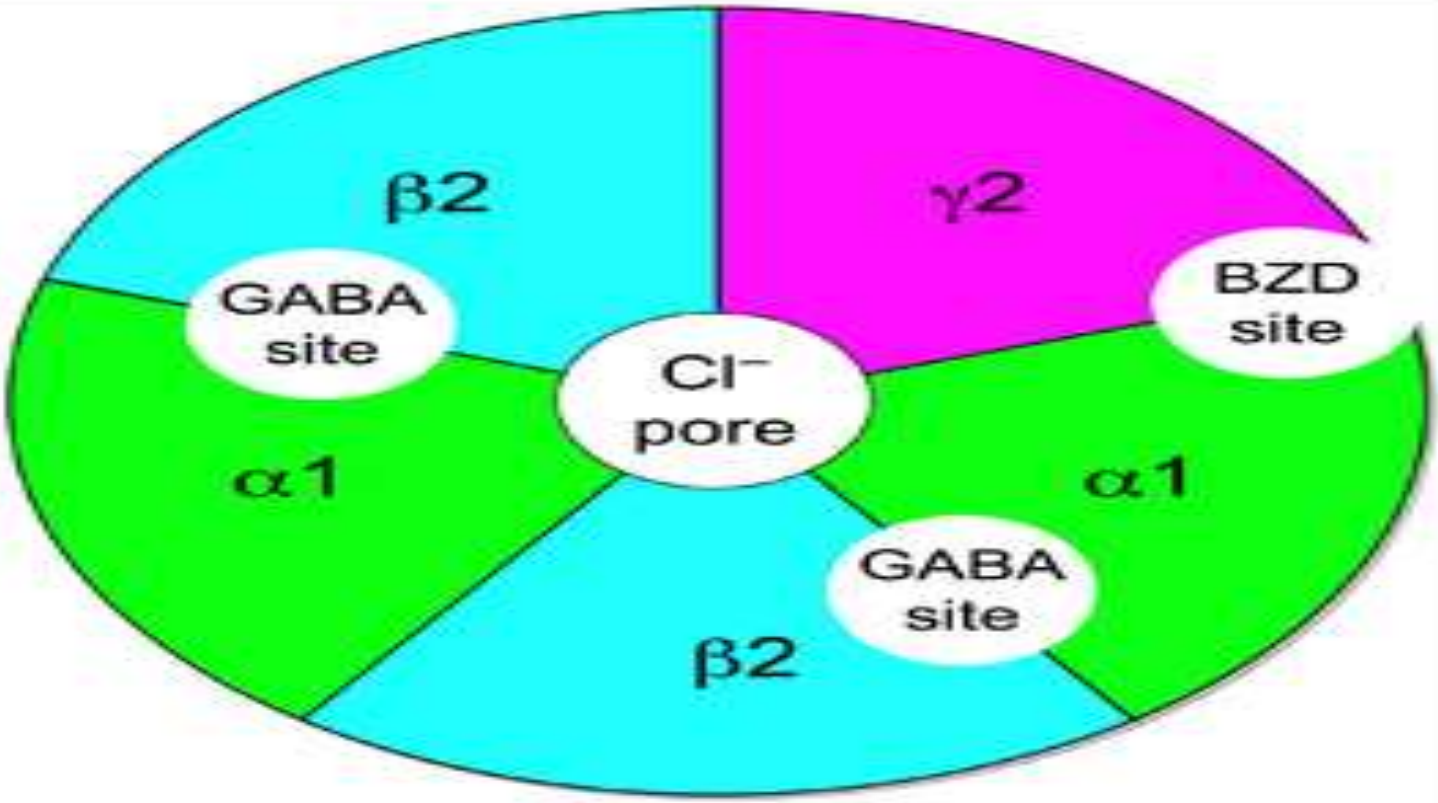
- *Meprobamate , C*lonidine,

Benzodiazepines

- Site of action: mid brain ,ascending reticular formation ,&limbic system

- MOA:

  By post synaptic inhibition through BZD receptor



Schematic diagram of a $GABA_A$ receptor protein ($(\alpha1)_2(\beta2)_2(\gamma2)$) which illustrates the five combined subunits that form the protein, the chloride (Cl^-) ion channel pore, the two GABA active binding sites at the α1 and β2 interfaces, and the benzodiazepine (BDZ) allosteric binding site at the α1 and γ2 interface.

PK of Benzodiazepines

- Given orally ,iv & im (lorazepam & temazepam)
- Oral absorption good
- Phase I & phase II metabolism
- Lorazepam & Oxazepam → no active metabolite → short acting

ADR

- Sedation
- Light headedness
- Cognitive impairment
- Vertigo
- Confusion
- Appetite & Wt gain
- Alt in sexual function
- Dependence

Advantages of BZD

- High therapeutic index
- Do not affect respiration or cardiovascular function
- No microsomal induction
- Low abuse liability
- Specific BZD antagonist **Flumazenil** is available

CHLORDIAZEPOXIDE

- First BZD used as an antianxiety agent
- Produce smooth long lasting effect
- Preferred in chronic anxiety states
- T1/2 :5-15 hours
- Dose : 20-100 mg

OXAZEPAM

- Hepatic metabolism is less significant
- It is preferred in the elderly and those with liver disease
- Short duration of action
- Used in short lasting anxiety state

LORAZEPAM

- Oral & IM administration
- No active mtb
- Short acting → preferred in elderly
- Used in short lasting anxiety ,Panic, OCD, tension syndrome
- Dose: 1 - 6mg/day

ALPRAZOLAM

- Anxiolytic + antidepressant
- High potency anxiolytic
- Useful in anxiety associated with depression
- Less drowsiness
- Dose : 0.25-0.5mg BD or TDS
- active mtb

AZAPIRONES

- Buspirone , Gepirone, Ipsapirone

MOA:

- Selective agonistic action on 5HT-1A receptor
- Weak D2 blocking action – no antipsychotic or extrapyramidal S/E

Site of action:

- Dorsal raphe seretoninergic neurones

Azapirones

Advantages:

- No sedation
- No tolerance or physical dependence
- No abuse liability
- Less psychomotor impairment
- Does not potentiate the effect of other CNS drugs

Disadvantages

- Slow onset of action
- not suitable for acute anxiety
- Requires thrice daily admin

PK

- given orally, rapidly absorbed
- Extensive first pass metabolism
- Excreted through urine and faeces

ADR

- Dizziness ,headache, Nausea
- Tachycardia , Pupillary Constriction

DOSE: 5-10mg OD-TDS

SSRI in Anxiety

- Preferred in chronic anxiety states
- Started in low dose
- Slow onset of action
- Started along with BZD

Beta blockers

- **Propranolol** :reduce the symptoms of anxiety
- They do not affect the psychological symptoms (worry ,tension, anxiety)
- Used for performance/situational anxiety
- Dose: 20-40mg 2hr before the performance

Different type of anxiety and its and its management

- **Generalized Anxiety Disorder**: persistent excessive, unrealistic worry associated with somatic symptoms.
- Acute phase – Benzodiazepines are preferred
  - Rapid onset of action
  - Eg: lorazepam, Oxazepam
  - Not ideal for long term treatment due to abuse liability & development of tolerance
- For long term use : Buspirone ,SSRIs .

Obsessive-Compulsive Disorder

- Obsessive thoughts and compulsive behaviors that impair everyday functioning
- Treatment
  - TCA (clomipramine)→ poorly tolerated
  - SSRI
    - Fluoxetine (5–60 mg/d),
    - fluvoxamine (25–300 mg/d),
    - sertraline (50–150 mg/d)
  - Buspirone
  - BZD

Panic Disorder:

- Recurrent and unpredictable panic attacks, with intense discomfort and fear of impending doom or death.

- Treatment
  - SSRIs →low doses
  - Eg: 5–10 mg fluoxetine, 25–50 mg sertraline, 10 mg paroxetine

Phobic Disorders

- Persistent fear of **objects or situations**, exposure to which results in an immediate anxiety reaction. The patient avoids the phobic stimulus, and this avoidance usually impairs occupational or social functioning.

- Treatment
  - Beta blockers : Propranolol 20–40 mg orally 2 h before the event (performance anxiety)
  - SSRIs
  - MAO inhibitors

Stress Disorders

- Anxiety following exposure to ***extreme traumatic events***. The reaction may occur shortly after the trauma (*acute stress disorder*) or be delayed and subject to recurrence (PTSD) . In both syndromes, individuals experience associated symptoms of detachment and loss of emotional responsivity.

- Treatment
  - Benzodiazepines and supportive/expressive psychotherapy
  - SSRI
  - MAO inhibitors