Sleep is a normal physiological phenoming. Sleeplessness (insomnia) may result from a variety of causes. in the treatment of insomnia, Anxiety, and genral type of epilepsy. A category of drug is used called sedative / Hypnotic.

⇒ Tranquillizer → in latin word,

Trangu = calm and quit.

⇒ All those drugs, which brings the excitate C.N.S into calm and quit state called Tranquillizer.

According to duration of action and potency of drug tranquiller divided -2.

A. Minor tranquillizer → Sedative
B. Major " → Hypnotics } called as

⇒ Sleep in classified into 4 step →

1. Step-I (Awakeful sleep) → it is the first step in which total conciousness remains and the person remains in a normal stage. duration of this stage about - 20 to 30 mi.

2. Stage -II (induce periode of sleep) → Just after the awakeful stage, the sleep induces and the person feel drowsy, Eyelid become heavy and C.N.S depression is observed.

3. NREM (Non Refrectty Eye movement) → This is (orthodox) the total sound sleep with C.N.S depressent and loss of conciousness. in this stage, the rate of respiration become deep and sallow.

4. REM → it is the last stage of sleep.
(Paradoxical sleep) in this stage total subconcious and maximum, C.N.S depression nerv and dreams take place.

⇒ in this stage Reflex action are observed and muscular activity become poor. R.E.M sleep occupies 25% of sleeping time.

[Hypnotic effect involves more pronounced depression of the CNS, than sedation. Sedative hypnosis can be achieved with most sedative drug simply by ↑ the dose.]

Sedative ⇒

⇒ All those drugs which reduces the stage one of sleep OR induces the sleep are called sedative.

Hypnotic → All those drugs which directly produces the normal sleep / NREM are called Hypnotic.

Classification of sedative / hypnotic →

Sedative / hypnotics are mainly classified 3 category

1. Barbiturates
2. Benzodiazepien
3. Miscellenous

1. Barbiturates → Barbiturates are further classi. into 4 category

long acting barbiturates (6 hours more) → Barbitone sodium
phenobarbitone
methobarbitone
methabital
primidone

intermediate bar. → Allobarbiton
(3 to 6 hour) Butabarbiton, Amobarbiton
Aprobarbiton, Argobarbiton

short acting → cyclobarbital, Hexobarbital
(less than 3 h) Pentobarbiton, Secobarbiton
with

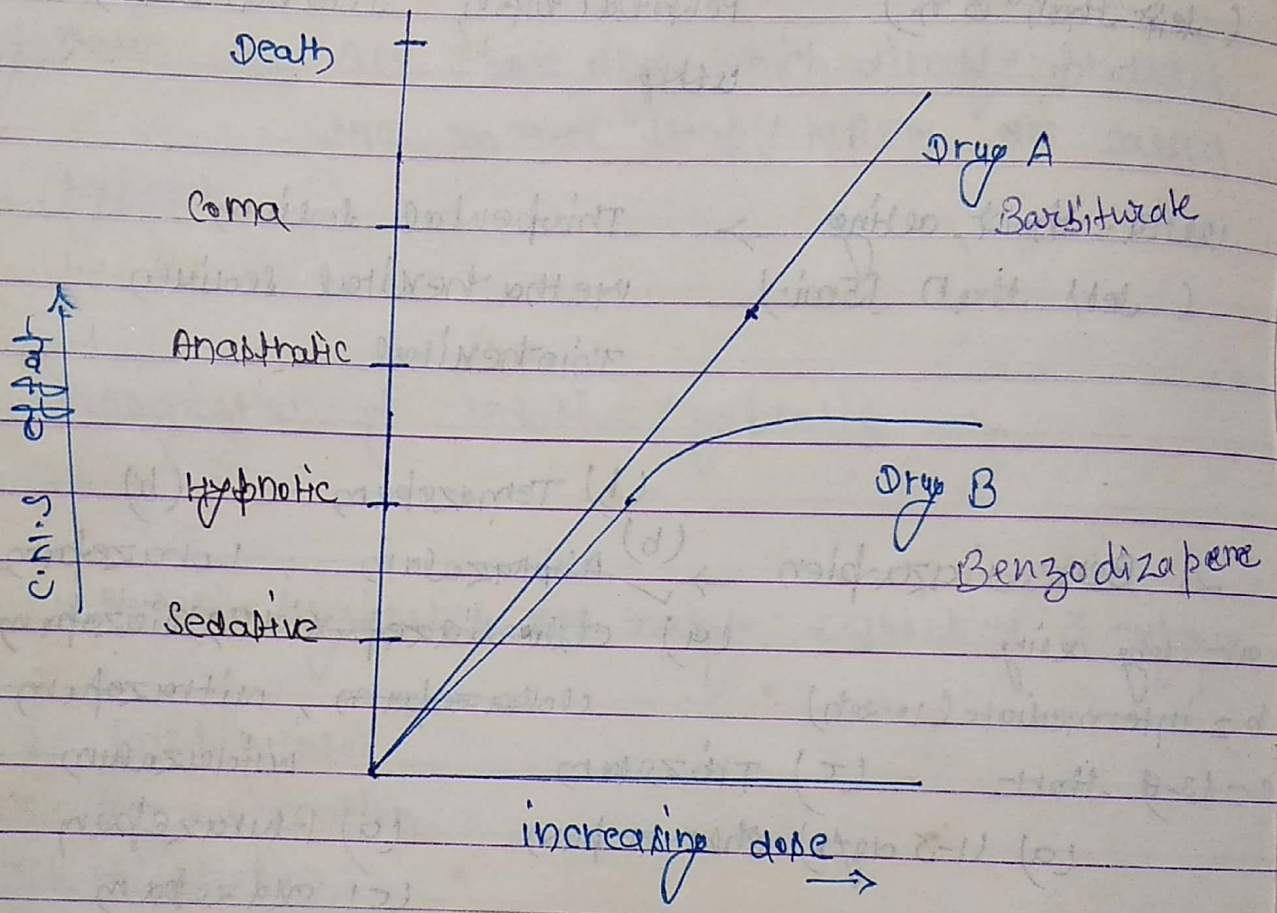
ultra-short acting → Thiopental sodium
(less than 15 min.) methathexital sodium
thiothexital

2. Benzodiazepien → (b) Temazepam (b)
(b) Nitrazolam, Lorazepam
(a) chlordiazepoxide/Diazepam
a = long acting clonazepam, nitrazepam
b = intermediate (1-3 h) midazolam
c = v.s short (c) Triazolam (a) Flurazepam
(a) (1-3 days) Chlorazepam (c) oxazepam

3. Miscellaneous → (A) inorganic salt → NaBr, KBr
(B) Chloral derivative → chloral hydrate
(C) Aldehyde derivative → paraldehyde
(D) Alcohol → Ethinamate, Ethchlorvynol
(E) Acyl-urea / Acety urea → Bromisoval
Carbromal
(F) Piridine dione deriv → Glutethimide
(G) Di-substituted quinazolon → methaqualone

Classification of ~~inter~~ Benzodiaza

Barbiturates →



Barbiturates → Barbo were discovered early in 20th century, hundreal of compound were made and tested in this periode. untill 1960 they form the largest group of hypnotics Sedative clinically.

Barbiturates produces effect in ranging from sedation, hypnosis and to unconsciousness and death. therefore dangerous in overdose. They causes death from respiratory and C.V depression if given in large dolgoe.

Therefore Barbiturates are very rarely used in nowadays. Pentobarbiton and similar typical Baro, with a duration of action of 6-12 hrs are still very occasionaly use. But they are less safe then Benzodaizapien.

Baro, which remains in white spread use are those which have specific property (Phenobarbitone used for convulsion).

Mechanism of Actions → Barbiturates action Benzodiazapien receptor resulting intance the action of GABA. Baro bind to a different site on Benzo.-GABA receptor and their action seems to be less specific than Benzo.

Baro. blocks the depolarization or prevent the gentation potential to excitatory post synaptic nerve.

Uses → They are effective sedative and hypnotics are

They are widely employed in a variety of dis. in a symptom where sedation/hypnotic needed.

2> They are useful in insomnia accute maniacal (उन्माद) state, and some Psicyconeurotic disorder.

2> They are also useful in anxiety associated with hypertension.

2> They are also useful in convulsion disorder.

Toxic effect → they produce respiratory and cardiack depression in large dosage.

2> They causes addiction.

Benzodiazapien → Nowadays many benzodiaz. are widely used as sedative hypnotic, Anasthetic Anticonvulsant, Muscle-Relaxant.

This is the safe drug in comparison to Barbiturate because :-

(a) Benzo, have high therapeutic index. They are not having unconciousness and Respiratory depression.

(b) hypnotic dose donot effect Respiration and C.V functions.

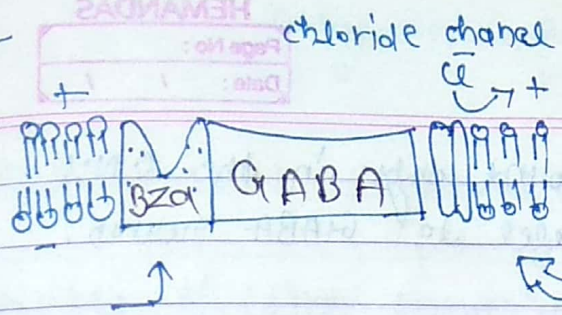
(c) Benzo, have practically no action on other body sys. only, even intravenous injection the B.P fall and cardiacs contractility dicreases.

(d) Benzo, donot alter disposition of other drug by microsomal enz.

(E) They have lower abuse liability.

Mechanism of action → Binding of GABA to its rece. on the cell membrane trigger and opening of a Cl chanel, which leads to an ↑ in Cl conduction. The influx of Cl ions, causes a small hyperpolarization that moves the post synaptic potential away from it firing threshold potential and thus inhibit the formation of action potential.

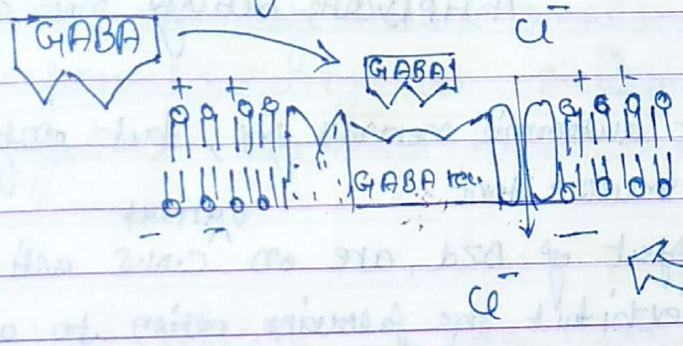
Bzd, bind to its receptor on the cell membrane which are seperate from GABA receptor,



Empty receptor is inactive and the coupled, Cl^- chanel is close.

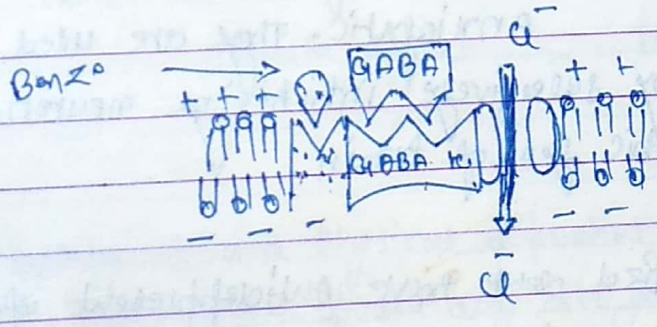
Bzd receptor

(B) Receptor binding GABA →



Binding of GABA causes the Cl^- ion chanel to open.

(C) Receptor binding GABA and Benzo. →



Binding of GABA is enhanced by Bzd resulting in a greater entry of chloride ion.

Entry of Cl^- hyperpolarized cell making it more difficult to depolarize and therefore reducing neural excitatory.

but adjacent to GABA receptor.

⇒ Binding of Bzd increases the activity of GABA receptor for Cl^- ions influx.

⇒ Benzodiazepines here, are found only in the C.N.S and their location parallel to GABA neuron.

(OR USES)

Pharmacological action → Benzo., have neither Antipsychotic activity nor any analgesic activity.

⇒ Bzd do not affect autonomic nervous sys, but only depress reduced skeletal muscle tone.

⇒ most imp effect of Bzd, are on various C.N.S activity.

⇒ all the Bzd exhibit the following action to a greater or lesser extent.

1. Reduction of Anxiety → At low dosage, Bzd are Anxiolytic. They are used to reduced anxiety, by selectively inhibiting neuronal circuit in the Limbic sys of brain.

2. Anti-depressent → Bzd do not have Antidepressent effect except alprazolam.

3. Sedative and hypnotic action → All the Bzd (used to treat anxiety) have sedative action. At higher dosage, certain Bzd, produced hypnosis.

⇒ Bzd, ↓, the time taken to get sleep and ↑ the total duration of sleep. Both effect tends to decline when benz. are taken regularly 1-2 weeks.

GABA Antagonist → Bicuculine, Flumazenil

HEMANDAS
Page No :
Date : / /

4. Anticonvulsent → Several of Bzd have anticonvulsent activity and are used to treat epilepsy & (other sevear disorder).

All the Bzd have anticonvulsent activity in experiment animal test. They are highly effective against chemicaly induced convulsent caused by Leptazal, Carrgennen, Bicuculine but less effective against electricaly induced convulsent in experimental model.

Muscle-Relaxant → Bzd relaxe the spasticity of skeletal muscle, probably by increasing presynaptic inhibition in the spinal chord.

Adverse effect → Toxic effect resulting from accute overdose. (24hrs)

2> Psychological and Physical dependent on Bzd, can develope if high dosage of the drug are given over a prolonged period. Abrupt discontinuation of Bzd result in withdrawal (cessation of use) symptoms such as confusion, Agitation, Restlessness insomnia, Anxiety and tension.

Drowsiness and confusion are the 2 most common side effect of Bzd. Ataxia occurs at higher (Loss of muscle control) dosage.

HEMANDAS
Page No:
Date: / /

Miscellenious → Zalpidem → it is not Bdz, but it act on Bzd receptor.
(other hypnotic agents)

⇒ it has no anticonvulsant or muscle-relaxant property.
⇒ it shows no or very little withdrawal symptoms.
⇒ zalpidem is rapidly absorbed from GIT, and has a rapid onset of action and short half life (3 hrs)
Adverse effect of zalpidem are GIT disturbance, agitation, Headathique, Day time drowsiness.
⇒ Although zal. has potentially advantages over the Bdz, but clinical experience is still limited.

Buspirone → Buspirone is useful in the treatment of anxeity disorder and has an efficacy comparable to Bzd.
Buspirone act by 5-HT_{1A} receptor. Buspirone also act on other receptor such as dopamine-2 receptor (D-2) and 5-HT_2 receptor.

⇒ Buspirone lacks anticonvulsant and muscle-relaxant property of Bdz, and causes only minimal sedation.
⇒ Adverse effect are headathique, Dizziness, nervousness and agitation.