

ACUTE POISONING OF BARBITURATES & BENZODIAZEPINES





BARBITURATES:

- ❖ Non-selective **CNS depressants**.
- ❖ Derivatives of barbituric acid (2,4,6- trioxo hexa hydro pyrimidine).
- ❖ Popular sedative & hypnotics up to 1960's.
- ❖ Can produce effects ranging from **sedation & reduction of anxiety** to **unconsciousness & death** from respiratory & cardio vascular failure.

USES:

- ✓ **Sedative & hypnotic.**
- ✓ **Pre operative sedation.**
- ✓ **Treatment of seizure disorders.**



MECHANISM OF TOXIC EFFECTS

- ❖ Direct CNS depressants.

- ❖ Bind to GABA receptors



Prolong the opening of chloride channel



Inhibiting excitable cells of the CNS

- ❖ Potent inducer of hepatic drug- metabolising enzymes especially CYP450 system, so liable to cause drug interactions.
- ❖ Precipitate attacks of acute porphyria.
- ❖ Tolerance & dependence occur.

CLASSIFICATION:

1. LONG ACTING: (6-12 hrs)

- ❖ Mephobarbitone
- ❖ Phenobarbitone

2. INTERMEDIATE ACTING: (3-6 hrs)

- ❖ Amobarbitone
- ❖ Aprobarbitone
- ❖ Butobarbitone

3. SHORT ACTING: (<3 hrs)

- ❖ Hexobarbitone
- ❖ Pentobarbitone
- ❖ Secobarbitone

4. ULTRA-SOUND ACTING: (<15-20 mins)

- ❖ Thiopentone
- ❖ Methohexitone



ADVERSE EFFECTS:

- Residual depression.
- Paradoxical excitement.
- Hypersensitivity reactions-localised swelling of eye lid,cheek or lip , erythematous or exfoliative dermatitis.
- Synergistic action with ethanol & antihistamines.

TOXIC EFFECTS:

- Slurred speech , ataxia, lethargy, confusion , headache , nystagmus .
- CNS depression,coma,shock.
- Pupils –first constricted , later dilate because of hypoxia.
- Hypothermia
- Cutaneous bullae (blisters)
- Death due to respiratory arrest or cardio vascular collapse.

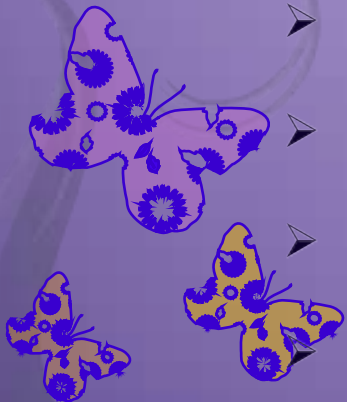
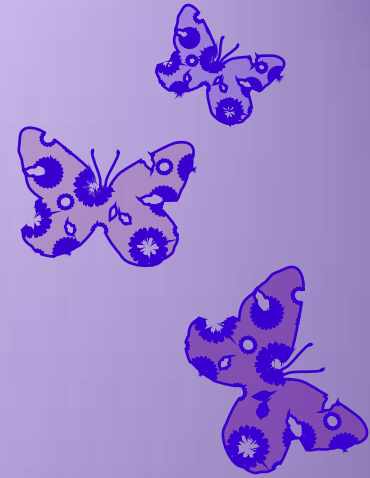
ACUTE BARBITURATE POISONING

- ❑ Leading cause of poisoning due to their ready availability.
- ❑ Most of the cases are suicidal but some are due to error or ungraded exploration in children.
- ❑ Short acting barbiturates are more dangerous than long acting.
- ❑ Shock & anorexia occur quickly.
- ❑ Coma is more severe with short acting barbiturates.



SYMPTOMS:

- Stupor or coma, areflexia.
- Peripheral circulatory collapse.
- Weak & rapid pulse.
- Cold clammy skin.
- Slow or rapid & shallow breathing.
- Pupils constricted & reacting to light initially but subsequently develops paralytic dilatation.
- Atelectasis.
- Pulmonary edema.
- Bronchopneumonia
- Acute renal shut down.



MANAGEMENT:

SCANDINAVIAN METHOD:

Hospitalisation

↓
Support vital functions

↓
Prevent further absorption

↓
Increase elimination of drug

↓
Conservative management with good nursing care

↓
Appropriate detoxification or psychiatric after care

◎ HOSPITALIZATION:

- Admitted to the hospital.

◎ SUPPORT VITAL FUNCTIONS:

- Consciousness.
- Airway , breathing , circulation.
- Blood pressure.

◎ PREVENT FURTHER ABSORPTION:

- Emesis.
- Gastric lavage.
- Activated charcoal & catharsis.

◎ INCREASE ELIMINATION OF DRUG:

- Forced diuresis.
- Alkalinization of urine.
- Prophylactic antibiotic.
- Peritoneal dialysis.
- Hemodialysis.
- Hemoperfusion.

◎ OTHER MEASURES:

- Psychiatric after care.

REFERENCES:

- *Pharmacology by H.P.Rang and M. M. Dale, 5th edition, page no:523.*
- *Principles of Clinical Toxicology by Thomas. A. Gossel , 2nd edition , page no:290-293.*
- *Textbook of Forensic Medicine and Toxicology by V.V. Pillay , 14th edition, page no:472-473.*
- *Essentials of Medical Pharmacology by K.D.Tripathi , 6th edition, page no:390-392.*
- *Pharmacology and Pharmacotherapeutics by R.S. Sathoskar, 19th edition, page no:114-115.*





BENZODIAZEPINES

- ❖ Anxiolytic & hypnotic agents.
- ❖ Wide therapeutic index.
- ❖ Safest of all sedative drugs.

USES:

Management of

- Anxiety disorders
- Seizure disorders
- Insomnia
- Movement disorders (adjunctive therapy)
- Mania (adjunctive therapy)

CLASSIFICATION:

HYPNOTIC:

- Diazepam
- Flurazepam
- Nitrazepam
- Alprazolam
- Temazepam
- Triazolam

ANTI-ANXIETY:

- Diazepam
- Chlordiazepoxide
- Oxazepam
- Lorazepam
- Alprazolam

CLASSIFICATION:(contd)

ANTICONVULSANT:

- Diazepam
- Lorazepam
- Clonazepam
- Clobazepam

MODE OF ACTION:

Benzodiazepines



Stimulating GABA b receptors



Opening up the chloride ion channel in the receptor complex



↑se conductance of chloride ion across the nerve cell membrane



Lowers the potential difference btwn the interior & exterior of the cell



Blocking the ability of the cell to conduct nerve impulses



ADVERSE EFFECTS:

- Weakness
- Headache
- Amnesia
- Vertigo
- Diplopia
- Nausea
- Diarrhoea
- Chest pain
- Paradoxical effects-restlessness ,agitation, hallucinations.
- Triazolam –delirium, toxic psychosis.

MECHANISM OF TOXICITY:

- ❖ Toxic symptoms-sedative action on the CNS.
- ❖ Large doses-neuromuscular blockade .
- ❖ Intravenous injection-peripheral vasodilation -fall in BP, shock.
- ❖ ↓se alveolar ventilation (↓se PO₂ , ↑se PCO₂).
- ❖ Induce CO₂ narcosis in persons with COPD.
- ❖ Respiratory depressant effect with sedative drugs-concomitantly taken.
- ❖ Death occurred in persons who concurrently injected ethanol / CNS depressant.
- ❖ IV dosing-hypotension & respiratory depression-death.

ACUTE POISONING:

SIGNS AND SYMPTOMS:

MILD: Drowsiness , Ataxia , Weakness

MODERATE TO SEVERE :Vertigo , slurred speech, nystagmus, partial ptosis, lethargy , hypotension, respiratory depression, coma (stage 1 & 2).

❑COMA 1 (Stage 1): Responsive to painful stimuli but not to verbal or tactile stimuli, no disturbance in respiration or BP.

❑COMA 2 (Stage 2):Unconscious, not responsive to painful stimuli, no disturbance in respiration or BP.



MANAGEMENT:

➤ LIFE SUPPORTIVE PROCEDURES & SYMPTOMATIC / SPECIFIC TREATMENT:

- ⊙ Airway , breathing & circulation.
- ⊙ Intravenous fluid administration.
- ⊙ Endotracheal intubation.
- ⊙ Assisted ventilation.
- ⊙ Supplemental oxygen.

➤ DECONTAMINATION:

- ⊙ Stomach wash within 6-12 hrs.
- ⊙ Activated charcoal.
- ⊙ Emesis is contraindicated.

- IV FLUIDS:
- CORRECTION OF HYPOTENSION WITH DOPAMINE OR LEVARTERENOL:
- ANTIDOTE TREATMENT: FLUMAZENIL
 - ⊙ Flumazenil -reversing the coma induced by benzodiazepines.
 - ⊙ Mode of action - competitive antagonism.
 - ⊙ Complete reversal of benzodiazepine effect with a total slow iv dose of 1mg.
 - ⊙ Administered in a series of smaller doses beginning with 0.2 mg & progressively increasing by 0.1- 0.2 mg every minute until a cumulative total dose of 3.5 mg is reached.
 - ⊙ Resedation occurs within ½ hr - 2 hrs.