GENERAL ANAESTHETICS

By

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GENERAL ANAESTHESIA

(AN + AESTHESIA)

Reversible :-

- * LOSS OF PAIN SENSATION
- * LOSS OF MEMORY(amnesia)
- * LOSS OF REFLEXES
- *LOSS OF CONSCIOUSNESS

GENERAL ANAESTHESIA
(History)

- **(A) In the past :-**
  - **(i) Non-drug method :-**
    - **(a) Asphyxia**
    - **(b) Concussion**
  - **(ii) Drugs/agents :-**
    - **(a) Opium**
    - **(b) Cannabis**
    - **(c) Alcohol**

GENERAL ANAESTHESIA
(History – contd..)

- **(B) In 19 th Century :-**
- **(i) 1844 – Horace Wells – N_2O**
- **(ii) 1846 – Morton – Ether**
- **(iii) 1847– Simpson – Chloroform**
- **(iv) 1929 – Cyclopropane**
- **(v) 1935 – Thiopentone (I.V.)**
- **(vi) 1956 – Halothane**
- **(vii) Enflurane, Isoflurane, Sevoflurane, Ketamine, Propofol**

GENERAL ANAESTHESIA (CLASSIFICATION)

I. INHALATIONAL :

1. Gas : N_2O, Cyclopropane
2. Liquids : . Ether , Chloroform
   . Halothane
   . Enflurane
   . Isoflurane
   . Desflurane
   . Sevoflurane

II - INTRAVENOUS

1. Inducing agents :(Barbiturates)
   . Thiopentone sodium

2. Slower acting drugs : (Non-Barbiturates)
   . Ketamine, Propofol, Fentanyl
   . Diazepam , Midazolam,Etomidate.

GENERAL ANAESTHETICS

(Site of Action)

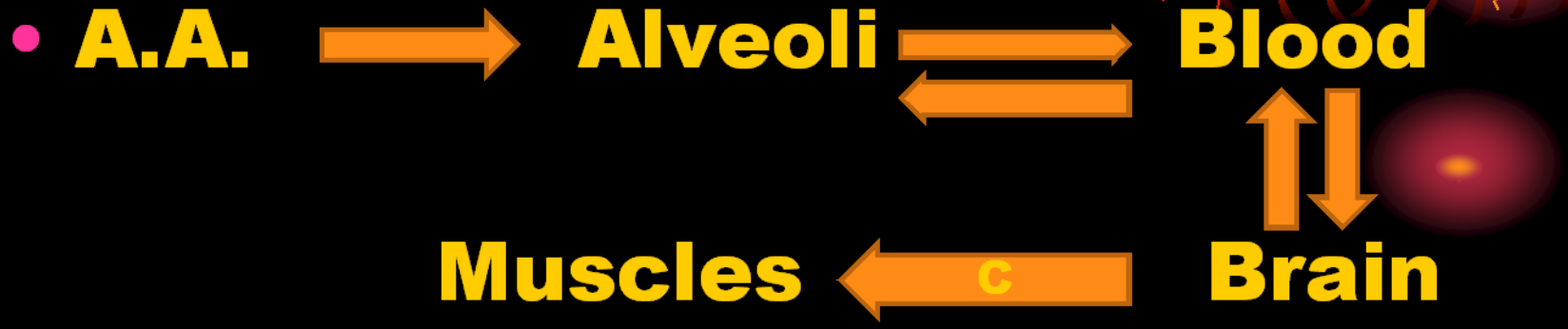
(I) Neuronal Actions

- Cortex, Thalamus, Hippocampus
- Peripheral sensory nerves, spinal cord and brain stem
- Inhalational GAs :-
- (i) Unconciousness – Thalamus & Reticular Activating system blockade
- (ii) Immobilization –Spinal cord, Medulla
- (iii) Amnesia – Hippocampus
- (iv) Analgesia – Opiate like substances

GAs - (Site of Action)
(II) Molecular Actions

- 1)GAs → Facilitates GABAnergic Neurotransmission → Unconsciousness.
- 2) In spinal cord → GAs → Facilitates Glycine mediated action → Inhibit noxious stimuli
- 3) GAs → Inhibit Nicotinic receptors → Produces Analgesic effect
- 4) GAs → Blocks NMDA receptors → Produces Unconsciousness (Ketamine, N2O)
- 5) GAs →Activates K- Channel → releases neurotransmitters → inhibit Hippocampus → Produces Amnesia

PHARMACOKINETICS OF G.A.



** Diffusion Hypoxia - 70% N_2O

PHARMACOKINETICS OF G.A. (Inhalational)

I. Depth of Anaesthesia depends:

(a) Potency of A.Agent (MAC)

(b) Partial Pressure in Brain

II. Induction/Recovery of A.A depends on :

(a) Rate of change of PP in brain

PHARMACOKINETICS OF G.A.

MAC

- It is the Minimum Alveolar Concentration of an Inhalant G.A. at 1 atmospheric pressure that produces immobility in 50% of patients exposed to noxious stimuli.
- Adequate MAC = 0.5 – 2.0
- Lower the MAC, More Potent is the Gas A.

PHARMACOKINETICS OF G.A.

Blood : Gas Partition Coefficient

(Solubility in blood + lipids)

PC = Amt. of Anaeth in Blood

Amt. of Anaeth in Gas

- **Determines Rate of Induction/Recovery**
- **Low B:G P.C = Rapid Induction/Recovery**

  (eg. N_2O, Desflurane,Sevoflurane)
- **High B:G P.C = Slow Induction/Recovery**

  (eg. Halothane)

PHARMACOKINETICS OF G.A.

- **(1) Balanced Anaesthesia :-**
- **The patient is kept in alighter planes of anesthesia → so that the patient is safe → and can be maintained as long as surgical procedure is carried out.**

- **(Preanaesthetic agents + Inducing agent + Muscle relaxant + Analgesic agent with suitable anaesthetic agent)**

PHARMACOKINETICS OF G.A.

- **(II) Basal Anaesthesia :-**

Is a type of pre-anaestheic medication administered in the ward before shifting the patient to the operation theatre → produces good sedation, smooth induction + reduction in anaesthetic dose).

- **(eg. Midazolam /Diazepam, Ketamine, Propofol)**

Pharmacokinetic Properties

- **III) SECOND GAS EFFECT :-**

N_2O → Insoluble in blood → Rapid induction & rapid uptake of N_2O from alveolar gas → leads to rapid ↑ in concentration of co-administered anaesthetic agent → ↑ speed of induction of second anaesthetic agent.

Pharmacokinetic Properties

- **IV) DIFFUSION HYPOXIA :-**

N2O (Low blood/gas partition coefficient) → On discontinuation → Diffuses more readily from blood to alveoli → Reduces alveolar partial pressure of oxygen → Causing transient Hypoxia (Diffusion Hypoxia)

Prevented by → administration of 100% oxygen → during the last few minutes of anaesthesia and in immediate post-anaesthetic period.

MECHANISM OF ACTION OF G.A.

- **DIFFERENT THEORIES :-**
- **(I) LIPID THEORY :**

G.A.

Dissolves in Lipid Cell Membrane

Alters Fns of Lipid Cell Membrane

Greater lipid solubility, Greater is the Anaesthesia (Overton-Meyer Theory)

MECHANISM OF ACTION OF G.A.

- **(II) HYDRATE (H_2O) THEORY :**

G.A.

▼

Freezing of Water Mol. on Cell Membrane

▼

Anaesthetic – hydrate Complex

▼

Disturbs Membrane Protein Functions

▼

Interfere with Ionic Movements

MECHANISM OF ACTION OF G.A.

- **(III) PROTEIN THEORY :**

G.A.

↓

Interferes Fns of Hydrophobic Domains of Protein Molecule

↓

Affects Fns of Protein Molecules

↓

Disrupts Normal Mechanism of Controlling Ion Permeability

MECHANISM OF ACTION OF G.A.

- **(IV) Inhibition of Ascending Reticulating System → producing Unconsciousness**

- **(V) Release of Opiates as Endogenous substances → Producing Analgesia**

MECHANISM OF ACTION OF G.A.

- **Recent Hypothesis :-**
- **(VI) Legand – gated ion (not voltage gated) channels**

- **(VII) Inhibitory $GABA_A$ receptor gated Cl- channels activated → Produces Unconsciousness**

(eg. BZD, Barbiturates, Propofol)

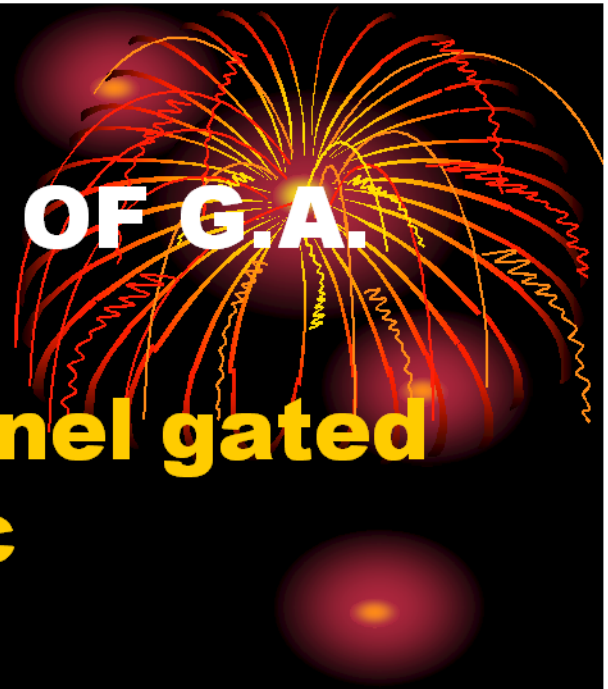
MECHANISM OF ACTION OF G.A.

- **(VIII) Inhibitory Glycine receptor gated Cl - channel in spinal cord & medulla activated → Loss of sensation (response to noxious stimuli).**

-→ Block painful stimuli
Produce immobility.

(eg. Propofol, BZD, Barbiturates)

MECHANISM OF ACTION OF G.A.



- (IX) Inhibit cation channel gated by nicotinic cholinergic receptors

- -→ mediates analgesia & `amnesia

- (eg. Fl. anaesthesia, Barbiturates)

MECHANISM OF ACTION OF G.A.

- (X) Inhibits excitatory NMDA type Glutamate receptor gated Ca++ selective cation channels

  (eg. N2O and Ketamine)

- (XI) Activation of K- Channel

  -→ Releases protein complexes → releases neurotransmitters→ inhibit Hippocampus → Produces Amnesia.

(XII) Acts by inhibiting synaptic transmission

STAGES OF ANAESTHESIA

1) Stage I = Stage of Analgesia
2) Stage II = Stage of Delerium
3) Stage III = Stage of Surgical Anaesthesia
4) Stage IV = Stage of Respiratory Paralysis

Clinical features of Anaesthesia

- **I) Inadequate Anaesthesia :**

  * **ANS Overactivity**
    (↑ BP, HR, Sweating)

  * **↑ Grimacing**

  * **↑ Muscular activity**

Clinical Features of Anaesthesia

- **II) Surgical Anaesthesia :**

  * **Loss of Eyelid/Lash Reflexes**

  * **Rhythmic Respiration**

  * **Relaxation of Sk. Muscles.**

Clinical Features of Anaesthesia

- **III) Deep Anaesthesia :**
  - * Respiratory Depression
  - * Hypotension
  - * Asystole
  - * Blood Loss + Hypoxia
  - * Death due to Resp. failure

COMPLICATIONS OF ANAESTHESIA

- **(I) During Anaesthesia :**
- **Respiratory depression**
- **Hypotension**
- **Cardiac arrhythmias**
- **Acid Pneumonia**
- **Laryngospasm, Asphyxia**
- **Fire, explosion (Ether)**
- **Delirium, convulsion**
- **Death**

COMPLICATIONS OF ANAESTHESIA

- **(II) Post Anaesthesia :**
- **Nausea, vomiting**
- **Persisting sedation**
- **Pneumonia**
- **Organ Toxicity**
  - * **Hepatotoxicity**
  - * **Nephrotoxicity**
- **Delirium**

AN IDEAL GENERAL ANAESTHETIC

- **(I) FOR PATIENT :-**

- **Effective , safe , pleasant**
- **Rapid & smooth induction**
- **Fast recovery**
- **No toxicity / less p.o. complications**

AN IDEAL GENERAL ANAESTHETIC

- **(II) FOR SURGEON :-**

- **Good anaesthesia**
- **Profound analgesia**
- **Less capillary bleeding**
- **Adequate muscular relaxation**
- **Unexplosive**

AN IDEAL GENERAL ANAESTHETIC

- **(III) FOR ANAESTHETIC :-**
- **Stable at room temperature**
- **Easily controllable**
- **Wide margin of safety**
- **Less resp. / cvs depression**
- **Non corrossive (rubber tubings , metals)**
- **No special apparatus required**

AN IDEAL GENERAL ANAESTHETIC

- **(IV) FOR MANUFACTURER :-**

- **Cost of production cheap**
- **Enough storage capacity**

PREANAESTHETIC MEDICATIONS

- **Objectives are :-**

1) To relieve anxiety + apprehension preoperatively without drowsiness

2) To induce amnesia for pre-op. and post – operative events

3) To supplement analgesic action of anaesthesia & potentiate them ... less anaesthetic required.

PREANAESTHETIC MEDICATIONS
(Objectives)

4) To decrease secretion & vagal stimulation caused by anaesthetic agents

5) To decrease post operative vomiting

6) To decrease acidity & volume of gastric juice ... to prevent aspiration pneumonia

7) To minimize undesirable side effects (salivation, bradycardia, coughing, vomiting)

8) For smooth , rapid induction & recovery.

DRUGS USED FOR PREANAESTHETIC MEDICATION

I) Opioids :- (Morphine, Buprenorphine, Pethidine)

- Allay anxiety & apprehension
- Produce Pre – post op. analgesia
- Smoothen induction
- Reduce dose of Anaesthetic agents.

DRUGS USED FOR PREANAESTHETIC MEDICATION

II) Anti-anxiety drugs :- (Diazepam, Lorazepam, Midazolam i.v.)

- **To produce loss of recall of pre-op. events.**

III) Sedatives – Hypnotics :- (Promethazine)

- **Antihistaminic, sedative, antiemetic & anti-arrhthymic properties**

(Used in children)

DRUGS USED FOR PREANAESTHETIC MEDICATION

IV) Anticholinergic Agents :-

(Atropine, Hyosine, Glycopyrrolate)

- ↓ Salivary and bronchial secretion
- Prevents vagal bradycardia & hypotension
- Prevents laryngospasm precipitated by respiratory secretions

- Hyoscine : - Amnesia , Antiemetic effect
- Glycopyrrolate :- Antibradycardia, Antisecretory, less CNS stimulant

DRUGS USED FOR PREANAESTHETIC MEDICATION

- **(V) H2 – Blockers :-**

  (Ranitidine, Famotidine)

- **↓Gastric, Salivary and bronchial secretions**

- **To prevent the risk of aspiration pneumonia (during prolonged surgery, C.S.).**

DRUGS USED FOR PREANAESTHETIC MEDICATION

- **(VI) Antiemetics :-**

  (Metoclopramide, Ondansatron)

- **Enhances gastric emptying & Lower Esophageal tone (LES)**

- **Reduces chance of reflux & aspiration pneumonia**

- **As entiemetic prevents P.O. vomiting**

DRUGS ADMINISTERED DURING ANAESTHESIA

- 1) Sk. M. Relaxants : - d-TC, Succinylcholone, Pancuronium
- 2) Antihypertensives : - Trimethaphan, Sodium Nitroprusside
- 3) Vasopressor agents : Methoxamine, Phenylephrine
- 4) Antiarryhthmics :- Quinidine, Lignocaine, Verapamil,Procainamide.

DRUGS ADMINISTERED DURING ANAESTHESIA

- 5) Anticonvulsants : - Diazepam, Phenytoin
- 6) Respiratory stimulants : - Doxapram
- 7) Ganglion Blockers :- Trimethaphan.

DRUGS TO BE DISCONTINUED BEFORE SURGERY

- 1) Combined Oral Contraceptives – 4 weeks
- 2) MAOIs – 2 weeks
- 3) Aspirin – 1 week

DRUGS TO BE CONTINUED DURING SURGERY

- 1) Glucocoticosteroids
- 2) Antiparkinsonian drugs
- 3) Antiglaucoma drugs
- 4) Thyroid & Antithyroid drugs
- 5) NSAIDs
- 6) Insulin

NITROUS OXIDE (N_2O) (ADVANTAGES)

** Joseph Priestley in 1776 .

Horace wells used it in 1884.

1. Non irritant, Non-inflammable, Non-explosive inhalational gas.

2. Rapid induction , rapid recovery (because of low blood solubility)

3. Good analgesic(Sub An. Dose)

4. Second - Gas Effect

NITROUS OXIDE (N_2O)
(Advantages)

5. Maintain BP & Respiration
6. Non toxic to Liver ,Kidney & Brain (Wide margin of safety)

7. Does not sensitize the heart to CAs – No Cardiac arrhythmias
8. Cost effective – Cheap.

NITROUS OXIDE (N_2O)

(*Disadvantages*)

1. Poor anaesthetic, weak SKMR
2. Diffusion Hypoxia
3. ↑ Megaloblastic anaemia, abortions & birth defects in female OT personnel
4. Causes expansion of air pockets in closed spaces(↑Vol.(pneumothorax) & ↑ Pressure (sinuses).

NITROUS OXIDE (N_2O)
(USES)

- As an adjuvant in :-
- 1) Dental analgesia
- 2) Obstetric analgesia and refractory pain in terminally ill patients (50% N_2O + O_2)
- 3) Most surgical procedures (70% N_2O +30% O_2)
- 4) As maintenance of anaesthesia in (30 – 60%) conc.

HALOTHANE

(Advantages)

1. Non-inflammable, Non-explosive (electro-cautery used)

2. Sweet odor liquid anaesthetic

3. Potent anaesthetic , rapid induction; smooth & pleasant recovery

HALOTHANE

(Advantages)

4. Non – irritant –
   Abolishes Pharyngeal, Laryngeal reflexes early, Bronchodilation –
   (safe in bronchial asthmatics)

5. Uterine smooth muscle relaxation- external version done in prenatal period – (used in Obstetrics)

6. Dose dependent ↓BP– (Useful in Plastic surgery)

7. No Hepatotoxicity in children, pleasant odor – (Useful in Pediatric Patients)

HALOTHANE

(DISADVANTAGES)

1. Narrow margin of safety

2. Direct CVS depression- Hypotension, Bradycardia

3. Halothane shake (shivering)

4. Halothane Hepatitis

HALOTHANE

(DISADVANTAGES)

5. Malignant Hyperthermia
6. Sensitizes myocardium to CAs
7. Sp. Apparatus required (Boyle's)
8. Poor analgesia & muscle relaxation
9. Cerebral vasodilatation – C/I in pts with↑Intracranial Pressure

OTHER INHALATIONAL ANAESTHETICS

1. Gas : N_2O, Cyclopropane
2. Liquids : . Ether , Chloroform
   . Halothane
   . Enflurane
   . Isoflurane
   . Desflurane
   . Sevoflurane

THIOPENTONE SODIUM

- It is an ultra - short acting barbiturate
- 2.5 % fresh soln - I.V 3-5 mg/kg
- Rapid OOA : 15-20 sec.
- DOA : 8- 12 min (Fast Recovery)
- Redistribution
- T1/2 : 7-10 hrs., CNS dep>12 hrs.

THIOPENTONE SODIUM

(Uses)

1. Induction of GA
2. For rapid control of convulsions.
3. Short Painless Operations :-
   - ** Fractures Reduction
   - ** Dilatation & Curettage (D & C)
   - ** Laryngoscopy/Bronchoscopy
   - ** Endotracheal intubation

THIOPENTONE SODIUM
(Uses)

4. I.V inf. of sub - anaesthetic dose facilitates verbal communication in psychiatric patients (acts by knocking off guarding)

** Preparation:0.5,1g powder (2.5 % fresh alkaline soln.)

*Local irritation, Thrombophlebitis.

THIOPENTONE SODIUM
(ADVANTAGES)

1. Potent I.V. anaesthetic (Smooth rapid induction, rapid recovery).
2. Non-inflammable, Non-explosive
3. Does not sensitize heart to Adr.

4. ↓ ICP **Preferred in Neurosurgery**
5. No CVS depression
6. No P.O. - N,V, Excitation.

THIOPENTONE SODIUM
(DISADVANTAGES)

1. Depresses Resp C,VMC, Myocardium
2. Poor analgesic (hyperalgesia).
3. Weak muscle relaxant.
4. SCH + Thiop Na --- Separate syringe
5. Ppt. Acute intermittent porphyria
6. Shivering , delirium during recovery.
7. CVS collapse in hypovolemia, shock or sepsis
8. Vasospasm, gangrene on leakage

KETAMINE

- Non – Barbiturate I.V./I.M. An. Agent
- 'Dissociative Anaesthesia' – (sedation, marked analgesia, immobility, amnesia and feeling of dissociation from the surroundings).
- Blocks NMDA type of Glutamate receptors.
- Ketamine HCl: 1-4mg /kg over 1 min I.V.
  6.5 - 13 mg/kg I.M.

KETAMINE
(ADVANTAGES)

1. Non inflammable, Non - explosive.
2. Rapid induction (1 min) & recovery (10 – 15 min) , Amnesia (1-2 hr)
3. Good analgesic (40 min)
4. No Broncho / Laryngospasm – (safe in Br. Asthmatics)
5. 'AOC' in extensive burns - dressing
6. Less vomiting, hypotension

('AOC' in Shock & dehydration)

KETAMINE

(ADVANTAGES)

8. 'AOC' in emergency situation like accidents, war
9. Cardiac arryhthmias are rare.
10. Retains Pharyngeal & laryngeal reflexes, while cough reflexes depressed.
11. High margin of safety - used in children (i.m.), elderly & poor risk patients.

KETAMINE (DISADVANTAGES)

1. Poor visceral analgesia - give opioids
2. Not suitable for orthopedic surgery -↑muscle tone – poor muscle relaxation.
3. Not suitable in cardiac disease Pts - IHD,HBP – (↑BP , HR, COP) – (Sympathetic stimulation) (Emergence phenomenon)
4. Not preferred in psychiatric Pts due to emergence delirium, hallucinations (disorientation, sensory illusions) and involuntary movements (Rx: Diazepam / Midazolam)

KETAMINE (DISADVANTAGES)

5. Not suitable for Neurosurgery :↑ ICP (Isoflurane suitable)
6. Regurgitation – if stomach is full .
7. ↑ salivation (R_x atropine)
8. Not suitable in Glaucoma :

   ↑ IOP

KETAMINE (USES)

1. Dressing of burns,accident wounds.
2. Short term minor & diagnostic procedures :-

** Angiography , ** Cardiac catheterization

** Trauma surgery, ** Tooth extraction etc...

3. Surgery of Head, Neck & Face
4. Children for diagnostic procedures
5. Dehydrated, shock & severe burns pts.

KETAMINE (USES)

4. Children for diagnostic procedures
5. Dehydrated,shock,severe burns pts.
6. Assisted vaginal delivery, c.s. (less foetal & neonatal depression)

(But C/I in pregnancy before term, eclampsia & pre-eclampsia – due to oxytocic effect)

PROPOFOL

An oily liquid as 1% emulsion.

1. Rapid induction & recovery (OOA : 15-45 secs, DOA :10 mins).

2. Rapid distribution (T1/2=2-4 min)
3. Rapid metabolism (El.t1/2 = 45 min)

4. As i.v. inducing & i.v. infusion for maintenance

PROPOFOL

- Faster recovery than thiopentone – due to high clearance & rapid metabolism
- Suppresses laryngeal reflexes – useful for endotracheal intubation

- Anti-emetic, anti-convulsant effects
- Safe in pregnancy though it crosses placenta

PROPOFOL (ADVANTAGES)

- 1) Rapid recovery
- 2) No hangover
- 3) No P.O. N,V.
- 4) No involuntary movements
- 5) No airway irritation
- 6) Useful for Day Care surgery (OPD anaesthesia).

PROPOFOL (DISADVANTAGES)

1. Excitatory effects
2. Induction apnoea lasts ~1 min.
3. ↓ BP, Bradycardia.
4. Respiratory depression.
5. Pain at the site of injection
6. Anaphylactoid reaction
7. C/I in children

PROPOFOL (USES)

Dose : 2mg/kg Bolus IV - induction
9mg/kg I.V – Maintenance

1. **Induction ,Maintenance of GA**
2. **Out pt. surgery (short surgical procedures)**
3. **Sub anaesthetic doses (2.4 mg/kg/hr) - for sedating intubated Pts in ICU (IV infusion).**
4. **Resistant Status Epilepticus**

MIDAZOLAM

- Short acting Benzodiazepines
- Water soluble injection

- Less irritant to vein unlike Diazepam
- Rapid acting, but short duration

- Suitable in pts with poor cardiac reserve (no cardiovascular or respiratory depression)

MIDAZOLAM (USES)

- I.M.- Pre-anaesthetic Medication(5mg)
- I.V. Induction of Anaesthesia(1-2.5mg)

- Sedation & amnesia without analgesia for Endoscopy, Bronchoscopy, cardiac catheterization (2.5-7.5mg)

- S.C. Infusion – As Anticonvulsant
- Resistant cases of status epilepticus

NEUROLEPTANALGESIA

- (Droperidol 2.5 mg + Fentanyl citrate 50 mcg)
- Droperidol – Neuraleptic agent
- Fentanyl citrate – Opioid analgesic
- Both are short acting (30 -50 min)
- I.V method to relieve pain
- Differs from classical G.A. :-
- ** Conscious & Cooperative
- ** Intense analgesia & indifference to external stimuli

NEUROLEPTANALGESIA (Advantages)

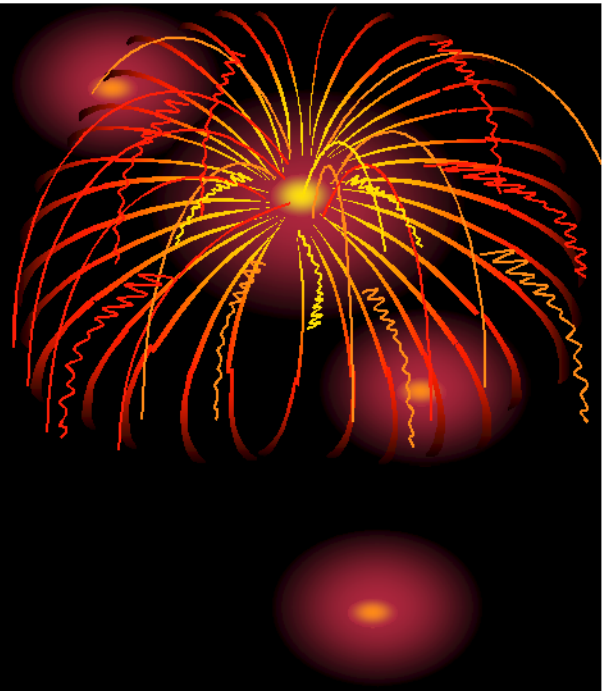
- Smooth onset, rapid P.O. recovery
- Less Hypotension,circulatory disturbances
- Suppression of vomiting,coughing
- Continued analgesia in P.O. period

NEUROLEPTANALGESIA (Advantages)

- Useful in old people, in 'Poor Risk' patients.
- Fentanyl+droperidol+65% N_2O +35% O_2 = Neuroleptanaesthesia
- Useful in operative procedures of :- Eyes, oral, orthopedics, angiography, myelography & bronchoscopy, wound & burn dressing.

NEUROLEPTANALGESIA (Disadvantages)

- Prolongs QTc interval – produces Torsade de Points
- Death could occur due to Ventricular Fibrillation in susceptible individuals
- Currently, its use has decline due to
- ** respiratory depression,
- ** hypotension and
- ** extrapyramidal side effects



THANK YOU

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Pharmacology - NHLMMC