Unit VIII – Problem 3 – Pharmacology: General Anesthesia

- **What is general anesthesia?**
  - It is a state induced with medication(s) characterized by:
    - ✓ Loss of consciousness.
    - ✓ Loss of all modalities of sensation.
    - ✓ And it is reversible.

  Note: general anesthesia is similar to coma, but in state of coma it is not always guaranteed to be reversible.
- **Requirements during anesthesia:**
  - Unconsciousness.
  - Analgesia.
  - Muscle relaxation.
  - Maintenance of physiological stability (the most important being cardiac reflex and blood pressure). Note that laryngeal and pharyngeal reflexes are inhibited so the process of intubation doesn't become difficult.

  Note: there is no single drug which can achieve all of those targets mentioned above. Therefore, a combination of 2 or more drugs is used to achieve them.
- **There are 4 stages of general anesthesia** (which were described by Guedel with the use of the drug diethyl ether. These stages are not seen nowadays because this drug is rarely used):
  - **Stage I** → induction/ analgesia: using some of general anesthesia drugs in sub-anesthetic doses can lead to pain relief (an example is nitric oxide).
  - **Stage II** → exaggerated sympathetic manifestations and delirium: this phase is kept as fast as possible to prevent the risk of cardiac arrest (which might happen in this phase).
  - **Stage III** → surgical anesthesia with 4 planes (plane 1, plane 2, plane 3 and plane 4). Notice that surgical anesthesia is mostly involving plane 2 and plane 3.
  - **Stage IV** → in which medullary paralysis might occur and this is irreversible.
- **Steps of anesthetic process:**
  - **Premedication (Why?):**
    - ✓ Relieving anxiety: if the patient is anxious → he has increased sympathetic activity → and anesthesia cannot be produced.
    - ✓ Reduce secretions: some anesthetics such as halothane and isoflurane can be irritating and produce secretions → these might be aspirated resulting in pneumonia. Notice that proton-pump inhibitors (PPIs) are given to suppress gastric secretions.
    - ✓ To suppress autonomic responses: which can be manifested as cardiac rhythm changes → for this reason, anticholinergics are administered.
    - ✓ To produce amnesia (فقدان الذاكرة): scopolamine produces temporary loss of memory and a sleeping state.
    - ✓ As adjuvant for maintenance of anesthesia.
  - **Induction of anesthesia.**
  - **Initiation and maintenance of muscle relaxation.**
  - **Maintenance of anesthesia.**
  - **Analgesia (as part of premedication, during operation and post-operation).**
  - **Other drug therapies may include:**
    - ✓ Reversal of neuromuscular blockade.
    - ✓ Prevention/ treatment of nausea and vomiting.
    - ✓ Reversal of the residual effect of opiate and benzodiazepine.
- **What is balanced anesthesia?**
  - A balanced combination of drugs with different actions is often used to provide the various components of general anesthesia (using smaller doses of each drug).

- ✓ e.g. if you are using an anesthetic which doesn't act as a good analgesic → you can combine it with an opioid to achieve a better effect.

- **Neuroleptanalgesia:**
  - In which a neuroleptic (antipsychotic) drug such as droperidol is combined with an opioid analgesic (fentanyl) → to produce a complete detachment with powerful analgesia (during this state the patient is conscious during the operation but he doesn't feel the surgical process. The surgeon can order different commands to the patient so he knows in which cortical area he is working and minimizing injuries which might happen to other areas).
  - **Neurolepanalgesia can be converted to nueoleptanesthesia** → by concurrent use of nitric oxide (NO) + oxygen inhalation.
- **Dissociative anesthesia:**
  - It is similar to neuroleptanalgesia but with increased muscle tone.
  - **It is induced by ketamine. This drug can lead to post-operative hallucination.**
- **Common pre-anesthetic drug combinations:**
  - **Benzodiazepine (alprazolam) + antiemetic (metaclopramide) + PPI (omeprazole) or H_2-blocker (ranitidine).**
  - **Intramuscular opioid (morphine) + antimuscarinic (atropine).**
  - **Neuroleptic (droperidol) + opioid (fentanyl) = neuroleptanalgesia.**
- **Intravenous anesthetics:**
  - Easy, rapid and quick.
  - **Propofol**: it has a rapid onset and rapid recovery. It is used for induction/maintenance, can cause hypotension and has an antiemetic effect.
  - **Thiopental**: it is the most common drug used in intravenous anesthesia. It is one of the barbiturates with rapid onset of action.
    - ✓ Kinetics: when it is given intravenously → the state of anesthesia is produced within seconds but the duration is very short (5-10 minutes) although the half life (t ½) is for 1 day! (How?)
      - ❖ Because the drug has a high perfusion rate and increased lipid solubility in the brain → this will result in increased induction to the brain leading to a rapid onset but a fast recovery will occur due to the redistribution of the drug within the tissue of the body.
- **Inhalation anesthetics:**
  - **Nitric oxide (NO):** it is a gas which is given mostly in dentistry and during labor (when a female is in a severe pain). It has to be given with oxygen otherwise hypoxia will result.
  - **Sevoflurane**: it has a rapid onset and recovery. It is unstable in soda-lime.
  - **Halothane**: it has a medium rate of onset and recovery.
- **Muscle relaxants (neuromuscular blockers):**
  - Why are they used during anesthesia? → to provide more area for exploration.
  - **They are classified to:**
    - ✓ Non-depolarazing (curare type): preventing the effect of acetylcholine on the motor end plate (by blocking nicotinic-m receptors present on the surface of muscle membrane). These are used for long procedures. To reverse the effect of these drugs → anticholineesterase inhibitor is administered (neostigmine).
    - ✓ Depolarizing succinylcholine: will bind to receptors of motor end plate providing an initial muscle twitching (mostly in muscles of the hand and face) but unlike acetylcholine it will not be degraded by acetylcholine-esterase. Therefore, it convert to express same effects of non-depolarizing drugs. This is used in short procedures. If a patient is suffering from the disease pseudocholinesterase and was given depolarizing succinylcholine → fresh plasma transfusion will be done to reverse the effect of this drug.

- **Mannitol:**
  - It is an osmotic diuretic given as IV.
  - It is filtered but not reabsorbed from renal tubules and thus producing an osmotic effect to drag water with it from the tubules.
  - **It decreases intracranial pressure but not used to treat pulmonary edema (Why?)**
    - ✓ Because with pulmonary edema there is already volume overload and we don't want to further increase the volume by administrating this drug as an IV fluid!
- **Morphine:**
  - **It is not preferred to be given (Why?)** → because it is constricting the pupils and thus initial clinical assessment of consciousness cannot be done/known.
  - It is causing increased intracranial pressure and respiratory depression (reversed by naloxone).