Drugs used in premedication

Preoperative medication consists of psychological and pharmacological preparation. The patient before entering the operation theatre should be free from apprehension, sedated and cooperative.

Goals of preoperative medication:

1)Relief of anxiety.
2)Sedation.
3)Amnesia.
4)Analgesia.
5)Drying of airway secretions.
6)Prevention of autonomic reflex response.
7)Reduction of gastric fluid volume and increased pH.
8)Antiemetic effects.
9)Reduction of anesthetic requirements.
10)Facilitation of smooth induction of anesthesia.
11)Prophylaxis against allergic reactions.

Psychological preparation:

1)Preoperative visit.
2)Interview.

Administration of premedication

1 – 2 hours before the surgery.
-Night before.

Prescribed medications:

Taken 2 hours prior to surgery, with small sip of water (<30 ml) orally.

Group of preanesthetics

1)Anxiolysis: Benzodiazepines (45 – 90 minutes preoperatively).
2)Amnesia: Benzodiazepines.
3)Analgesia: Opioids.
4)Anti-autonomic: Anticholinergic, beta-blockers.
5)Antiemetic: Dopamine antagonists, 5HT antagonist, antihistaminic, anticholinergic.
6)Antacid: H_2 blocker, PP1, sodium citrate.

Anxiolytics/ Sedatives/ Hypnotics

<u>1)Benzodiazepines (still commonly used):</u>
a) Diazepam
b) Lorazepam

c) Midazolam
d) Alprazolam
2) Barbiturates (not used much):
a) Secobarbital
b) Pentobarbital

Benzodiazepines

General characteristics:

-Produce anxiolysis, amnesia and sedation.
-Act predominantly on GABA receptors in the CNS.
-Minimal respiratory and cardiac depression.
-Do not produce nausea and vomiting.
-They are not analgesics.
-Crosses placental barrier and may cause neonatal depression.

Diazepam (Valium®):

Diazepam is used for premedication in a dose of 0.25-0.5 mg/ kg orally or 0.25 mg/ kg intramuscularly.
Beside it is used as a premedication, intra venous diazepam can be used as a sole agent as for catheterization, cardioversion, bronchoscopy……etc. and as an adjuvant to light anesthesia. Dose of diazepam as an inducing agent is 0.3-0.6 mg/ kg IV, dose requirements decrease with aging, cirrhosis of liver leads to up to fivefold increase in elimination half-life.
Dose requirements decrease 10% per decade of patient's age. Flumazenil is effective in reversing the sedative.

Midazolam:

Water soluble benzodiazepine with painless administration, its amnesic effects are more potent than sedative effects. Patients with decreased intracranial compliance show little or no change in ICP with midazolam. It is the drug of choice for outpatient surgery and pediatric premedication. It is capable of crossing Brain-Blood Barrier with effects ranging from tranquillization to full anesthesia.
Usual dose is 0.15 - 0.3 mg/ kg intravenously for induction of anesthesia, lesser dose to be used in elderly and obese patients. 0.5 – 0.75 mg/ kg orally produces anxiolysis and degree of tranquility within 30 minutes, pediatric dose is 0.1 mg/ kg IV or IM. Intranasal midazolam 0.3 mg/ kg has quicker onset of action than oral midazolam.
Midazolam is respiratory depressant. Midazolam is relatively doesn't affect heart rate and blood pressure much, but it is hazardous in patients with hypovolemia as it may aggravate hypotension.

Opioid analgesics The most common opioids are fentanyl, pethedine and morphine, they differ in duration of action, and can be given parentally. Opioids administered preoperatively for:

1)Sedation.

2)To control hypertension during tracheal intubation.

3)Analgesia.

For preoperative analgesia, the use of IV fentanyl is preferred because it's rapid onset and short duration.

Fentanyl:

A potent narcotic analgesic, it is 100 times more potent than morphine, and produces less nausea and vomiting than it.

Fentanyl dose is 1-5 μg/ kg IV (μg = microgram = 1/ 1000 of mg). It metabolized in liver and excreted through urine and feces. It may result in respiratory depression and rigidity of respiratory muscles (which can be treated with naloxone). It is used cautiously in patients with COPD (chronic obstructive pulmonary disease), head injury and patients on MAO inhibitors (a group of antidepressant drugs). Fentanyl is also available as transdermal patches.

Anticholinergic drugs

There are 3 drugs in use as pre-anesthetic:

1)Atropine.

2)Hyocine.

3)Glycopyrrolate.

While the first two cross the BBB*, glycopyrrolate does not cross it and is not absorbed from the gastrointestinal tract.

Clinical effects:

1) Antisialogogoue effects (decreasing the flow rate of saliva and their effect): Glycopyrrolate and hyoscine are more potent than atropine, reduce secretions and bradycardia after succinylcholine.

2)Sedative and amnesic effect: In combination with morphine, hyoscine produces powerful sedative and amnesia effects.

3)Prevention of reflex bradycardia: Atropine is used it prevent oculocardiac reflex in eye surgery and is used to prevent halothane bradycardia.

Doses:

Atropine: In adults 0.3 – 0.6 mg, in children 0.01- 0.02 mg/ kg (maximum 0.6 mg per dose) IV: has vagal inhibition, CNS stimulations. (Dosage should be adjusted according to the patient's response and tolerance).

Hyoscine: adults - 0.4 mg IV, children - 0.015 mg/ kg IM: more antisialogoue action with less vagal inhibition and causes sedation and amnesia, so avoided in elderly patients.

Glycopyrrolate: 0.004 mg/ kg IV, infants of 1 month to 2 years of age may require up to 0.009 mg/ kg IM: have no central action, longer duration of action, and less tachycardia.

Side effects:

1)CNS toxicity: Atropine produces central anticholinergic syndrome of the CNS, producing restlessness, agitation, somnolence (strong desire to sleep) and convulsions.

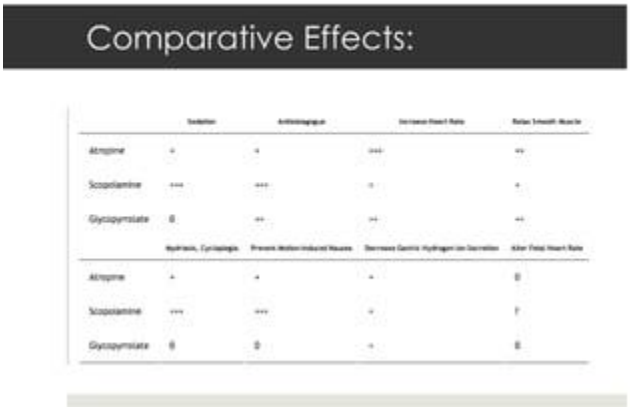
2)Tachycardia and hyperthermia.

3)Reduction in lower esophageal sphincter tone.

4) Mydriasis (dilation of the pupil) and cycloplegia (paralysis of the ciliary muscle of the eye).

5)Unpleasant and excessive drying of mouth.

Comparative effects of anticholinergics



Antiemetics

Antiemetics and antihistamenics enhance gastric emptying and are used to prevent nausea and vomiting. Additional usage includes sedative property and relieving anxiety.

Metoclopramide, ondansetron and phenothiazines are antiemetics used preoperatively.

Ondansetron:

It is high effective in managing of vomiting related with chemotherapy and radiotherapy, used also for prevention of postoperative nausea and vomiting in a dose of 4 mg IV, in children, a dose of 0.1 mg /kg up to 4 mg may be used in vomiting prone children. Elimination half-life is 3.5 to 4 hours in adults. Side effects include headache, constipation, diarrhea, sedation, a sense of flushing, warmth .

Metoclopramide (Plasil®):
It is the most common antiemetic, used parenterally, orally and even rectally, the IV dose is 0.15 – 0.3 mg/ kg, its effect lasts for 12 hr. Metoclopramide increases the rate of gastric emptying and causes some increase in peristalsis of gut. It may be used in emergency anesthesia, and indicated in patients with hiatus hernia, obese, parturient and duodenal ulcer.
Metoclopramide acts both centrally and peripherally:
A) Central action: Acting as dopamine antagonist, acts on medullary vomiting center, producing antiemitic.
B) Peripheral action: Enhances gastric emptying, so that gastric components are passed earlier, preventing gastric aspiration.
Note: Atropine should be withheld until induction of anesthesia as it blocks effects of metoclopramide.
Side effects include abdominal cramps following IV injection, occasional neurological.

Prevention of pulmonary aspiration

There is no drug or combination is absolutely reliable in preventing the risk of aspiration, patients with no apparent risk of aspiration, these drugs are not recommended.
Cimetidine (Tagamet®) and Ranitidine (Zantac®) are the two drugs in common clinical use which when used as premedication may increase the gastric pH higher than 2.5 and decrease the gastric volume < 25 ml.
Reduce the secretion of acid into the stomach by about 70% by blocking the effect of histamine on receptors in the stomach wall, used to prevention of acid aspiration syndrome.
Ranitidine seems to be better than cimetidine due to:
1) Its longer duration of action.
2) Its lower incidence of side effects and drug interactions.
Doses: cimetidine – 400 mg (oral)
Ranitidine – 150 mg (oral),
90 – 150 minutes before induction of anesthesia, also effective when given IV 45 to 60 minutes before induction, but are unable to influence acid already present in the stomach, which depends on gastric emptying.
Oral sodium citrate 15 – 30 minutes before induction can also be used for this purpose.
Factors predisposing to aspiration:
1)Emergency surgery.
2)Inadequate anesthesia.
3)Abnormal pathology.

4)Obesity.
5)Pregnancy.
6)Large abdominal mass.
7)Opioid premedication.
8)Neurological deficit.
9)Lithotomy.
10)Difficult intubation/ airway.
11)Hiatus hernia.

Premedication in pediatric patient

Include age-specific psychological preparation and an emphasis on oral medications when sedation is desired. Topical anesthetic creams are often prescribed for children before cannulation.

A) Psychological factors:

1) Age: most important factor in the success of preoperative visit and interview.
2) Children who do not ask questions during preoperative interview may be masking high levels of anxiety.
3) It may be helpful to have the parents accompany these children to the operating room.

B) Pharmacological preparation:

Their use is controversial. (Oral premedicaton is preferred for patients without IV access).

1)Midazolam: (0.5 – 0.75 mg/ kg) in a flavored oral preparation produces sedation. Intranasal midazolam has faster onset but causes nasal burning.
2)Paracetamol: syrup: (5 – 10 mg/ kg).
(10 – 15 mg/ kg) rectally produces analgesic effect.
3)Ketamine: (5 – 10 mg/ kg) IM prescribed 20 to 30 minutes before induction facilitates smooth separation from parents.
4) Opioids: In the absence of an IV catheter, transmucosal administration of fentanyl (lollipop) is effective in producing sedation.

Preoperative medication instruction guideline

A) Medication to be continued on day of surgery:

1) Antihypertensive
2) Diuretics
3) Cardiac medication
4) Antidepressant – antianxiety
5) Thyroid, asthma medication
6) Steroids (oral, inhaled)

B) Medication to be discontinued before surgery:

1) Aspirin: 7 days before surgery.

2) Non-steroidal anti-inflammatory drugs (NSAIDs): 48 hours before surgery.
3) Oral hypoglycemic drugs: on the day of surgery.
4) Insulin: 1/3rd dose in morning.
5) Warfarin: 4 days before surgery.
6) Heparin: 4 – 6 hours before surgery.
7) Monoamine oxidase inhibitors (MAO inhibitors): 2 weeks before surgery.