WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 6, 988-1006. Research Article ISSN 2277– 7105

PREANASTHETICS: A REVIEW ON CURRENT PRACTICE

Nandan H. N.*[1], Dr. Suresha B. S.[2], Monisha M. N[3]., Mazhar Anwar C.[3], Mohammed Ismail[3] and Uthkarsha Vinesh[1]

*[1,1,3]Pharm D, Department of Pharmacy Practice, Bharathi College of Pharmacy, Bharathinagara, K. M. Doddi, Mandya, Karnataka, India – 571422.

[2]Prof & HOD, Department of Pharmacy Practice, Bharathi College of Pharmacy, Bharathinagara, K. M. Doddi, Mandya, Karnataka, India – 571422.

Article Received on
22 Jan. 2018,

Revised on 12 Feb. 2018,
Accepted on 05 March 2018,

DOI: 10.20959/wjpr20186-11493

***Corresponding Author**
Nandan H. N.
Pharm D, Department of Pharmacy Practice, Bharathi College of Pharmacy, Bharathinagara, K. M. Doddi, Mandya, Karnataka, India – 571422.

ABSTRACT

The practice of preanaesthetic medication embarked upon soon after ether and chloroform were introduced as general anesthetics in the middle of the 19th century. Premedication was originally introduced to facilitate induction of anaesthesia with agents, such as chloroform and ether, that are irritant and produce copious amounts of secretions. Preanaesthetic medications are a group of drugs administered before anaesthesia to make it more pleasant and safe. The major objectives of preanaesthetic medication are to decrease the stress response with preservation of hemodynamic parameters, facilitate anaesthesia induction and produce amnesia. Major concerns during surgical procedures include anxiety among patients, post-operative pain, post-operative nausea and vomiting and the risk of aspiration pneumonitis.

Preanaesthetic medicines are generally given to avoid the adverse events associated with general anaesthesia, facilitate surgery and reduce the risk of post-operative complications. The preoperative preparation of a patient for anaesthesia and surgery includes both psychologic and pharmacologic components. The psychologic aspect of preoperative preparation is provided by the anaesthesiologist's visit and interview. In addition, a wide spectrum of pharmacologic agents[e.g., barbiturates, benzodiazepines, major tranquilizers, opioid (narcotic) analgesics, anticholinergics, histamine H_2-blockers, gastrokinetic drugs] are administered to facilitate the process of preoperative preparation. The preanaesthetic medication correlates with various outcomes like patient's clinical status, the type and duration of operation, duration of post-operative recovery, post-operative analgesia

requirement and hospital stay. Our study gives an insight to the various premedications used before anaesthesia to minimize its side effects.

KEY WORDS: Preanaesthetics, Anaesthesia, Psychologic aspect, Anaesthesiologist's, Side effects, Hemodynamic parameters.

INTRODUCTION

Preanaesthetic medication refers to the use of drugs before anaesthesia to make it more pleasant and safe.[1] Premedication was originally introduced to facilitate induction of anaesthesia with agents, such as chloroform and ether, that are irritant and produce copious amounts of secretions. Modern induction methods are simple and not unpleasant.[2] The major objectives of preanaesthetic medication are to decrease the stress response with preservation of hemodynamic parameters, facilitate anaesthesia induction and produce amnesia.[3] Preanaesthetic medication is also defined as a group of drugs that are used before anaesthesia to prepare the patient, administered from half an hour before the surgery to the night before.[4] Anaesthesia is defined as a state of temporary induced loss of sensation or awareness. It may include analgesia (relief from or prevention of pain), paralysis (muscle relaxation), amnesia (loss of memory), or unconsciousness.[5] Major concerns during surgical procedures include anxiety among patients, post-operative pain, post-operative nausea and vomiting and the risk of aspiration pneumonitis. Preanaesthetic medicines are generally given to avoid the adverse events associated with general anaesthesia, facilitate surgery and reduce the risk of post-operative complications.[6] The preoperative preparation of a patient for anaesthesia and surgery includes both psychologic and pharmacologic components. The psychologic aspect of preoperative preparation is provided by the anaesthesiologist's visit and interview. In addition, a wide spectrum of pharmacologic agents[e.g., barbiturates, benzodiazepines, major tranquilizers, opioid(narcotic) analgesics, anticholinergics, histamine H_2-blockers, gastrokinetic drugs] are administered to facilitate the process of preoperative preparation.[7] The preanaesthetic medication correlates with various outcomes like patient's clinical status, the type and duration of operation, duration of post-operative recovery, post-operative analgesia requirement and hospital stay.[6,8]

Literature on the current pattern of use of preanaesthetic is not well documented and limited to few Indian, British and American Surveys. This study was conducted to understand the prescription and utilization patterns of preanaesthetic medications and anaesthetics for different surgical procedures with prime focus on preanaesthetics.

PAST, PRESENT AND FUTURE OF PREANAESTHETIC MEDICATION

HISTORY OF PREANAESTHETICS

The concept of anaesthetic premedication was initially developed to counteract the side effects of general anaesthesia when ether and chloroform were widely used as inhalational anaesthetics in the 1850s. Two physicians, Nussbaum in Germany and Bernard in France, in 1864 simultaneously found that subcutaneous morphine can relax patients and intensify chloroform anaesthesia. At the same time, another French scientist Dastre found that atropine can decrease salivation and antagonize the effects of respiratory depression and vomiting associated with morphine. As a result, morphine and atropine became popular as anaesthetic premedication in the late 19th century. It was not until 1911 when Dudley Buxton published the first paper regarding the use of morphine, atropine, scopolamine and other similar agents prior to inhalation anaesthesia that anaesthetic premedication became a debated issue and drew more attention of anaesthesiologists.

CURRENT PRACTICE OF PREANAESTHETICS

The practice of anaesthetic premedication in surgical patient is no longer a routine procedure today. There are several reasons to explain why we do not give medication to every patient before sending them to the operating theater. The main reason is that the induction time of general anaesthesia in current practice is much shorter than that of ether anaesthesia. We now routinely use intravenous anaesthetics as induction agents; for most intravenous agents, onset of action occurs within 60 seconds. Patients who do not have venous access, such as children undergoing an operation in an outpatient setting, can be given sevoflurane as an induction agent via a face mask. Despite having some involuntary movements (excitement stage of Guedel's sign), these children can easily be made sleep in 1 minute due to the low blood solubility of sevoflurane. The issue of patient safety is another concern of anaesthetic premedication. When patients are premedicated, they must be put into surveillance to monitor the vital signs and the potential side effects of medication when they are in the ward, during transport to operating theater, or when they are in the waiting area of the operating theater. We usually do not monitor vital signs of patients while they are still in the waiting lounge. If premedication becomes a routine practice in a hospital, more manpower is needed to take care of these patients, leading to an increase in costs; for this reason most of the hospitals do not perform this at present. From the viewpoint of efficacy of medication, patients will not obtain the beneficial effects of premedication if they receive their medication too early or too late prior to operation. In a busy operating theater of a medical center where a lot of patients

are ready to undergo surgery, the operation is often delayed or conducted earlier, making the efficacy of premedication unpredictable. We should also take "street readiness" of patients into account. At present, more operations are performed on an outpatient service basis in medical centers. After surgery, patients need to resume their normal daily activity as soon as possible. If the side effects of a premedication affect the functional recovery following an outpatient operation, most patients will not be willing to accept the medication.

FUTURE DIRECTION OF PREANAESTHETICS

Although premedication was initially developed to fight back the adverse effects of anaesthesia, we now emphasize more about the efficacy of premedication in improving the general wellbeing of patients and patient satisfaction after their surgery. There are still many people in whom the quality of recovery from anaesthesia is not good and many of them have not been treated adequately. Although we already have guidelines for some preventive measures, for instance, to manage postoperative nausea and vomiting (PONV) or to deal with a difficult airway, we have yet to develop a complete list of statements or guidelines on premedication to manage all possible anaesthesia-related side effects. It is clear that new consensus guidelines need to be established and more clinical trials on anaesthesia premedication need to be conducted.[3]

PREANAESTHETIC MEDICATION

1) Opioids: Morphine, Pethidine, Fentanyl & its congeners.
2) Sedative-antianxiety drugs: Diazepam, Lorazepam, Alprazolam, Midazolam, Promethazine.
3) Anticholinergics: Atropine, Hyoscine, Glycopyrrolate.
4) Neuroleptics: Chlorpromazine, Triflupromazine, Haloperidol.
5) Histamine H2 blockers: Ranitidine, Famotidine, etc.
6) Proton pump inhibitors: Omeprazole, Pantoprazole, etc.
7) Antiemetics: Metoclopramide, Domperidone, Ondansetron, Granisetron.[4,10]

PURPOSES OF PREMEDICATION

The two general purposes of preanaesthetic medication proposed by Beecher in 1955 are as follows: (1) to present a tranquil and wellrested patient to the surgeon and (2) to decrease the hazards incurred by anaesthesia and surgery. Atropine was once used before anaesthesia to prevent "vagal inhibition" and to decrease secretion induced by chloroform or ether. Morphine had also been used to reduce reflex irritability of patients and decrease the amount

of ether requirement. As the new halogenated inhalational anaesthetics and intravenous anaesthetics have dramatically shortened the induction time of anaesthesia, the main purpose of premedication today is no longer to prevent radical movement or reduce secretion of patients, but to allay patient fears and lessen patient anxiety.

Other purposes of anesthetic premedication, as found in the literatures, are to: (1) prevent postoperative pain, (2) provide effective prophylaxis against PONV, (3) decrease perioperative shivering, (4) decrease postoperative pruritus, (5) decrease gastric secretions, (6) prevent allergic reactions, (7) suppress reflex responses to surgical stimuli, and (8) decrease anesthetic requirement for the surgical procedure.[9]

TO DECREASE ANXIETY

Preoperative anxiety can occur in as high as 80% of surgical patients. Two vulnerable groups of patients are females and children. Both psychological and pharmacological approaches are effective in decreasing preoperative anxiety. Midazolam has been proved to be effective in reducing the preoperative anxiety level in many studies. Except for midazolam, α_2-agonists, antidepressants, and anticonvulsants are all effective in reducing the preoperative anxiety level.

TO REDUCE POSTOPERATIVE PAIN

The concept of preemptive analgesia to deliver an analgesic regimen prior to the surgical stimulus to reduce the severity and duration of postoperative pain originated with the goals of (1) inhibiting the development of chronic postsurgical pain (CPSP), (2) decreasing acute postoperative pain after peripheral nerve damage and tissue injury, (3) preventing central neuron sensitization. The concepts of preventive analgesia that adopt a multimodal approach combining several interventions, which will produce a sufficiently dense, extensive and long duration of blockade, will pave the way for future direction of postoperative analgesia.

TO PREVENT CPSP

CPSP is a pain persisting for >3 months after surgery. Nerve damages and central sensitization play important roles in the development of CPSP. Pharmacological strategies to prevent CPSP include: (a) regional anaesthesia (b) NMDA receptor antagonists (c) gabapentinoids

TO PROVIDE FOR PROPHYLAXIS AGAINST PONV

i. Postoperative Nausea And Vomiting

About one-third of surgical patients who receive a general anaesthesia consisting of inhalational anaesthetics and opioids experience PONV. The incidence of PONV will dramatically escalate to 70-80% in a high-risk group of patients without PONV prophylaxis. Based on these findings, modern PONV prophylaxis adopts the principle of multimodal approach to treat high-risk patients with at least two or three different kinds of receptor antagonists, rather than just increasing the dosage of one single receptor antagonist, to prevent the occurrence of PONV.

ii. Postdischarge Nausea And Vomiting

Postdischarge nausea and vomiting (PDNV) receive more attention when more surgical procedures are conducted on an outpatient basis. The overall incidence of PDNV was 37% in the first 48 hours after discharge from hospital. The five independent risk factors for PDNV are (1) female sex, (2) age 50 years, (3) a history of PONV, (4) opioid use in the postanaesthesia care unit, and (5) nausea in the postanaesthesia care unit. Depending on the number of risk factors, the risk of PDNV can be predicted as 10%, 20%, 30%, 50%, 60%, and 80%, respectively.

TO DECREASE PERIOPERATIVE SHIVERING

Both general and regional anaesthesia can impair thermoregulation during cold exposure, and postanaesthetic shivering has been reported in 40-64% of patients (average 55%) with no prophylaxis. A variety of pharmacological and nonpharmacological interventions were tested to prevent patients from developing hypothermia, which showed equal effectiveness. Here, we describe the effects of pharmacological prophylaxis only. Antishivering medications found in the literatures can be categorized into several classes: (1) opioid receptor agonists or antagonists, (2) other centrally acting analgesics such as tramadol and nefopam, (3) α2-receptor agonists such as clonidine and dexmedetomidine, (4) cholinesterase inhibitors such as physostigmine and anticholinergic: atropine, (5) central nervous stimulants such as methylphenidate, (6) N-methyl-D-aspartate receptor antagonists such as ketamine and magnesium sulfate, (7) antiserotonergic agents such as ondansetron, granisetron, dolasetron, and urapidil, (8) g-aminobutyric acid receptor agonists such as midazolam and propofol, (9) sodium channel blockers such as lidocaine, (10) benzodiazepine receptor antagonists such as flumazenil, and (11) anti-inflammatory agents such as dexamethasone.

TO DECREASE POSTOPERATIVE PRURITUS

Pruritus is the most common side effect of neuraxial opioids, with an incidence varying from 30% to 100%. Parturients seem to be more susceptible to pruritus, with an increased incidence between 60% and 100%, and it appears to be estrogen related and dose dependent. Pharmacological strategies to prevent or treat such an event include the following: 5-HT3 receptor antagonists, opioid antagonists, antihistamines, NSAIDs and droperidol.

TO DECREASE GASTRIC SECRETIONS

Prevention of aspiration pneumonitis caused by regurgitated gastric juice from the full stomach of inadequately fasting patients or from the stomach of a parturient is always a challenge for anaesthesiologists. Except for fasting, appropriate measures to prevent aspiration include gastric decompression, acceleration of emptying, and application of the technique of rapid sequence intubation along with Sellick's maneuver. Premedication that can inhibit gastric juice secretion and reduce gastric juice volume and acidity, such as H2-receptor antagonists (H2RAs) or proton pump inhibitors (PPIs) are also given.[9]

PSYCHOLOGICAL APPROACH

Psychological education before an operation is a major part of premedication in terms of reducing the level of anxiety. Women and children are two vulnerable groups; most of the patients (as high as 70-80%) of these groups usually suffer from anxiety prior to operation. Psychological effects of a preoperative visit include not only building a friendly rapport among patients and anaesthesiologists, but also reducing anxiety through reassurance about anaesthesia from an anaesthesiologist. Compared to adults, psychological preparation can be more difficult in pediatric patients, as reassurance will not be effective in such young patients and separation anxiety can exist in parents and children. Some behavioral programs had been developed, such as parental presence during induction of anaesthesia and clown intervention and distraction techniques, with varying results.[9]

PHARMACOLOGICAL APPROACH

SEDATIVE-ANTIANXIETY DRUGS

The most popular premedicants belong to the sedative- hypnotic group of drugs, which includes both the benzodiazepines and the barbiturates. All sedative hypnotics produce a similar dose-dependent spectrum of central nervous system (CNS) activity. Although the slopes of their individual dose-response curves may differ, all drugs in this group produce a similar pattern of CNS depression. Comparative studies have indicated that benzodiazepines

are more effective in producing anxiolysis and amnesia and are associated with higher patient acceptance than the barbiturates. More recent data indicate that the benzodiazepines (e.g., flurazepam, triazolam, lorazepam) may also be superior to the barbiturates as hypnotics on the evening prior to surgery.[7]

Benzodiazepines

Benzodiazepines belong to a broad category of drugs that are referred to as gamma-amino butyric acid (GABA) agonists. GABA is the principal inhibitory neurotransmitter in the central nervous system (CNS). They bind to GABA receptors which causes an influx of chloride ions. This influx causes the post-synaptic nerve to be hyperpolarized, which increases the level of stimulation required to depolarize the nerve. GABA-A receptor subtypes have been identified, which are alpha-1 and alpha-2. It is thought that alpha-1 receptors mediate sedation and alpha-2 receptors are responsible for anxiolysis. Currently available formulations of benzodiazepines are not selective for GABA receptor subtypes.

Benzodiazepines bind to specific binding sites in the $GABA_A$ receptor–chloride channel complex in the brain, and facilitate the opening of the channel in the presence of GABA; this increases hyperpolarization-induced neuronal inhibition[11]. Benzodiazepines are the most commonly used drug for anxiolysis of children prior to induction of GA. Their properties consisting of: anxiolysis, sedation, muscle relaxation, anti-convulsant effect, and anterograde amnesia confer their popularity. The large therapeutic window in combination with minimal respiratory and cardiac depression makes them an excellent choice in the preoperative phase where monitoring is minimal. Benzodiazepines should be administered under direct supervision with the patient placed in a closely monitored bed space in the preoperative holding area.[3,12]

Midazolam

Is a water-soluble benzodiazepine with a short elimination half-life (2-4 hr). Midazolam is approximately twice as potent as diazepam with respect to its sedative and anxiolytic properties. Because of its rapid onset of sedative-anxiolytic effect and low incidence of postoperative side effects, midazolam appears to be an excellent intramuscular premedicant for pediatric patients.[7] Commercially prepared midazolam formulation is rapidly absorbed with patients demonstrating a satisfactory degree of sedation and anxiolysis within 10 minutes of consumption with a higher percentage at 20 minutes.[3]

Diazepam

Is the prototypic benzodiazepine which produces dose-dependent anxiolysis, sedation, and amnesia with a plasma half-life of 1.5–2.5 hours.[2.7] Diazepam has a greater fat solubility than midazolam and a faster CNS effect after intravenous administration (1.6 min); however it is metabolized to desmethyldiazepam with a pharmacologic activity equal to the parent compound. When administered rectally, diazepam appears to be less effective than rectal midazolam. The intramuscular route is not recommended because it is painful and absorption is erratic.[3]

Lorazepam

Is a potent short half-life benzodiazepine. Should generally be avoided for more than very short-term use, as it causes intense withdrawal phenomena and dependence.[11]

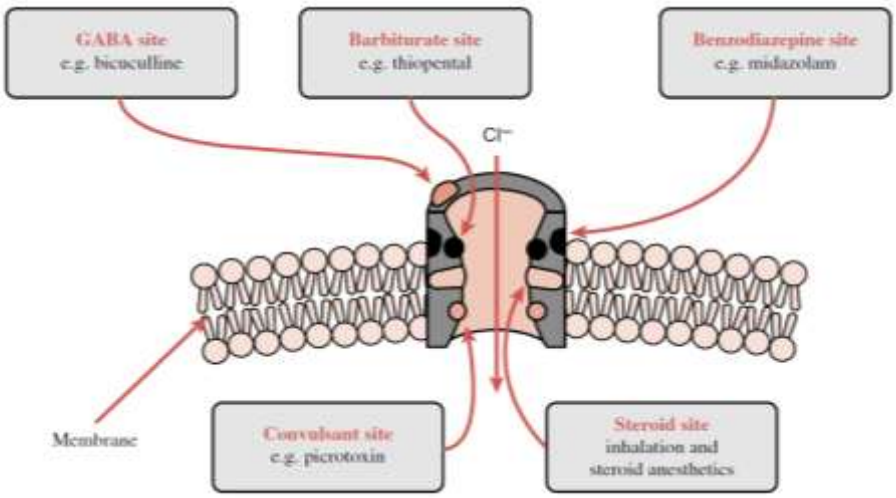

Figure 1: The GABAA-receptor-chloride ionophore sites of drugs action.[13]

Phenothiazine

Promethazine is a widely used phenothiazine which improves the relief of anxiety and the level of sedation as well as patient acceptance when added to morphine premedication[7]. In addition to being a sedative, promethazine has the advantage to possess several beneficial effects such as being an antihistaminic (H1blocker), an antiemetic, anti-motion sickness, and an anticholinergic.[3]

OPIOIDS

Opioids have been prescribed for premedication in an effort to facilitate the induction of anaesthesia and to decrease the inhaled anaesthetic requirement.[7] Opioids are substances that

act on opioid receptors to produce morphine-like effects that are blocked by antagonists such as naloxone. Cohen and Beecher stated many years ago that "unless there is pain, there is no need for a narcotic in preanaesthetic medication." Opioids bind to specific opioid receptors in the nervous system and other tissues.[7,14]

Morphine

Is the principal alkaloid in opium and still widely used[15]. It relieves both the perception of pain and the emotional response to it. Morphine sulfate may be administered intramuscularly (0.1 to 0.2 mg/kg) or intravenously (0.05 to 0.1 mg/kg) or orally**.** Absorption may not be adequate when given rectally.[11]

Pethidine

The actions of pethidine are similar to those of morphine. It causes similar respiratory depression, vomiting and gastrointestinal smooth muscle contraction to morphine, but does not constrict the pupil, release histamine or suppress cough. It produces little euphoria, but does cause dependence. Pethidine is sometimes used in obstetrics because it does not reduce the activity of the pregnant uterus, but morphine is often preferred.[11]

Fentanyl is a synthetic opioid and is the most commonly employed analgesic supplement during anaesthesia which may be administered by parenteral, transdermal, nasal, and oral routes. Fentanyl is strongly lipophilic, and is readily absorbed from the buccal mucosa with an overall bioavailability of approximately 30-50%. Fentanyl is rapidly and extensively metabolized, the $t_{1/2}$ being two to four hours, the short duration of action (the peak effect lasts only 20–30 minutes) being explained by redistribution from brain to tissues.The optimal dose as a preanesthetic medication with minimal desaturation and preoperative nausea appears to be 10 to 15 µg/kg.[3,11]

Tramadol is a weak µ-opioid receptor agonist whose analgesic effect is mediated via inhibition of norepinephrine reuptake and stimulation of serotonin release. Intravenous tramadol (1.5 mg/kg) given before induction of general anesthesia has been as effective as local infiltration of 0.5% bupivacaine (0.25 ml/kg) for ilioinguinal and iliohypogastric nerve blocks for pain control, but associated with a higher incidence of nausea and vomiting.[3]

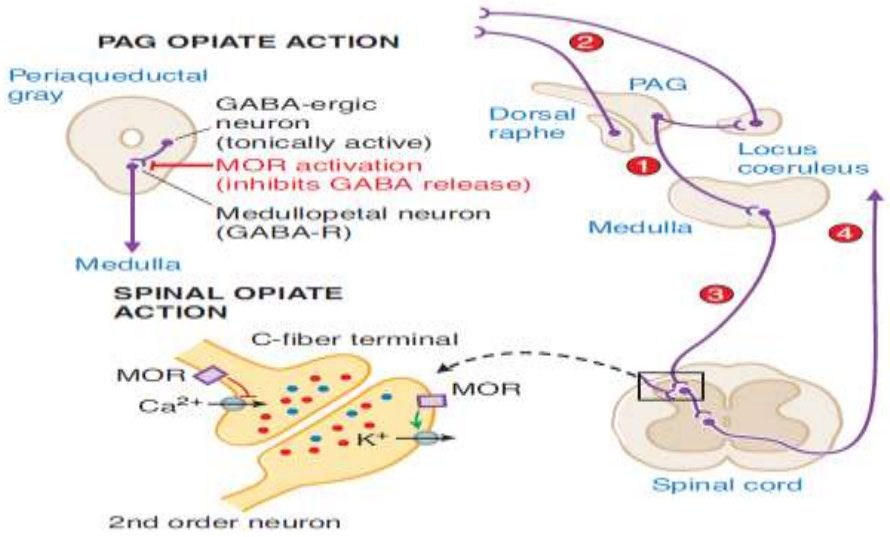

Figure 2: Mechanisms of opiate action in producing analgesia.[16]

Top left

Schematic of organization of opiate action in the periaqueductal gray.

Top right

Opiate-sensitive pathways in PAG Mu opiate actions block the release of GABA from tonically active systems that otherwise regulate the projections to the medulla (1) leading to an activation of PAG outflow resulting and activation of forebrain (2) and spinal (3) monoamine receptors that regulate spinal cord projections (4) which provide sensory input to higher centers and mood.

Bottom left

Schematic of primary afferent synapse with second order dorsal horn spinal neuron, showing pre- and post-synaptic opiate receptors coupled to Ca2+ and K+ channels, respectively. Opiate receptor binding is highly expressed in the superficial spinal dorsal horn (substantia gelatinosa). These receptors are located presynaptically on the terminals of small primary afferents (C fibers) and postsynaptially on second order neurons. Presynaptically, activation of MOR blocks the opening of the voltage sensitve Ca2+ channel, which otherwise initiates transmitter release. Postsynaptically, MOR activation enhances opening of K+ channels, leading to hyperpolarization. Thus, an opiate agonist acting at these sites jointly serves to attenuate the afferent-evoked excitation of the second order neuron.

The **sedative-narcotic** combinations are probably of more clinical importance to practicing anesthesiologists. Because pain results in increased anxiety and anxiety exacerbates pain, combinations of sedative- ankiolytics and narcotics may act synergistically. There is an additive (or supraadditive) action between narcotics and sedatives in terms of their analgesic effectiveness.[7]

ANTICHOLINERGICS

The use of anticholinergic compounds as part of routine preanesthetic medication stems mainly from their antisialagogue and vagolytic actions.[7] Anticholinergic drugs are those which block actions of ACh on autonomic effectors and in the CNS exerted through muscarinic receptors. Although the tertiary amine and quaternary ammonium groups of anticholinergic drugs bind to the same anionic site on the receptor that agonists occupy, these drugs do not fit into the narrow cleft and consequently cannot activate the receptor. Atropine or scopolamine was routinely administered before the induction of general anesthesia to block excessive salivary and respiratory secretions induced by certain inhalation anesthetics.[17-18]

Atropine (0.02 mg/kg) and **scopolamine** (0.01 mg/kg) both have CNS effects, although the sedating effect of scopolamine is 5 to 15 times greater than atropine. Atropine is more commonly used and is a better vagolytic agent than scopolamine, whereas scopolamine is a better sedative, antisialagogue, and amnestic. **Glycopyrrolate** is the only agent that does not cross the blood-brain barrier, so it does not cause confusion. When compared to atropine, it is less effective in attenuating bradycardia during induction. The central sedative effects of both atropine and scopolamine may be antagonized with physostigmine. Preoperative administration of oral atropine or oral glycopyrrolate does not alter the incidence or degree of hypotension during induction of anesthesia. Anticholinergic agents are very useful as an adjuvant to ketamine anesthesia because of their antisialagogue and central sedative effects. The recommended doses of anticholinergics are scopolamine, 0.005 to 0.010 mg/kg, atropine, 0.01 to 0.02 mg/kg and glycopyrrolate 0.01 mg/kg IV, IM.[3]

NEUROLEPTICS

Neuroleptics or antipsychotic drugs such as haloperidol and chlorpromazine tend to block dopamine D_2 receptors in the dopaminergic pathways of the brain. This means that dopamine released in these pathways has less effect. In addition to the antagonistic effects of dopamine, antipsychotics (in particular atypical neuroleptics) also antagonize 5

HT_{2A} receptors. Typical antipsychotics are not particularly selective and also block dopamine receptors in the mesocortical pathway, tuberoinfundibular pathway, and the nigrostriatal pathway. Atypical antipsychotic drugs have a similar blocking effect on D_2 receptors, however, most also act on serotonin receptors, especially 5-HT_{2A} and 5-HT_{2C} receptors.[19]

HISTAMINE H2 BLOCKERS

The H2-blocking drugs have been administered preoperatively to patients considered to be at increased risk to aspiration pneumonitis. The histamine H_2 receptor antagonists competitively inhibit histamine actions at all H_2 receptors, but their main clinical use is as inhibitors of gastric acid secretion. They can inhibit histamine-, gastrin- and acetylcholine-stimulated acid secretion; pepsin secretion also falls with the reduction in volume of gastric juice.[20]

The use of H2-receptor antagonists can increase gastric fluid pH during the preoperative period by producing dose related decreases in basal and nocturnal gastric acid production. In general, multiple dose regimens (e.g., a nighttime dose on the evening prior to surgery and a morning dose on the day of surgery) are more effective than single dose regimens in decreasing gastric acidity and volume. Parenteral administration is more effective than oral when a rapid onset of effect is desired. Both of the commonly used H2-receptor antagonists, cimetidine, 150-300 mg, and ranitidine, 50-100 mg, significantly increase gastric fluid pH within 1 hr after parenteral administration.[7]

Ranitidine

Is a nonimidazole (has a furan ring) H2 blocker which as has several desirable features compared to cimetidine (about 5 times more potent than cimetidine). Though its pharmacokinetic profile and $t_{1/2}$ of 2-3 hr is similar to cimetidine, a longer duration of action with greater 24 hr acid suppression is obtained clinically because of higher potency.[21]

PROTON PUMP INHIBITORS

Proton pump inhibitors are benzimidazoles which inhibit the final common step in gastric acid secretion. They react covalently with SH groups of the H^+K^+ATPase enzyme and inactivate it irreversibly. After diffusing into the parietal cell from blood, proton pump inhibitors gets concentrated in the acidic pH of the canaliculi because the charged forms generated there are unable to diffuse back. Moreover, it gets tightly bound to the H^+K^+ATPase enzyme. It also inhibits gastric mucosal carbonic anhydrase.

Pantoprazole

Is a newer H^+K^+ATPase inhibitor, similar in potency and clinical efficacy to the prototype, omeprazole, but is more acid stable and has higher oral bioavailability. It is also available for i.v. administration.[21]

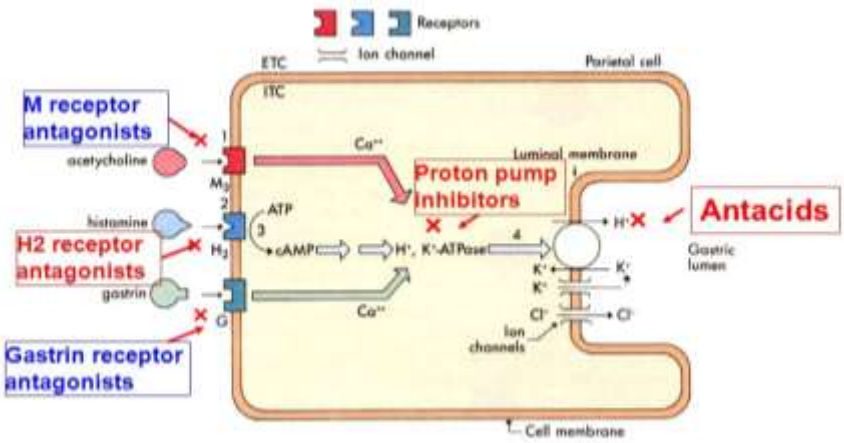

Figure 3: Mechanism of drugs that suppress gastric acid secretion.

ANTIEMETICS

These are the drugs used to prevent or suppress vomiting. Prokinetic drugs promote gastrointestinal transit and speed gastric emptying by enhancing coordinated propulsive motility. They acts through both dopaminergic and serotonergic receptors and causes D2 antagonism, 5-HT4 agonism and 5-HT_3 antagonism. Neuroleptics are potent antiemetics which act by blocking D2 receptors in the CTZ, antagonize apomorphine induced vomiting and have additional antimuscarinic as well as H1 antihistaminic property. 5-HT_3 antagonists block the depolarizing action of 5-HT through 5-HT_3 receptors on vagal afferents in the GIT as well as in nucleus tractus solitarius (NTS) and chemoreceptor trigger zones (CTZ).

Ondansetron

Is the prototype of 5-HT_3 antagonists of antiemetic drugs found to be highly effective in PONV. It blocks the depolarizing action of 5-HT through 5-HT. receptors on vagal afferents in the g.i.t. as well as in NTS and CTZ. Oral bioavailability of ondansetron is 60-70% due to first pass metabolism. It is eliminated in urine and faeces, mostly as metabolites; $t_{1/2}$ being 3-5 hrs, and duration of action 4-12 hr.

Metoclopramide

Acts through both dopaminergic and serotonergic receptors. It is rapidly absorbed orally. It is partly conjugated in liver and excreted in urine within 24 hours ($t_{1/2}$ is 3-6 hr). Orally it acts in 1/2-1hr, but within 10 min after i.m. and 2 min after i.v. injection. The action lasts for 4-6 hours.[21]

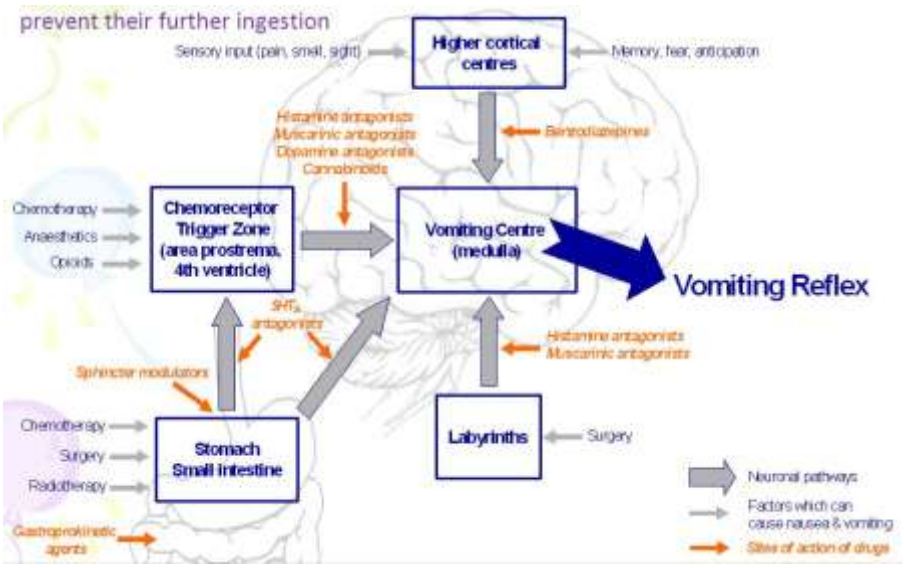

Figure 4: Factors inducing nausea and vomiting.

α_2-ADRENERGIC RECEPTOR AGONISTS

Clonidine: is an α_2-agonist, causes dose-related sedation by its effect in the locus ceruleus through its inhibition of adenylate cyclase. The plasma concentration peaks at 60 to 90 minutes after oral administration and at 50 minutes after rectal administration. The need to administer clonidine 60 minutes before induction of anaesthesia makes its use impractical in most clinical settings. An oral dose of 3 µg/kg given 45 to 120 minutes before the surgery produces comparable sedation to that of diazepam or midazolam. Clonidine acts both centrally and peripherally to reduce blood pressure and therefore it attenuates the hemodynamic response to intubation. It is usually administered in combination with atropine.[3]

Dexmedetomidine

Compared to clonidine, dexmedetomidine is a more selective α_2-adrenergic receptor agonist with a faster onset of action, quicker time to reach the peak plasma concentration, and a shorter elimination half-life. Dexmedetomidine premedication can decrease the severity of acute postoperative pain and reduce analgesic requirement.[9]

USE OF PREANAESTHETICS IN OUTPATIENTS

It is frequently stated that premedication should be minimized or avoided in outpatients because it prolongs the recovery period. Data available in the anaesthesia literature do not support this hypothesis. Recent studies indicate that premedication with a short acting opioid analgesic (e.g., fentanyl, 1-2 μg/kg IV) might decrease recovery time as a result of the analgesic's ability to decrease the anesthetic requirement. Clarke and Hurtig reported that intramuscular premedication with meperidine, 1 mg/kg, and atropine, 0.01 mg/kg, did not prolong recovery to "street fitness" after outpatient surgery. In a retrospective study, Meridy reported that preoperative administration of diazepam or hydroxyzine did not appear to significantIy prolong recovery. In pediatric outpatients, oral diazepam, 0.1 mg/kg, or hydroxyzine, 0.5 mg/kg produced only minimal decreases in anxiety but did not delay emergence or discharge. More recently, oral premedication with a combination of diazepam, 0.2 mg/kg, meperidine, 1.5 mg/kg, and atropine, 0.02 mg/kg, was shown to decrease perianaesthetic problems without prolonging recovery in pediatric outpatients.[7]

PREANAESTHETIC CLINIC

In India and in many other developing countries, anaesthesiologists are poorly recognized. Many studies have demonstrated poor knowledge of anaesthesia and anaesthesiologists among general public in developing countries, despite their increasing involvement in perioperative care, resuscitation, intensive care, acute and chronic pain management. Patients who are scheduled for elective surgery are usually referred from various surgical specialities to anaesthesiologists for evaluation before the surgical procedure. In pre anaesthesia clinic (PAC) patients are prepared both physically and psychologically for surgery and it is ensured that they are in most favourable condition to withstand the stress of surgery. Patients in general have poor understanding about anaesthesiologists and pre anaesthetic clinics. Such patients do not know the importance of pre anaesthesia check-up and try to fruitlessly rush through it resulting in incomplete assessment. Many a times pre-operative investigations are seen as wastage of time and money. On the other hand, some patients think that, they will be anaesthetised in pre-anaesthetic clinics. This not only undermines the purpose of pre-anaesthetic clinic but also increases perioperative morbidity and mortality.[22] preanaesthetics clinics help in arranging evaluation of underlying medical conditions (seizure disorder, asthma, diabetes, severe cardiac, pulmonary, renal, hepatic, neurological, metabolic or haematopoietic problems).[23]

CONCLUSION

Most anesthesiologists would agree that relief of anxiety is an important objective of preoperative preparation. Both psychologic support and pharmacologic agents are useful in minimizing anxiety during the preoperative period. Other goals of premedication include sedation; analgesia; amnesia; antiemetic and antisialagogue actions; increased gastric fluid pH (>2.5) and decreased gastric fluid volume (<20 ml); and prophylaxis against allergic reactions. The drug choice and dosage will depend on the patient's age, weight, ASA physical status, current medications, and history of adverse drug reactions, as well as the type and duration of the surgical procedure. The timing and route of drug administration may be as important as the drugs actually chosen for premedication. If the premedicant is properly selected and administered in an appropriate fashion, it can produce the desired pharmacologic actions without adverse side effects or drug interactions. Contrary to popular opinion, most commonly used premedicants do not significantly delay recovery after anesthesia. Even though benzodiazepines and narcotic analgesics produce dose-dependent central nervous system depression, these agents do not necessarily prolong the recovery period because of their ability to decrease the patient's anesthetic requirement. Thus, the rational use of premedication can make the experience of surgery safer and more pleasant for our patients without increasing health care costs. By limiting one's practice to one or two drugs in each of the various premedicant drug groups, the practicing anesthesiologist will become more familiar with the effects of these drugs and be better prepared to alter their "premedication routine" to meet the specific needs of the individual patient.

ACKNOWLEDGEMENT

I wish to express my sincere gratitude to my family and my bestfriend Uthkarsha vinesh for their continuous support.

CONFLICT OF INTEREST

We have no conflict of interest.

BIBLIOGRAPHY

1. K D Tripathi. Drugs acting on central neruous system. General anaesthetic. Essentials of medical pharmacology. 6th edn. India. Jaypee brothers medical publisher (P) LTD., 2008: 378.
2. James M Ritter, Lionel D Lewis, Timothy Gk Mant, Albert Ferro. The nervous system. Anaesthetics and muscle relaxants. A Textbook of Clinical Pharmacology and

Therapeutics. 5th edn. Great Britain. Hodder Arnold, an imprint of Hodden Education, part of Hachette Livre UK., 2008: 149-150.

3. C Abdallah, R Hannallah. Premedication of the child undergoing surgery. M.e.j. anesth., 2011; 21(2): 165-176.
4. Preanesthetic Medication. Available from: http://howmed.net/pharmacology/preanesthetic-medication/
5. Anesthesia. Available from: https://en.wikipedia.org/wiki/Anesthesia
6. Kulkarni M, Patil A. A Cross-Sectional Pharmacoepidemiological Study of the Utilization Pattern of Pre-Anesthetic Medications in Major Surgical Procedures in a Tertiary Care Hospital. Cureus., 2017; 9(6): 1344.
7. Paul F. White. Pharmacologic and Clinical Aspects of Preoperative Medication. ANESTH ANALG., 1986; 65: 963-974.
8. Biswas p, Niveditha, Shivamurthy MC. A study to evaluate the pattern of pre Anaesthetic medication in various surgical specialties in a Tertiary Care Hospital. Int J Pharm Sci Res., 2014; 5(6): 2441-2446.
9. Michael J, Sheen, Fang-Lin Chang, Shung-Tai Ho. Anesthetic premedication: New horizons of an old practice. Acta Anaesthesiologica Taiwanica., 2014; 52: 134-142.
10. K D Tripathi. Preanaesthetic Medication. Pharmacological Classification of Drugs with doses and preparations. 4th edn. India. Jaypee brothers medical publisher (P) LTD., 2010: 52.
11. James M Ritter, Lionel D Lewis, Timothy Gk Mant, Albert Ferro. The nervous system. Hypnotics and Anxiolytics. A Textbook of Clinical Pharmacology and Therapeutics. 5th edn. Great Britain. Hodder Arnold, an imprint of Hodden Education, part of Hachette Livre UK., 2008; 108: 160-161.
12. Joonyoung Ji. Dexmedetomidine as an Oral Premedication to Facilitate Mask Induction for General Anesthesia for Pediatric Dentistry. University of Toronto., 2014; 1-56.
13. David J. Smith, Michael B. Howie. General Anesthesia: Intravenous and Inhalational Agents. Charles R. Craig, Robert E. Stitzel. Modern Pharmacology with Clinical Applications. 5th edn. 307, 297.
14. Opioid. Available from: https://en.wikipedia.org/wiki/Opioid
15. K D Tripathi. Drugs acting on central neruous system. Opioid Analgesics. Essentials of medical pharmacology. 6th edn. India. Jaypee brothers medical publisher (P) LTD., 2008: 454.

16. Tony L. Yaksh, Mark S. Wallace. Opioids, Analgesia, and Pain Management. Goodman & Gilman's. The Pharmacological Basis of Therapeutics. Laurence L. Brunton. 12th edn. New York. MC Graw Hill Medical., 2011: 491.
17. K D Tripathi. Drugs acting on Autonomous neruous system. Anticholinergic Drugs. Essentials of medical pharmacology. 6th edn. India. Jaypee brothers medical publisher (P) LTD., 2008: 106.
18. William F. Wonderlin. Muscarinic Blocking Drugs. Charles R. Craig, Robert E. Stitzel. Modern Pharmacology with Clinical Applications. 5th edn., 137.
19. Antiphyscotic. Available from: https://en.wikipedia.org/wiki/Antipsychotic
20. Lisa M. Gangarosa, Donald G. Seibert. Drugs Used in Gastrointestinal Disorders. Charles R. Craig, Robert E. Stitzel. Modern Pharmacology with Clinical Applications. 5th edn., 270-283.
21. K D Tripathi. Gastrointestinal Drugs. Essentials of medical pharmacology. 6th edn. India. Jaypee brothers medical publisher (P) LTD., 2008: 627-650.
22. Taneja R, Kumar A, Sood S. A study of patient's perception about pre anaesthesia clinic in a tertiary care hospital of a developing country. J. Evid. Based Med. Healthc., 2017; 4(56): 3416-3420.
23. C J Cote. Preoperative Preparation and Premedication. British Journal of Anaesthesia., 1999; 83(1): 16-28.