Review of anticholinergic drugs: Their use and safe omittance in preoperative medications

DAVID D. ROSE, CRNA, MA
Spokane, Washington

The routine use of anticholinergics as part of preoperative medication is deep-rooted and widespread in anesthesia practice. The current trend is toward a more rational approach to their use. The purpose of this article is to review the pharmacodynamics of anticholinergics and cite recent literature regarding their addition or safe omittance from a preoperative medication.

The addition of anticholinergics as part of "routine" premedication is probably the most widely used drug application in anesthesia. Originally, atropine, the classic representation, was used for both its antisialagogue effect in preventing an abundance of secretions frequently seen with ether and cyclopropane, and for its vagolytic properties. However, the replacement of ether and cyclopropane by the newer volatile agents has virtually eliminated the problem of secretions. In addition, current thought regarding vagal blockade reveals that bradycardia should be treated as it occurs, rather than that all surgical patients should be given an unnecessary drug.

Despite current information available, as many as 60% of anesthetists continue to order anticholinergics as part of their routine premedication. The trend, however, is toward a more rational approach to anticholinergic use. Nevertheless, anticholinergics do have an important place in the anesthetist's armamentarium.

Airway secretions
Ciliary movement is depressed in the presence of thickened secretions. Therefore, it is not advantageous to use anticholinergics in those patients who could benefit from less viscous secretions. These would include smokers, patients with chronic obstructive pulmonary disease, and in the pediatric group, those with cystic fibrosis.

Antisialagogue
The newer anesthetic agents do not have the tendency to increase upper airway secretions. Consequently, it is felt by many clinicians that it is a more logical practice to treat excessive secretions once they occur, rather than exposing all patients to a drug they do not need.

Some indications for anticholinergics occur in patients undergoing intraoral surgical procedures where excessive secretions can be an interference. Another indication may be when topical anesthetics are used intraorally. The antisialagogue effect inhibits secretions which might otherwise impair the onset of the anesthetic by diluting the agent.

Body temperature
An increase in body temperature may occur with anticholinergic use because of the suppression of sweat glands, which are innervated by the sympathetic nervous system through cholinergic...
pathways. Also, larger doses may cause hyperpyrexia through a central effect on the temperature regulating mechanism.

In a febrile child requiring atropine as a premedicant, the sympathetic discharge may increase body temperature. For this reason, children requiring such therapy should have both constant temperature monitoring as well as a means of controlling the temperature immediately available throughout the surgical procedure. Glycopyrrolate may be substituted in this instance; recent studies indicate that it has a lesser incidence of hyperpyrexia and virtually no central mediating effects.

General nervous system

Signs of central nervous system (CNS) toxicity may include delirium, excitement, hallucinations, ataxic gait, fever, coma, and occasionally death.

CNS toxicity is more likely to be seen with the tertiary amines such as atropine, because tertiary amines are lipophilic and can easily cross the blood-brain barrier. Glycopyrrolate, however, being a quaternary amine, is not likely to produce the central effects as it is unable to penetrate the blood-brain barrier.

Gastric pH

The elevation of gastric pH by anticholinergics remains questionable. Earlier studies suggest that large doses of glycopyrrolate or atropine increase gastric pH and decrease gastric volume. These higher doses, however, may cause the toxic side effects often seen with larger doses of anticholinergics. More recent studies reveal that glycopyrrolate and atropine, given in premedicant doses to adults, have no significant effect in elevating the gastric pH or decreasing gastric volume. However, recent studies in children reveal that glycopyrrolate given in premedicant doses both increases gastric pH and decreases gastric volume as compared to atropine.

Gastroesophageal sphincter tone

A decrease in gastroesophageal sphincter tone has been reported with premedicant doses of both atropine and glycopyrrolate. The risk of gastroesophageal reflux is present due to a decrease in intraluminal pressure caused by anticholinergics. The risk can further increase if premedication includes such drugs as morphine, meperidine (Demerol), droperidol, or promethazine, since these drugs have also been found to decrease gastroesophageal tone. Additional consideration should be used when administering anticholinergics to the patient with already compromised gastroesophageal sphincter tone, that is, the patient who has a hiatal hernia with esophageal reflex.

Heart rate

There is usually an increase in heart rate associated with the administration of anticholinergics. Recent studies, however, reveal that glycopyrrolate is associated with less of an initial increase in heart rate, and its vagolytic effects last significantly longer than those of atropine.

In addition, glycopyrrolate, being a quaternary amine, has been found to exhibit less placental transfer than atropine, a tertiary amine. Therefore, the resultant loss of fetal beat-to-beat variability is not manifested with glycopyrrolate, and early signs of fetal distress from hypoxia will not be masked.

However, there are precautions regarding heart rate changes that the anesthetist should consider when ordering anticholinergics as part of a premedicant. First, tachycardia may be more undesirable than bradycardia in patients with borderline congestive heart failure or a tendency toward supraventricular arrhythmias. Because glycopyrrolate exhibits a more gradual onset of effects as compared with atropine, there is a lower incidence of tachycardia associated with its use. It thus may be advisable to consider glycopyrrolate in these situations if a premedicant anticholinergic is needed.

Second, patients with coronary artery disease need special attention when anticholinergics are used. Patients with three vessel disease may reveal a decreased chronotropic response to atropine. On the other hand, a patient in the post-myocardial infarction period may unmask strong sympathetic discharge resulting in severe ventricular arrhythmias when a relatively small dose of atropine is administered for vagal blockade. Also, it has been shown that elderly patients with no history of heart disease can exhibit a negative or diminished positive chronotropic response to atropine. The explanation for these findings is not clear. Studies, however, reveal that the cause may be due to a dysfunctional cardiac pacemaker resulting from ischemic changes to this area of the heart.

It appears that stenosis and/or occlusion of the right coronary artery can produce ischemia, hypoxia, acidosis, and a build-up of metabolites in the area of the S-A node and the posterior A-V groove. Experimental data from animal studies on coronary occlusion has shown decreases, increases, and inconsistent heart rate changes resulting from these conditions. The addition of an an-
Anticholinergic may produce unpredictable responses in these cases. Such considerations should enter into the decision to use anticholinergics as a premedicant in patients with cardiovascular disease, in patients scheduled for revascularization of the myocardium, and in elderly patients.

Third, large intramuscular or small intravenous doses of atropine may produce bradycardia. This can be associated with a shift of the pacemaker below the sinoatrial node, leading to supraventricular arrhythmias that can jeopardize the circulation, particularly in conjunction with vascular disease.1,10,20

Finally, special attention should be given to these patients when considering the reversal of non-depolarizing neuromuscular blocking agents. Since the response to atropine is unpredictable in some cardiovascular patients and possibly lethal in those patients with severe coronary stenosis and/or occlusion, anticholinergic drugs should be used with caution. Glycopyrrolate should be considered due to its lesser effect on cardiovascular dynamics and prolonged vagolytic properties when an anticholinergic is necessary in combination with an anticholinesterase for the reversal of neuromuscular blockade.9,11,20 However, recent documentation in the literature reveals that atropine and neostigmine may be used for the reversal of pancuronium in patients undergoing coronary artery bypass graft surgery without any significant cardiovascular effects.21

**Pediatric use**

Infants and children need to be treated separately in a discussion of anticholinergic drugs. Secretions present in small airways may enhance the risk of increased airway resistance or possibly even obstruction of these smaller airways.8 Evaluation of the patient with increased secretions may indicate the need for an anticholinergic.

In addition, anticholinergics are used in the infant to block cholinergic challenges to the heart. There are studies, however, revealing that intravenous administration of atropine prior to halothane anesthesia may increase the incidence of ventricular arrhythmias.1,20

Finally, infants and younger children are more likely to encounter bradycardic episodes following the administration of succinylcholine.3,10 The episodes are usually quickly treated by administering either intravenous or intramuscular atropine.8

**Physiologic dead space**

Atropine has been shown to increase physiologic dead space 20-25%. A compensatory increase in minute ventilation avoids any alterations in the PaCO2.2,25 This increase in minute ventilation should not be mistaken for some compensatory mechanism thought to be caused by depressed ventilation produced by a concomitant narcotic in the premedicant.

Alone, therefore, anticholinergics exhibit no altering effect on ventilatory responses to carbon dioxide. Oxygen consumption and carbon dioxide production also are unchanged.2,3,25

**Reflex bradycardia**

It is presently felt that, if an anticholinergic is indicated to prevent reflex bradycardia, the intravenous administration is more logical either shortly before its anticipated need or when the symptom presents itself.1-6,9,11

Indications for anticholinergic use in this setting would be in procedures where pressure, either on the eye or carotid bodies, or traction on abdominal viscera, may elicit strong vagal discharge. Another example is in the repeated bolus doses of succinylcholine, which may also produce vagal stimulation resulting in bradycardia. This is especially critical in the pediatric patient.19

In summary, anticholinergics are not harmless drugs. In some circumstances, they may even be dangerous. Thus, they should be used discriminately, and their omission from a "routine" premedicant regimen should be considered during the preoperative evaluation.

**REFERENCES**


AUTHOR

David D. Rose, CRNA, MA received his BSN in 1973 from California State University at Fresno. When this paper was written, he was a senior nurse anesthesia student at Sacred Heart Medical Center in Spokane, Washington. He received his master's degree in anesthesiology education from Gonzaga University. He is also a captain in the Army Nurse Corps of the United States Army Reserve in Spokane.