NEUROMUSCULAR BLOCKING AGENTS (Systemic)

Atracurium Besylate¾Atracurium besilate
Succinylcholine¾Suxamethonium
VA CLASSIFICATION (Primary)
Atracurium¾MS300
Gallamine¾MS300
Pancuronium¾MS300
Succinylcholine¾MS300
Tubocurarine¾MS300/DX900
Vecuronium¾MS300
Commonly used brand name(s):Anectine4; Flaxedil2; Norcuron6; Pavulon3; Quelicin4; Sucostrin4; Tracrium1.
Other commonly used names are: Atracurium besilate Atracurium Besylate.

Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

Accepted

Skeletal muscle paralysis¾The neuromuscular blocking agents are indicated as adjuncts to anesthesia to induce skeletal muscle relaxation and to facilitate the management of patients undergoing mechanical ventilation 1, 2, 3, 4, 5, 6, 7, 8, 9, 10.

Generally, a relatively short-acting nondepolarizing neuromuscular blocking agent or a single dose of the depolarizing neuromuscular blocking agent succinylcholine is used to facilitate endotracheal intubation. Continuous infusion of succinylcholine may be used for short surgical procedures requiring muscle relaxation. Nondepolarizing neuromuscular blocking agents, or, less commonly, succinylcholine administered by continuous infusion, are used for surgical procedures requiring an intermediate or prolonged duration of muscle relaxant action and to facilitate controlled ventilation.

Convulsions (treatment)¾[Atracurium] *, 14 [gallamine] , 2, 4 [pancuronium] * , 14 [succinylcholine] , 7 tubocurarine, 8, 13 and [vecuronium] * 14 are indicated to reduce the intensity of muscle contractions of pharmacologically or electrically induced convulsions. Succinylcholine is generally preferred because of its short duration of action.
[Neuromuscular blocking agents are also used to decrease the muscular manifestations of persistent convulsions associated with toxic reactions to other medications 11 .] *

Myasthenia gravis (diagnosis)¾Tubocurarine is indicated as a diagnostic aid for myasthenia gravis when the results of tests with neostigmine or edrophonium are inconclusive 8, 9.

* Not included in Canadian product labeling.

Pharmacology/Pharmacokinetics

Precautions to Consider

Cross-sensitivity and/or related problems

Patients sensitive to bromides may be sensitive to the bromide salts of pancuronium or vecuronium also.
Patients sensitive to iodine or iodides may be sensitive to the iodide salt of gallamine also.

Mutagenicity

Atracurium¾Mutagenic activity was observed in the mouse lymphoma assay under conditions in which more than 80% of the treated cells were killed, i.e., a relatively strong effect with concentrations of 80 and 100 mcg per mL in the absence of metabolic activation and a much weaker effect with concentrations of 1.2 mg per mL or higher in the presence of metabolic activation. However, mutagenic activity has not been demonstrated in the Ames test or in a rat bone marrow cytogenicity assay 1.

Pregnancy/Reproduction

Pregnancy¾Atracurium: Adequate and well-controlled studies have not been done in humans. However, studies in rabbits (doses of 0.15 mg per kg of body weight [mg/kg] once a day or 0.1 mg/kg twice a day on Day 6 through Day 18 of gestation) have shown that atracurium causes visceral and skeletal anomalies. Also, postimplantation losses were greater in the group given 0.15 mg/kg once daily than in controls.
FDA Pregnancy Category C 1.

Gallamine: Problems in humans have not been documented. However, it has been determined that gallamine crosses the placenta 2.

Pancuronium: Studies have not been done in either animals or humans. However, problems in humans have not been documented. 38

FDA Pregnancy Category C 38.

Succinylcholine: Studies have not been done in humans. However, succinylcholine has been shown to cause intrauterine growth retardation and limb deformities resembling clubfoot when administered to the rat fetus between the 16th and 19th days of gestation or when injected in chick embryos from the 5th to 15th days of incubation 12.

FDA Pregnancy Category C 12.

Tubocurarine: Although adequate and well-controlled studies have not been done in humans, it has been determined that tubocurarine crosses the placenta. In animal studies, intramuscular injection of tubocurarine into the intercapsular region of the rat fetus on the 16th and 19th days of gestation caused growth retardation (incidence 21 to 23%) and limb deformity (incidence 7 to 8%), respectively. Tubocurarine has also caused growth retardation and limb deformities when injected into chick embryos from the 5th to the 15th day of incubation.

Tubocurarine may cause congenital fetal contractures if large and repeated doses are administered during the early months of pregnancy, possibly by immobilizing the fetus at the time of joint formation 8.

FDA Pregnancy Category C 8.

Vecuronium: Vecuronium crosses the placenta. Studies have not been done in either animals or humans.
FDA Pregnancy Category C 39.

Labor and delivery¾Atracurium has been shown to cross the placenta in small quantities following administration to pregnant women for delivery by cesarean section. Although no adverse effects in the neonates were reported with atracurium, tubocurarine has been reported to cause diminished skeletal muscle activity leading to respiratory difficulty in the newborn when large and repeated doses are given near delivery. The possibility of neonatal respiratory depression or reduced skeletal muscle activity should be considered when any of these agents is used near delivery.

Breast-feeding

It is not known whether neuromuscular blocking agents are distributed into breast milk. However, problems in humans have not been documented.

Pediatrics

Atracurium, gallamine, and tubocurarine: Neonates up to 1 month of age may be more sensitive to the effects of nondepolarizing neuromuscular blocking agents 5, 8.

Older infants are more sensitive than children to the effects of nondepolarizing neuromuscular blocking agents 28.

Pancuronium: The prolonged use of pancuronium to facilitate mechanical ventilation in neonates has been associated with myopathy 5.

Some premature neonates administered pancuronium for emergency anesthesia and surgery subsequently developed methemoglobinemia 5.

The cause of the methemoglobinemia has not been established 5.

Succinylcholine: Hyperkalemic rhabdomyolysis resulting in cardiac arrest and death has occurred in apparently healthy pediatric patients after administration of succinylcholine 12, 27.

The adverse events occurred in pediatric patients with previously undiagnosed skeletal muscle myopathy (e.g., Duchenne's muscular dystrophy) 12, 27.

Because it is not possible to predict when a pediatric patient may experience a serious adverse reaction, it is recommended that the use of succinylcholine be restricted to emergency situations or other situations where the immediate securing of the airway is needed (e.g., laryngospasm) 12, 27.

Vecuronium: Pediatric patients 7 weeks to 1 year of age are more sensitive to the effects of vecuronium (on a mg-per-kg basis) than are adults. Recovery time may be 11/2 times that of adults. 39

Geriatrics

Although appropriate studies with neuromuscular blocking agents have not been performed in the geriatric population, geriatrics-specific problems that would limit the usefulness of these medications in the elderly are not expected. However, elderly patients are more likely to have age-related renal function impairment, which may decrease the rate of clearance of gallamine, pancuronium, succinylcholine, or tubocurarine from the body and thereby prolong their effects.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):