

# Anaesthesia and the brain

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## ABSTRACT

The brain is often a window to early changes in blood flow, tissue perfusion, or early neural damage manifested by a decline in higher cortical functions including recall memory and cognitive processing. The elderly population is particularly at risk of central nervous system injury, which may manifest as stroke and/or cognitive deterioration due to reduced cognitive reserve, as seen with aging-related cognitive decline. These changes in cognitive function are associated with reduced activities in daily living that substantially reduce the quality of life of the elderly, and can be magnified by physical or emotional stress in high-risk individuals.

The safety of anaesthesia and surgery has progressed over several decades to the point that today elderly and debilitated patients may safely undergo increasingly complex procedures with low

risk of major morbidity or mortality. However, anaesthesia and surgery appear to be associated with risk of brain injury, including stroke, and changes in cognitive functioning that outlast the effects of anaesthesia or pain medications, inflammation and the healing response. Several excellent studies have investigated the aetiology of the changes associated with cardiac and non-cardiac surgery. Understanding this decline and its aetiology is complicated by the fact that anaesthesia and surgery are rarely separated, indicating that the differences may be due to the stress response associated with surgery or the administration of anaesthetics. The focus of this lecture is on the complex field of neuroscience, and particularly cognitive neurosciences, in the elderly population, and the complex process of measuring and defining change in the perioperative period. Different types of surgery, implications for quality of life, as well as aetiological factors and how they relate to treatment, will be discussed.

## Product information (See page 91)

**S4** MIVACRON 5. Reg. No. 27/17.1/0569. Each ampoule contains 2 mg/ml Mivacurium (as the chloride). **PHARMACOLOGICAL CLASSIFICATION:** A 17.1 Peripherally-acting muscle relaxants. **INDICATIONS:** Used as an adjunct to general anaesthesia to relax skeletal muscles and to facilitate tracheal intubation and mechanical ventilation. **CONTRA-INDICATIONS:** Use in children under the age of 2 years. Patients known to have a sensitivity to mivacurium chloride, other benzyl isoquinolinium derivatives, benzyl alcohol. Patients known to be homozygous for the atypical plasma cholinesterase gene. **WARNINGS:** MIVACRON paralyses the respiratory muscles as well as other skeletal muscles, but has no effect on consciousness. MIVACRON should be administered only by, or under close supervision of an experienced anaesthetist, with adequate facilities for tracheal intubation & artificial ventilation. Monitoring of neuromuscular (NM) function is recommended during use. **INTERACTIONS:** NM block may be potentiated by concomitant use of inhalational anaesthetics e.g. enflurane, isoflurane, sevoflurane and halothane. Evidence of spontaneous recovery from succinylcholine should be observed prior to MIVACRON administration. A depolarising muscle relaxant e.g. suxamethonium chloride should not be administered to prolong the NM blocking effects of non-depolarising agents, as may result in a prolonged & complex block which can be difficult to reverse with anticholinesterase drugs. Magnitude and/or duration of NM block may be increased with antibiotics (aminoglycosides, polymyxins, spectinomycin, tetracyclines, lincomycin & clindamycin, anti-arrhythmic drugs (propranolol, calcium channel blockers, lignocaine, procainamide & quinidine), diuretics, magnesium salts, ketamine, lithium salts, ganglion blocking medicine (trimetaphan, hexamethonium). Anti-mitotic medicine, monoamine oxidase inhibitors, ecothiopate iodide, pancuronium, organophosphates, anticholinesterases, certain hormones, bantamadol may prolong the NM block. Certain medicine may aggravate or unmask latent myasthenia gravis or actually induce a myasthenic syndrome, increasing sensitivity to MIVACRON e.g. various antibiotics, beta-blockers (propranolol, oxprenolol), anti-arrhythmic medicine (procainamide, quinidine), antirheumatic medicine (chloroquine, D-penicillamine), trimetaphan, chlorpromazine, steroids, phenytoin & lithium. Onset of block may be lengthened & duration of block shortened with chronic phenytoin or carbamazepine therapy. **PREGNANCY AND LACTATION:** Safety in pregnancy and lactation is not established. **DOSAGE AND DIRECTIONS FOR USE:** For single patient use, under full aseptic conditions and any dilution carried out immediately before use. Discard any unused solution in open ampoules or in infusion solutions. May be used undiluted for infusion. Refer to package insert for diluting instructions and compatibility. Should not be mixed in the same syringe or administered simultaneously through the same needle with highly alkaline solutions (e.g. barbiturate salts). Where other anaesthetic agents are administered through the same indwelling needle or cannula and compatibility has not been demonstrated, each agent must be flushed through with physiological saline. Compatible with fentanyl, alfentanil, sufentanil, droperidol and midazolam. Refer to package insert for dosage recommendations in adults (by injection and by infusion); children 2–12 years; elderly; patients with cardiovascular disease; patients with reduced renal and/or hepatic function; patients with reduced plasma cholinesterase activity (e.g. organophosphate exposure); obese patients. **SIDE-EFFECTS AND SPECIAL PRECAUTIONS:** Skin flushing, erythema, urticaria, hypotension, transient tachycardia or bronchospasm are dose-related. Severe anaphylactic or anaphylactoid reactions reported in conjunction with one or more anaesthetic agents. Caution should be exercised in administering MIVACRON to patients with a history suggestive of an increased sensitivity to the effects of histamine and patients who are unusually sensitive to falls in arterial blood pressure, e.g. hypovolaemia. Increased sensitivity to MIVACRON can be expected in patients with myasthenia gravis, other forms of NM disease and cachectic patients. Severe acid-base or electrolyte abnormalities may increase or reduce sensitivity to MIVACRON. Reversal of Neuromuscular Block: Evidence of spontaneous recovery should be observed prior to the administration of reversal agents (e.g. neostigmine). The use of a peripheral nerve stimulator to evaluate recovery prior to and following reversal of neuromuscular block is recommended. **MANAGEMENT OF OVERDOSE:** Prolonged muscle paralysis and its consequences are the main effects. Risk of haemodynamic side-effects, may be increased. Essential to maintain a patent airway together with assisted positive pressure ventilation until spontaneous respiration is adequate. Full sedation may be required since consciousness is not impaired. Recovery will be hastened by the administration of anticholinesterase agents accompanied by atropine or glycopyrrolate once evidence of spontaneous recovery is present. Cardiovascular support may be provided by proper positioning of the patient and administration of fluids or vasopressor agents as required.

**S4** TRACRIUM Injection 2.5 ml. Reg. No. R/17.1/209. Each ampoule contains 25 mg atracurium besylate. **PHARMACOLOGICAL CLASSIFICATION:** A17.1 Peripherally-acting muscle relaxants. In anaesthesia to relax skeletal muscles and to facilitate controlled ventilation. Suitable for endotracheal intubation especially where subsequent muscle relaxation is required. **CONTRA-INDICATIONS:** Known sensitivity. **WARNINGS:** Atracurium paralyses the respiratory muscles as well as other skeletal muscles but has no effect on consciousness or pain threshold. Should only be administered by, or under the supervision of an anaesthetist. Facilities for tracheal intubation & maintenance of pulmonary ventilation & adequate arterial oxygenation must be available. Monitoring of neuromuscular function is recommended in order to individualise dosage requirements. Must not be administered into the infusion line of a blood transfusion. **DOSAGE AND DIRECTIONS FOR USE:** Use by injection (IV); intravenous injection. It must not be mixed with thiopentone or any alkaline agents. When small vein is selected as the injection site, TRACRIUM should be flushed through the vein with physiological saline after injection. Where other anaesthetic drugs are administered through the same in-dwelling needle or cannula as TRACRIUM, it is important that each drug is flushed through with physiological saline. The dosage range recommended for adults is 0.3 to 0.6 mg/kg on the duration of complete neuromuscular block (full block) required and will provide muscle relaxation for 15 to 35 minutes. Complete neuromuscular block (full block) can be prolonged with supplementary doses of 0.1 to 0.2 mg/kg as required. Endotracheal intubation can usually be accomplished within 90 seconds from the intravenous injection of 0.5 to 0.6 mg/kg. The neuromuscular block produced by can be reversed by standard doses of anti-cholinesterase agents such as neostigmine and edrophonium preceded or accompanied by atropine. **Use in Infusion:** After an initial bolus dose of 0.3 to 0.6 mg/kg. To maintain neuromuscular block during long surgical procedures, by administration as a continuous infusion at rates of 0.3 to 0.6 mg/kg/hr (0.005 to 0.01 mg/kg/minute). Refer to package insert for compatibility and dilutions with other infusion solutions. Refer to package insert for dosage recommendations in children, in elderly and high risk patients and long-term use in ICU. Monitoring of neuromuscular blockade recommended during use, in order to individualise dosage requirements. **SIDE-EFFECTS AND SPECIAL PRECAUTIONS:** Skin flushing, instances of transient hypotension and bronchospasm, anaphylactoid reactions. Use with caution in patients with myasthenia gravis, other neuromuscular diseases and severe electrolyte disorders in which potentiation of other non-depolarising agents has been noted. Resistance to non-depolarising neuromuscular blocking agents may develop in burn patients. Increased doses of non-depolarising muscle relaxants may be required in burn patients and are dependent on the time elapsed since burn injury and the size of the burn. Caution should be exercised in administering to patients with a history suggestive of an increased sensitivity to the effects of histamine. **Interactions:** The NM block may be increased by the concomitant use of inhalation anaesthetics such as halothane, isoflurane and enflurane. NM block may be increased with antibiotics (aminoglycosides, polymyxins, spectinomycin, tetracyclines, lincomycin & clindamycin, anti-arrhythmic drugs (propranolol, calcium channel blockers, lignocaine, procainamide & quinidine), diuretics, magnesium salts, ketamine, lithium salts, ganglion blocking medicine (trimetaphan, hexamethonium). Certain medicine may aggravate or unmask latent myasthenia gravis or actually induce a myasthenic syndrome, increasing sensitivity to MIVACRON e.g. various antibiotics, beta-blockers (propranolol, oxprenolol), anti-arrhythmic medicine (procainamide, quinidine), antirheumatic medicine (chloroquine, D-penicillamine), trimetaphan, chlorpromazine, steroids, phenytoin & lithium. Onset of block may be lengthened & duration of block shortened with chronic anticonvulsant therapy. A depolarising muscle relaxant e.g. suxamethonium chloride should not be administered to prolong the NM blocking effects of non-depolarising agents, as may result in a prolonged & complex block which can be difficult to reverse with anticholinesterase drugs. Use in pregnancy and obstetrics: Safety not established. Intensive Care Unit (ICU) Patients: Reports of seizures when receiving concurrently with other agents; muscle weakness and/or myopathy following prolonged use of muscle relaxants in severely ill patients in the ICU. **MANAGEMENT OF OVERDOSE:** Prolonged muscle paralysis and its consequences are the main signs of overdosage. It is essential to maintain a patent airway together with assisted positive pressure ventilation until spontaneous respiration is adequate. Full sedation will be required since consciousness is not impaired. Recovery may be hastened by the administration of anti-cholinesterase agents accompanied by atropine or glycopyrrolate, once evidence of spontaneous recovery is present.