THE USE OF MUSCLE RELAXANTS IN INFANTS AND CHILDREN

BY

GORDON H. BUSH

Department of Anaesthesia, University of Liverpool, England

The belief that the use of muscle relaxants in infants and children is both unnecessary and dangerous has not been substantiated by subsequent clinical experience. The important advances that have been made recently in paediatric anaesthesia are due largely to the introduction of muscle relaxants, which have reduced the need for toxic agents to a minimum and have emphasized the importance of control of pulmonary ventilation. Furthermore, muscle relaxants now play an important role in the management of a wide variety of medical and surgical conditions.

GENERAL CONSIDERATIONS

Muscle relaxants are absolutely contraindicated when the ability to ventilate the lung is in doubt, either because of the lack of means of pulmonary ventilation or failure to establish an airway. This occurs particularly in children with upper airway obstruction and to a lesser degree in the neonates. Endotracheal intubation must be performed whenever muscle relaxants are used and pulmonary ventilation maintained by intermittent positive pressure respiration throughout the period of action of the muscle relaxant. Intubation is rarely difficult and can be performed without haste or hypoxia, even in small infants, if the lungs have been previously ventilated with 100 per cent oxygen (McCaughey, 1962). The residual effects of drugs of the antidepolarizing group must be antagonized by the use of an anticholinesterase drug at the termination of the operation, as partial neuromuscular block carries grave risks in the immediate postoperative period and increases the incidence of pulmonary complications.

THE NEONATE

The early use of antidepolarizing relaxants in the neonate, which by definition is an infant less than 28 days old, was abandoned following reports of failure to re-establish respiration (Roberts, 1950; Rickham, 1952). Stead (1955) showed that compared with the adult the neonate is sensitive to d-tubocurarine and resistant to the effects of suxamethonium. He emphasized the advantages of the use of relaxant drugs in neonatal surgery and recommended suxamethonium in doses of 5 mg intravenously up to a total not exceeding 15–45 mg. Rees (1957) suggested that incremental doses should be kept as low as 1–1.25 mg because the neonate showed an increased liability to develop a phase II block. Hellings, Cope and Hawksley (1958) discussing the anaesthetic management of neonates undergoing repair of oesophageal atresia recommended an initial dose of 0.5 mg/lb. (1.1 mg/kg) body weight of suxamethonium with increments of 1 mg/lb. (2.2 mg/kg) body weight which later should be reduced to 0.5 mg/lb. (1.1 mg/kg) or less; the total dose used should not exceed 50 mg and the drug should be used as a 0.5 per cent solution. In 23 patients given suxamethonium only one developed any postoperative pulmonary complication, whilst of 18 patients given gallamine or d-tubocurarine, 8 developed postoperative respiratory difficulties. This trend was confirmed by Salanitre and Rackow (1961) who showed that of 89 patients, aged less than 13 weeks, who were given suxamethonium 20 per cent developed respiratory difficulties compared with 80 per cent of the 17 patients given d-tubocurarine. Intermittent suxamethonium is widely believed to be the relaxant of choice in neonatal anaesthesia, and, in an attempt to reduce the total dose used, small concentrations of halothane are often added to the inspired gas mixture. McCaughey (1962) uses intermittent doses in the range 1 mg/8–10 lb. (0.22–0.27 mg/kg) body weight and found the hourly consumption of suxamethonium to be only 12–14 mg, which is considerably smaller than that noted by the other workers. The advantages of any reduction in dosage by this amount can only be achieved by forfeiting one advantage...
THE USE OF MUSCLE RELAXANTS IN INFANTS AND CHILDREN

of the employment of muscle relaxants, namely the avoidance of potent and unselective agents. Intermittent suxamethonium must be given intravenously and the presence of a cut-down infusion in these cases makes administration relatively easy. The danger of intramuscular suxamethonium is well illustrated by the case described by Heifetz and Birkhan (1962) in which 80 mg of suxamethonium was given intramuscularly for a 140-minute procedure in a 6.6 lb. (3 kg) neonate, in whom respiratory insufficiency lasted for 16 hours postoperatively. Reduction in muscle blood flow (Churchill-Davidson and Richardson, 1952) and the effects of hypothermia (Zaimis, Cannard and Price, 1958) must inevitably prolong the action of intramuscular suxamethonium.

Churchill-Davidson and Wise (1962) investigated neuromuscular transmission in the newborn by means of electromyography, and found that there was a marked tolerance to the depolarizing action of decamethonium and appeared to be no obvious sensitivity to the antidepolarizing action of d-tubocurarine compared with the adult when dosage was calculated on a body weight basis. The premature infant in particular showed evidence of a dual type of block following the injection of a depolarizing drug. These findings suggested that the full value of the clinical use of d-tubocurarine remained to be studied. Antidepolarizing relaxants had been used successfully by a number of anaesthetists in the newborn (Auld, 1952; Fairlie, 1954; Dinsdale, 1954; Payne, 1955). Recently in an unselected series of 215 neonates only two instances of immediate postoperative difficulties were observed following the use of d-tubocurarine (Bush and Stead, 1962).

It was also noted that, using adequate operating conditions as the criteria for assessment, the neonate in the first few days of life required less d-tubocurarine than the older child but, as might be expected, this sensitivity had largely diminished by the end of the neonatal period of life. d-Tubocurarine may well challenge the position of intermittent suxamethonium as the preferable relaxant for long neonatal operations because administration is technically easier and relaxation is more consistent. The initial dose of d-tubocurarine should be 0.25 mg in premature and 0.5 mg in full-term neonates and supplementation may be with 0.125 mg and 0.25 mg respectively. Such a scheme prevents overdosage and only the minimum effective dose need be given. The residual curarization is reversed at the end of the operation with neostigmine 0.036 mg/lb. (0.08 mg/kg) preceded by atropine 0.008 mg/lb. (0.018 mg/kg) body weight intravenously. Potentiating factors such as inhalational agents should be avoided and the tendency to hypothermia, which is marked when controlled ventilation is used, countered by appropriate means.

For procedures lasting up to 30 minutes intermittent suxamethonium is preferable.

INFANTS AND CHILDREN

There is evidence that, compared with the adult, infants and children are more resistant to the actions of both types of neuromuscular blocking agents and this resistance gradually declines as adolescence is approached. Thus Salgado (1962) found that the dose of gallamine fell from 0.55 mg/kg/min at 18 months to 0.03 mg/kg/min at the age of 14 years. Telford and Keats (1957) found that the mean suxamethonium requirements for cardiovascular surgery fell from 278 µg/kg/min at the age of 1–6 months to 98 µg/kg/min at the age of 12–16 years. This may represent a true reduction in suxamethonium sensitivity but there is a possibility that in older children the muscle endplate may react differently to repeated doses of suxamethonium.

The choice of relaxant depends on the expected duration of the operative procedure and the absence of specific contraindications. Antidepolarizing relaxants are indicated when the operation is likely to exceed 30 minutes duration whilst for shorter procedures the depolarizing relaxants are preferable. The recommended doses of relaxants for infants and children show considerable variation, which can be explained by the different dosages of other drugs used in the premedication, induction and maintenance of anaesthesia and by the fact that, regrettably, pulmonary ventilation is not always controlled.

d-Tubocurarine and gallamine.

The initial dose of d-tubocurarine is stated to be 0.1–0.2 mg/kg (Foldes, 1957), 0.22 mg/kg (Smith, 1959), 0.4 mg/kg (Anderson, 1951), and 0.3–0.6 mg/kg (Booth, Nisbet and Wilson, 1960).
In the absence of large doses of premedicant drugs and using only 1.8 mg/lb. (3.9 mg/kg) of thiopentone, an intravenous injection of d-tubocurarine of 0.65 mg/kg in younger and 0.6 mg/kg in older children will be required to produce ideal conditions for intubation and control of pulmonary ventilation for 30–45 minutes. Increments should be one-quarter to one-eighth of the initial dose. In younger children a solution of 3 mg/ml of d-tubocurarine is convenient and easily prepared. The dose of relaxant must be reduced by one-half to one-quarter when administered together with halothane or ether, and in patients suffering from a reduction in respiratory reserve, as occurs in progressive muscular dystrophy or following poliomyelitis.

When a vagolytic effect is desired, as in the reduction of reflex bradycardia during ophthalmic surgery, gallamine in a dose of 1 mg/lb. (2.2 mg/kg) may be preferable (Deacock and Oxer, 1962). This relaxant must not be used in the presence of impaired renal function since accumulation may produce a persistent myoneural block of many hours duration.

Following gallamine or d-tubocurarine, intravenous neostigmine 0.036 mg/lb. (0.08 mg/kg) preceded by atropine 0.008 mg/lb. (0.018 mg/kg) should be administered routinely, though a period of at least 20 minutes should elapse between the administration of d-tubocurarine and neostigmine. This dose of neostigmine will guarantee adequate reversal of the neuromuscular block. Respiratory acidosis must be avoided because neuromuscular block is potentiated and anticholinesterase drugs, under these circumstances are not only less effective as antidepolarizing antagonists but, as in adults, may produce serious cardiac arrhythmias (Riding and Robinson, 1961).

Suxamethonium. Bradycardia following suxamethonium must be prevented by the previous administration of vagolytic drugs in doses related to body weight. This relaxant is contraindicated when a rise in intraocular pressure is harmful as in patients with congenital glaucoma and penetrating eye injuries. Since suxamethonium also causes a rise in cerebrospinal fluid pressure (Halldin and Wählín, 1959) and may cause apnoea due to medullary "coning" (Filis and Jorgensen, 1961), this drug is contraindicated in patients with raised intracranial pressure.

Smith (1959) recommends that the dose range should be 1 mg/lb. (2.2 mg/kg) for a 10 lb. infant falling to 0.5 mg/lb. (1.1 mg/kg) for a 100 lb. child, and subsequent doses should be one-half to one-quarter of the original. McAughhey (1962) suggests that an initial dose of suxamethonium of 1 mg/4–5 lb. body weight will produce ideal conditions for intubation in 95 per cent of cases of all ages and an apnoea lasting 60 to 90 seconds. Because of the dangers of the semi-paralyzed state, an initial dose of 1 mg/2 lb. is preferable and subsequent doses may be reduced to 1 mg/6–8 lb.

Intramuscular suxamethonium has been advocated for endotracheal intubation. Beldays (1962) found that using 1.5 mg/lb. body weight there was complete paralysis after 1 minute or less in infants under 1 year old. With 2 mg/lb. body weight complete paralysis occurred after 2 minutes or less in the age group 1–5 years and up to 3 minutes in children of 6 years and over. Adequate spontaneous respiration returned in 15–19 minutes when 1.5 mg/lb. body weight of 10 per cent suxamethonium was used in children under 3 years and after the same time when 2 mg/lb. body weight was used in children over 4 years of age (Beldays, 1959). In certain circumstances such as the presence of convulsions the intramuscular route may be justified. The intravenous route of administration produces a rapid onset and recovery and the effect is more predictable. As pointed out by Foldes and Brown (1961) it avoids the possibility of an apnoea of many hours duration in an individual who is sensitive to suxamethonium.

Suxamethonium is often used to produce suitable conditions for intubation prior to the administration of gallamine or d-tubocurarine. There is no clinical evidence at present to suggest that any harm results from this sequence providing the depolarizing myoneural block is waning before the antidepolarizing drugs are administered. The excellent conditions for intubation produced by d-tubocurarine and gallamine are not widely appreciated. However, the administration of suxamethonium after antidepolarizing relaxants is pharmacologically unsound. Antidepolarizing relaxants may
be indicated in certain circumstances following repeated suxamethonium injections. Under these conditions the initial dose of antidepolarizing drug should be one-half to one-third of the recommended dose.

Decamethonium.

This drug is seldom used in infants and children since intermittent suxamethonium is more controllable for short procedures, and for longer action the antidepolarizing drugs are more predictable and reversible. Smith (1955) recommends 0.5 mg for a 10 lb. (4.5 kg) infant and 3 mg for a 100 lb. (45 kg) child, whilst Foldes (1957) suggests doses of 0.11–0.18 mg/lb. (0.23–0.40 mg/kg) body weight.

COMPLICATIONS

Certain complications following the use of muscle relaxants in children require special emphasis.

Muscle pains.

Postoperative myalgia following intravenous suxamethonium is considerably less frequent in children compared with adults. Bush and Roth (1961) found that in children between the ages of 5 and 9 years the incidence was only 3 per cent whilst in the 10–14 year age group the incidence was 23 per cent. The reason for this difference is obscure.

Prolonged apnoea.

Apart from overdosage, potentiation of muscle relaxants by various chemical and physical agents is a frequent cause of prolonged respiratory insufficiency. The enhancement of the neuromuscular blocking effects of antidepolarizing drugs by ether and halothane has already been mentioned.

Antibiotics, in particular neomycin and streptomycin, are well established as neuromuscular blocking drugs and prolonged apnoea has been reported in children following the intraperitoneal installation of these drugs (Pridgen, 1956; Bush, 1961a). This effect is especially liable to occur in children because antibiotics are commonly believed to possess little or no toxic action and a gross overdose is inadvertently administered. The dose of antibiotic must be related to body weight.

Young infants and neonates often sustain a fall in body temperature during anaesthesia, which is most marked in children under 20 lb. (9 kg) in body weight (Harrison, Bull and Schmidt, 1960). At body temperatures below normal, infants are lethargic, drowsy, with depressed respirations, which may proceed to apnoea. The effects of muscle relaxants are prolonged due to a reduction in muscle blood flow. These ill effects of inadvertent hypothermia must be prevented by adequate precautions against heat loss.

Prolonged apnoea following a single dose of suxamethonium may occur in children of all ages, though the youngest to be reported so far occurred in an infant of 6 months (Kaufmann, Lehmann and Silk, 1960). Kalow (1959) has shown that this prolonged action of suxamethonium is due to the inheritance of an atypical pseudocholinesterase which does not hydrolyze this drug in concentrations encountered clinically. The importance of this finding lies in the fact that this hereditary trait occurs approximately in 1 in 3000 persons and more than one child in a family may be affected (Power, 1958; Bush, 1961b). Patience and continued pulmonary ventilation will ensure recovery and polypharmacy is to be deprecated and may prolong the apnoea further.

THERAPEUTIC USES

The use of relaxant drugs to enable pulmonary ventilation to be controlled by mechanical means has a number of important clinical applications in infants and children. d-Tubocurarine is the most suitable relaxant in long-term cases and may be administered intramuscularly, the dose and interval of administration depending on the weight and condition of the patient.

The mortality from neonatal tetanus can be considerably reduced if a full regime of total paralysis is instituted (Smythe and Bull, 1959; Sykes, 1960).

Respiratory inadequacy may also occur in a variety of other conditions in the newborn, such as in infants suffering from diaphragmatic hernia, and following the surgical repair of a trachoo-oesophageal fistula, or exomphalos. Curarization may be necessary in these patients to allow effective mechanical ventilation of the lungs in the postoperative period. Together with the correction of the biochemical disturbances, curarization and IPPR has been reported to be successful in two cases of the respiratory distress syndrome of the newborn (Hesse et al., 1963).
In infants and older children curarization will be required to allow effective IPPR in patients with severe bronchiolitis or pneumonia.

Convulsive states due to such causes as status epilepticus (Nisbet, 1959; Evanson, 1959) or strychnine poisoning (Hawkins, 1962) can be controlled by adequate pulmonary ventilation following the use of muscle relaxants.

The hyperventilation of severe salicylate poisoning, with its dangers of hyperpyrexia, exhaustion and gross biochemical disturbances, may be averted by correct pulmonary ventilation, assisted by the use of muscle relaxants (Frier et al., 1957; Celander and Haglund, 1958).

The use of muscle relaxants for these purposes imposes considerable strain on the medical and nursing staff and this form of treatment should be undertaken only where suitable facilities exist. Nevertheless this method of therapy can be extremely rewarding and its use will undoubtedly increase in the future.

REFERENCES


(1962). Intramuscular succinylcholine for endotracheal intubation in infants and children—II.


Pridgen, J. E. (1956). Respiratory arrest thought to be due to intraperitoneal neomycin. Surgery, 40, 571.


THE USE OF MUSCLE RELAXANTS IN INFANTS AND CHILDREN


---

LIVERPOOL SOCIETY OF ANAESTHETISTS

Programme for Session 1963–1964

1963

**FRIDAY, OCTOBER 11, 8 P.M.**
Ordinary General Meeting at the Liverpool Medical Institution.
**Speakers:** Dr. A. BARAKA, Dr. G. H. BUSH and Dr. J. E. UTTING.
Recent developments in the field of muscle relaxants.

**THURSDAY, NOVEMBER 7, 8 P.M.**
Joint Meeting with the Liverpool Medical Institution at the Liverpool Medical Institution.

**Symposium:** The management of some respiratory emergencies.
**Speakers:** Dr. J. S. ROBINSON, Dr. E. SHERWOOD JONES, Mr. B. J. BICKFORD and Dr. G. JACKSON REES.

**FRIDAY, DECEMBER 6, 8 P.M.**
Ordinary General Meeting at the Liverpool Medical Institution.

**Symposium:** Progressive Patient Care.
**Speakers:** Professor CECIL GRAY, Dr. GEORGE J. C. BRITAIN, Miss A. M. W. WHITE, S.R.N., R.F.N., S.C.M., Mr. MARK WELLS, M.A., A.R.I.B.A.

1964

**FRIDAY, JANUARY 24, 8 P.M.**
Ordinary General Meeting at the Liverpool Medical Institution.
**Speaker:** Dr. JOHN CLUTTON-BROCK.
Consciousness and anaesthesia.

**FRIDAY, MARCH 20, 8 P.M.**
Ordinary General Meeting at the Liverpool Medical Institution.

**Papers to be presented in Competition for the Registrar’s Prize.**

**THURSDAY, APRIL 16, 8 P.M.**
Combined Meeting with the Anaesthetic Section of the Manchester Medical Society at Manchester.
**Speaker:** Dr. J. S. ROBINSON.
Controlled profound hypotension with halothane.
**Speaker:** Dr. A. R. HUNTER.
THA (tetrahydro-aminoacridine) — a disappointment.

**FRIDAY, MAY 8, 8 P.M.**
Thirty-second Annual General Meeting at the Liverpool Medical Institution.