DECAMETHONIUM IODIDE: A REAPPRAISAL

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Decamethonium iodide (C.10) was first described by Barlow and Ing, and by Paton and Zaimis, in 1948. The following year it was introduced into anaesthesia as a result of the work of Organe, and of Hewer, Lucas, Prescott and Rowbotham. Apart from the initial enthusiasm decamethonium has never found much favour with anaesthetists. In 1950 an editorial in the Lancet, comparing it with Gallamine, stated that the position of decamethonium was "less happy, mainly because no satisfactory antidote for it had yet been found". It went on to mention reports of delayed recovery and to conclude that "much more experience will be needed before its place in anaesthesia can be fully assessed".

The position has changed little since. Two years later the same journal stated in an annotation that "of the depolarizing group decamethonium had a brief period of popularity", and again the reason given for its failure to replace other relaxants was lack of a suitable antidote. Then in 1954, describing the Cardiff anaesthetic record system, Mushin, Lewis-Faning and Morgan wrote, "decamethonium, though commonly used at the time our card was first designed, is now little used and has been deleted from the record in the latest edition"; and Lee (1953), in his Synopsis of Anaesthesia, remarks that he seldom feels the need of this relaxant. It is hardly surprising that Burroughs Wellcome & Co. are ceasing to market their preparation, Syncurine (personal communication).

CRITICISM OF DECAMETHONIUM

It is interesting to consider the reasons for the fall from grace of decamethonium. The principal one is that it has no suitable antidote, a shortcoming which was aggravated by the almost simultaneous introduction of gallamine (Mushin, Wien, Mason and Langston, 1949), a drug effectively antagonized by neostigmine. It will be recalled that hexamethonium and pentamethonium bromide were at one time considered as possible antidotes to decamethonium but proved to be unreliable and indeed, owing to their hypotensive dangerous action.

The employment of decamethonium in anaesthesia was further discouraged by reports of persistent intercostal paralysis (Gray, 1950; Harris and Dripps, 1950; Hunter, 1950; Vetter and Nicholson, 1950; Barry, Straton and Sutherland, 1951; Guerrier and Mason, 1952), and of cardiovascular effects, viz., tachycardia, bradycardia and hypotension (Hunter, 1950; Guerrier and Mason, 1952) following the use of the drug. Finally, there were some who regarded its sharp end-point as an embarrassment to the smooth conduct of anaesthesia.

It is my opinion that a disproportionate amount of attention has been paid to the possible disadvantages of decamethonium. This view is supported by my own experience and that of my colleagues in the Dundee Teaching Hospitals who have used the drug extensively over the years. In proper dosage it has been found to be a reliable relaxant with no apparent side-effects, and to have a unique and valuable place in clinical anaesthesia.

The criticisms which have been levelled against decamethonium are not difficult to answer. The fact that it has no antidote is a poor objection to its employment in anaesthesia; to state that it does not need one is to present a more accurate picture of the situation. It is the only relaxant of reasonable duration of action which, even after full paralyzing doses, possesses this advantage. The sharp end-point, far from being an embarrassment, constitutes the most attractive
characteristic of decamethonium in anaesthesia. The complication of persistent intercostal paralysis is completely avoidable if dosage is not excessive. We have encountered no evidence of cardiovascular effects, and it is my firm opinion that they must be rare and of no practical significance.

SOME PHARMACOLOGICAL CONSIDERATIONS

The chemistry and pharmacology of decamethonium iodide have been thoroughly described (Paton and Zaimis, 1949; Burns and Paton, 1951; Paton, 1952; Foldes, 1954; Hunter, 1954; Paton, 1956; Burn, 1957). It is, however, relevant to mention certain characteristics of importance to its clinical use.

Injected intravenously, decamethonium iodide reaches its maximum effect in about 5 minutes. In a lightly premedicated adult of average build, following an induction dose of up to 750 mg, 5 mg decamethonium produces apnoea of approximately 20 minutes duration, provided slight hyperventilation with nitrous oxide/oxygen through a soda lime absorber is maintained. Within 5 minutes of the start of diaphragmatic contractions the effects of the drug have generally disappeared.

Although decamethonium is a depolarizing type of relaxant, the occurrence of obvious muscle fasciculations following induction with the normal dose of thiopentone is unusual. However, I have frequently succeeded in demonstrating them by giving a full dose of decamethonium (5 mg) immediately after a small amount of thiopentone (150 mg). The conscious person feels these as cramps (Organe, Paton and Zaimis, 1949; Hewer, Lucas, Prescott and Rowbotham, 1949), and the administration of a “test dose” of 1 mg was described by Gray (1950) as unpleasant for the patient. For this reason it is inadvisable to inject decamethonium before inducing sleep. The incidence of fasciculation seems to be related to the blood-level of adrenaline (Paton and Zaimis, 1950). Postoperative muscle pain does not appear to follow the use of decamethonium.

Decamethonium and Neostigmine.

Decamethonium (like suxamethonium) iodide is a relaxant of the depolarizing type, its effect being potentiated by the anticholinesterases. Therefore neostigmine must not normally be used in an attempt to reverse its action. However, in 1952, following experiments on animals, Zaimis reported that decamethonium and suxamethonium could no longer be described as purely depolarizing, and postulated the development in certain circumstances of a “dual block”, first of all depolarizing and later changing to a competitive type reversible by anticholinesterases. At the same time Churchill-Davidson and Richardson (1952) drew attention to the fact that in myasthenic patients the affinity of the motor endplate for decamethonium changes and a block characteristic of competitive inhibition occurs, reversible by neostigmine. Subsequent to numerous clinical reports of neostigmine (or edrophonium—Bullough, 1957) effectively dispelling “prolonged apnoea” following suxamethonium (Grant, 1952; Ruddell, 1952; Hodges, 1953; Cowan, 1954; Argent, Dinnick and Hobbiger, 1955; Hodges, 1955; Brennan, 1956; Paletz, 1956; Bullough, 1957; Jowell and Wood-Smith, 1957), it seems reasonable to accept that the depolarizing relaxants sometimes produce a block reversible by anticholinesterases, particularly if given in large doses. Of especial interest is Ruddell’s patient in whom a paralysis caused by heavy dosage of decamethonium (13 mg) and suxamethonium (250 mg) was dramatically reversed by neostigmine (6 mg).

Case Reports.

The following is a report of two similar examples.

The first concerns an elderly man undergoing hemicolectomy to whom I illadvisedly gave a total of 12.5 mg decamethonium over a period of 90 minutes. At the end of the operation his general condition was good but his respirations were only diaphragmatic and they remained so for half an hour. Neostigmine 2 mg was then cautiously injected intravenously with the result that normal breathing was restored immediately.

The second case is better documented and is given in detail.

The patient was a healthy woman aged 35 years for ureterolithotomy, an operation expected to last about 45 minutes; in fact, it occupied over 2 hours.

Premedication was pethidine 100 mg and atropine 0.6 mg. Anaesthesia was induced by thiopentone 500 mg and decamethonium 7.5 mg. The patient was intubated and respiration controlled with a 2:1 mixture of nitrous oxide and oxygen through a circle absorber. The operation was being done through a paramedian incision and 45 minutes later the surgeon complained of “tightness”, and, as the end was not in sight, the anaesthetist gave a further 5 mg of relaxant, making
the total dose of decamethonium 12.5 mg. Approximately 75 minutes after induction (half an hour after the second dose of C.10) the patient began to breathe spontaneously but inadequately, and anaesthesia was continued with cyclopropane and oxygen, and assisted respiration. For the final 15 minutes the patient breathed only oxygen. At the end of the operation her condition was good, but her respirations remained completely diaphragmatic, with marked "chin tug", and this state persisted for the next quarter-hour. The anaesthetist then felt that neostigmine might be worth trying but he was naturally diffident about giving it and decided to wait a little as "she was bound to breathe properly soon". However, 10 minutes later there was no improvement and 2.5 mg of neostigmine was injected slowly intravenously. Almost immediately there was an obvious change in respiration in that inspiration, instead of being a sudden jerk, became drawn-out and deeper. Within 3 or 4 minutes breathing was normal and the patient's reflexes had returned.

It cannot be emphasized too strongly that the fact that neostigmine can sometimes reverse decamethonium should be of little more than academic interest. The above report concerns cases of frank overdosage which need never occur; in such instances the administration of the short-acting anticholinesterase edrophonium and observation of its effect before giving neostigmine would appear to be a better procedure.

CLINICAL CONSIDERATIONS

Advantages of Sharp End-Point.

From the point of view of the practising anaesthetist the outstanding characteristic of decamethonium iodide is that it is the only relaxant available which will produce total relaxation of about 20 minutes duration, and, within 5 minutes or so of beginning to wear off, have left no trace of its effect. This abrupt wearing-off, far from being an embarrassment, is a real advantage. The only jarring note in modern relaxant techniques with tubocurarine or gallamine is that they frequently depend on the use of neostigmine, with its undesirable side-effects. The employment of decamethonium in suitable cases can reduce considerably our dependence on this drug; the rapid, complete recovery without neostigmine of a patient who, following a single injection of relaxant, has been totally paralyzed for a reasonable time puts the finishing touches to an anaesthetic pattern of undoubted usefulness. It may also be noted that patients who have been spared neostigmine seem to be less restless in the immediate postoperative period. Anyone who has experienced the intense colic and general wretchedness which follows the intravenous injection of 2.5 mg (preceded by atropine 0.6 mg) will agree that there may be something in this observation.

Dosage of Decamethonium.

The usual dose of decamethonium iodide is 5 mg, and this is not often exceeded. Hunter's advice, given in 1950, that 10 mg should be regarded as the absolute maximum, still holds good. Allowance must be made for the general condition and age of the patient; children are relatively resistant, and, as is to be expected (Rees, 1954; Stead, 1955), infants appear to show a resistance to this depolarizing relaxant.

If the above rule is followed and overdosage avoided, no side-effects will be encountered; there will be no persistent intercostal paralysis and no worries from cardiovascular disturbances. In our experience there have been no cases of prolonged apnoea.

Should the initial dose wear off prematurely, in a fit subject it may be repeated up to a total of 10 mg where the end of the operation is not in sight, but generally it is better to continue with an inhalational agent such as cyclopropane, or with suxamethonium. The introduction of cyclopropane, even in the unintubated, can usually be accomplished smoothly, but there is no doubt that the advent of suxamethonium has given us more confidence in dealing with this situation. Decamethonium is clearly not the relaxant of choice for operations likely to last longer than 30 to 45 minutes and it sometimes happens that one is caught out, e.g., the closure of a perforation develops into a partial gastrectomy. In this event it is best to proceed as outlined above.

Occasionally a patient is still apnoeic at the end of operation. If the technique outlined above has been followed this is never more than a minor inconvenience lasting only a few minutes. It is as well to remember that the relaxant drugs are not infrequently blamed for this state when attention to other possible causes, e.g., an excess of premedication or anaesthetic, or inadequate resuscitation of an ill case, would be of more value.

Indications for Decamethonium.

Decamethonium iodide has a definite place in anaesthesia for many operations of medium duration. It is not suitable for either very brief or prolonged procedures. Even in cases where
full relaxation is not required it can be a useful drug, facilitating the administration of the lightest possible anaesthetic combined with perfect operating conditions and consequently the minimum after-effects.

The claims of decamethonium are enhanced when it is particularly desired to avoid the use of neostigmine, e.g., in patients suffering from asthma or bronchitis, and in those with cardiac disease.

Decamethonium is not entirely suitable for intubation. Even 2 or 3 minutes after injection the jaw may still retain tone and it sometimes exhibits clonus (Doughty, 1950). Suxamethonium surmounts this difficulty; although the mixing of drugs is criticized by some, it must be said that suxamethonium together with decamethonium in a syringe forms a most effective combination.

It is impossible to present a clear-cut list of operations in which the use of decamethonium is especially suitable. Examples are appendicectomy, closure of a perforated peptic ulcer, herniorrhaphy (simple and strangulated), cystoscopy and some prostatectomies. Decamethonium is also of value in bronchography under general anaesthesia by virtue of its profound relaxant effect and sharp end-point without recourse to neostigmine.

Illustrative Cases.

The typical use of decamethonium in anaesthesia is illustrated as follows:

The patient was a healthy man aged 23 years.

Premedication was pethidine 100 mg and atropine 0.6 mg. Anaesthesia was induced with thiopentone 500 mg, followed by decamethonium 5 mg, and respiration was controlled with a 2:1 mixture of nitrous oxide and oxygen.

Twenty minutes later, just before closure, diaphragmatic respirations were beginning. A 50 per cent mixture of cyclopropane and oxygen was introduced until the peritoneum was closed, the remainder of the operation being covered by nitrous oxide and oxygen. At the end of the operation there was no evidence of its action and the child was opening his eyes.

An alternative to cyclopropane would have been the injection of a small amount of suxamethonium.

Decamethonium iodide is, in my opinion, the preferable relaxant for Caesarean section. The following is a description of the technique employed:

Premedication is with atropine only.

For a few minutes before induction the patient is encouraged to breathe a 2:1 mixture of nitrous oxide and oxygen. Thiopentone 150 mg is rapidly injected, followed by a mixture of decamethonium 5 mg and suxamethonium 50 mg. A cuffed endotracheal tube is at once introduced and respiration controlled with nitrous oxide (4 l.) and oxygen (2 l.) with the absorber off, in order to spare the infant the effects of hyperventilation. When the baby has been delivered (a procedure which may be performed at leisure) the mother is generally beginning to breathe and the anaesthetic is continued in the usual manner with cyclopropane.

With the minimum basal sedation normally used in these cases it is of importance to give nitrous oxide in a concentration over 50 per cent.

On the other hand, if the patient has for any reason been appreciably sedated pre-operatively, thiopentone should be avoided and induction carried out by means of nitrous oxide and oxygen, with a little cyclopropane where necessary.

Decamethonium may be injected intramuscularly with hyaluronidase in infant anaesthesia and has the advantage over suxamethonium of providing a longer period of relaxation. The same sharp end-point is observed. Its use in infants is illustrated as follows:

The first case was a baby of 8 lb. 12 oz. (4 kg) for a Ramstedt operation.

After premedication with atropine 0.3 mg, anaesthesia was induced with cyclopropane and the baby intubated. Decamethonium 0.5 mg plus "Wydase" 0.5 ml was injected intramuscularly, and anaesthesia continued with twenty per cent cyclopropane. Respiration continued, but was obviously depressed after five minutes and it remained so for a further fifteen. Relaxation was good. Twenty-five minutes after injection of the relaxant the operation was over and the child was opening his eyes.

The second patient was a baby of 13 lb. (6 kg) for reduction of an intussusception. Premedication and induction were as in the previous case. Decamethonium 0.5 mg plus Wydase 0.5 ml was injected intramuscularly; 4 minutes later the baby was still breathing so another identical dose of relaxant with hyaluronidase was given. In 2 minutes there was apnoea and anaesthesia was continued with nitrous oxide and oxygen. After a quarter of an hour respirations returned and cyclopropane was reintroduced. Thirteen minutes later the abdomen, on closure, was still lax, but at the end of the operation, three-quarters of an hour after the first injection of relaxant, there was no evidence of its action and the child was opening his eyes.

I think that there is a place for decamethonium iodide in anaesthesia for infants. The weight/dose relationship in the above cases indicates that they are relatively resistant to its action.

SUMMARY

(1) Since a brief period of popularity following its introduction in 1949, decamethonium iodide has been used progressively less by anaesthetists. The evidence for this is presented and the reasons
discussed. The principal of these is that too great an emphasis has been placed on its disadvantages, which have been exaggerated and misrepresented in the minds of the majority of anaesthetists. (2) Pharmacological points of importance to the use of decamethonium in anaesthesia, including its relation to neostigmine, are described. (3) Indications for the use of decamethonium iodide in anaesthesia are discussed. It is a reliable relaxant for many of the shorter surgical procedures. Its use for Caesarean section and in infants is described.

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REFERENCES