"BREVIDIL M" AS A MUSCLE RELAXANT IN ELECTRO-SHOCK TREATMENT.

By J. J. DANIK, M.B., CH.B., D.P.M.,
The Towers Hospital, Leicester.

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As modification of electro-shock is becoming a routine procedure in every patient undergoing this therapy, it is necessary to find a muscle relaxant, or as it has been commonly called a "curarizing agent," which will be ideal for this purpose. Ideal should mean no toxicity, rapid onset, short duration and rapid termination of neuro-muscular blocking action.

Muscle relaxants in use at present form two groups according to their mode of action. Some of them, like D-tubocurarine, diminish the depolarising action of acetylcholine so that the amounts discharged are unable to evoke end-plate potentials sufficiently large for the excitation of muscle-fibre. Others like decamethonium iodide exert an action analogous to that of a large dose of acetylcholine. They cause a persistent depolarization accompanied by neuro-muscular block (Paton and Zaimis, 1950; W. Feldberg, 1951).

To the latter group belong the succimethonium salts or bis (2-dimethyl-aminoethyl) succinate bismethhalides, which were described for the first time by Hunt and Taveau in 1911. In 1949 Bovet and Bovet-Nitti described their pharmacodynamic properties, showing that they possess a fairly potent though short-lasting inhibitory action on myoneural junctions, that the substances are inactivated by cholinesterase, and that the inactivation is prevented by anti-cholinesterases (physostigmine, neostigmine).

Castillo and de Beer (1950) in their experiments on animals found that a rapid intravenous injection of 0·2 mgm./kgm. body-weight of succimethonium iodide caused a short-lasting paralysis of the muscles of the head, neck and extremities in rabbits, but had no paralysing effect on respiration. Their further experiments on anaesthetized cats and dogs showed that the drug had an insignificant effect on blood pressure, its blocking action was considerably prolonged by the previous injection of physostigmine, and that 0·25 mgm. of succimethonium iodide was inactivated *in vitro* by 1 ml. of cats serum during an 18-hour incubation period.

From clinical investigations on man when the drug was used for muscular relaxation in about 30 laparotomies and over 500 electro-shocks (Thesleff, 1951; Holmberg and Thesleff, 1951) it has been found that the neuromuscular blocking action of succimethonium iodide starts almost immediately after intravenous injection and lasts from 1–6 minutes according to the dose.

With a dose of 0·1–0·2 mgm./kgm. body weight muscular paralysis first affects eye and throat muscles, then peripheral musculature, leaving respiration

almost unaffected, and only larger doses (0·4–0·6 mgm./kgm.) bring about respiratory paralysis. Even these comparatively large doses have never had any significant effect on the circulation, beyond a small and brief rise in blood-pressure and some bradycardia, and there have been no post-operative complications which could be attributed to the drug.

One of the succimethonium salts was presented for clinical investigation in this country a year ago and has subsequently appeared on the market under the designation " Brevidil M," which a is brand of succimethonium bromide or bis (2-dimethylaminoethyl)-succinate bismethobromide.

I have used " Brevidil M " as a muscle relaxant in electro-shock therapy for various mental disorders in 116 patients, both men and women, giving altogether 472 electro-shocks. The age of the patients ranged from 17 to 76 years. Some of them—mostly elderly people—were very debilitated and had considerable hypertension.

The effect of the action of " Brevidil M " was carefully observed in the first 42 patients, who received altogether 120 treatments. The pulse and blood-pressure were taken before the injection of " Brevidil M " and immediately afterwards.

The following method of administration is used : The patients have a light breakfast and the treatment is carried out about 2 hours later. A subcutaneous injection of atropine sulphate $\frac{1}{100}$ gr. is given 30–40 minutes before treatment. In the treatment room the patient receives an intravenous injection of freshly prepared solution containing 2 mgm./stone body-weight (0·3 mgm./kgm.) of " Brevidil M " mixed immediately before the injection in the same syringe with 3·5 cc. of 5 per cent. solution of soluble thiopentone. The injection is given comparatively slowly (30 seconds), and about 30 seconds after the completion of the injection the electro-shock is induced. From the beginning of the injection till the induction of the shock the patient is given oxygen by means of a mask. After the shock is over the oxygen is given again until the return of normal respiration.

Results.

About 30 seconds after the beginning of the injection delicate and short-lasting muscular fibrillation appears.

In all cases the pulse remains full and regular after injection, but slows by 10–20 beats per minute.

The blood-pressure in 35 patients was slightly raised (5–20 mm.) ; in 7 patients it remained unchanged.

It was found during the fit that with a dose of 2 mgm./stone (*a*) in 33 patients there were no muscular movements except blinking of eyelids, clonic twitchings of facial muscles and contractions of arrectores pilorum (goose-flesh) (*b*) in 7 patients, besides blinking of eyelids, twitchings of the facial muscles and contraction of arrectores pilorum, there were clonic movements of the upper and lower limbs, but in all these cases the muscles remained flaccid, and flexion of the spine was never noticed. In only 3 patients had the dose to be increased to 2·4 mgm./stone (0·35 mgm./kgm.) in order to reach muscle relaxation as

described at (*b*). In the other 2 cases (an old woman of 76 and another women who was fairly stout) muscular relaxation as at (*a*) was obtained with a dose of 1·4 mgm./stone (0·2 mgm./kgm.).

In 90 per cent. of the cases spontaneous breathing returned almost at once after the fit and regular respiration was established within a minute of the end of the shock. In the remaining 10 per cent. return to normal breathing was never delayed beyond 2 minutes. When the patient's breathing became regular he did not require further active attention other than that normally provided after electro-shock.

A fleeting erythema on the neck and the upper chest persisting for about 30 minutes after the injections was noticed in 6 patients, salivation was found to be fairly profuse in one of them, and in 2 of the patients a mild hiccup occured which passed off in a few minutes.

In the remaining 72 patients two different methods were applied. In some of them, after the premedication with $\frac{1}{100}$ gr. of atropine sulphate, 3 c.c. of 5 per cent. soluble thiopentone was given intravenously, followed by the injection through the same needle of freshly prepared solution of "Brevidil M," which was injected rapidly, and 20 seconds later the electro-shock was induced.

Others were given $\frac{1}{200}$ gr. of atropine sulphate and $\frac{1}{200}$ gr. of hyoscine hydrobromide as a premedication; about half an hour later "Brevidil M" was given by rapid intravenous injection and after 20 seconds the electro-shock was induced.

In neither of these two methods was oxygen used till after the shock was over.

The dose of "Brevidil M" used was a constant one—15 mgm. in man and 12 mgm. in women—and only in exceptionally large and muscular persons did it have to be increased by 2–3 mgm.

The results were exactly the same as those produced in the first 42 patients. It has only to be stressed that the patients prefer to be given E.C.T. under this light anaesthesia (thiopentone), because of the unpleasant feeling of apprehension which they otherwise experience after the injection of "Brevidil M."

In all cases in which soluble thiopentone was given, this comparatively small dose of 0·15 gm. (3 c.c. of 5 per cent. solution) was sufficient to prevent the patients from having any unpleasant recollection afterwards.

Conclusions and Summary.

"Brevidil M" was given to 116 patients, both men and women, as a muscle relaxant in E.C.T.

In 42 patients atropine sulphate was used as a premedication to prevent the usual parasympathetic stimulation associated with E.C.T. The average dose of "Brevidil M" was 2 mgm./stone (0·3 mgm./kgm.), giving in a majority of cases complete muscular relaxation, and in only 3 cases had this to be increased to 2·4 mgm./stone (0·35 mgm./kgm.) in order to achieve sufficient modification of the fit.

In 72 patients different methods were applied; in some of them soluble thiopentone and "Brevidil M" were given by two syringes after the premedication with $\frac{1}{100}$ gr. of atropine sulphate; others had "Brevidil M" injected

without thiopentone, and in these cases $\frac{1}{200}$ gr. of atropine and $\frac{1}{200}$ gr. of hyoscine were used as premedication. The dose of "Brevidil M" was constant, 15 mgm. in men, 12 mgm. in women.

The results achieved are very encouraging. The action of the drug on the circulation is insignificant. No side-effects which would need intervention were noticed.

The drug has a constant and certain action, gives the desired degree of muscular relaxation, even when it has been mixed with soluble thiopentone in the same syringe, and spares respiration; its action ceases soon after the shock is over.

To a large extent it can be mixed with thiopentone in the same syringe, although this should be done immediatley before the injection.

Because of the rapid onset, brief duration and rapid termination of neuromuscular blocking action, and because of its safety, "Brevedil M" seems to be ideal as a muscle relaxant in E.C.T. The fact that it is cheap is also not unimportant.

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