CLINICAL OBSERVATIONS ON SUXETHONIUM IN E.C.T.

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BECAUSE of their rapidity of onset, brevity of action and relative safety, the choline succinic ester derivatives, in the last two years, have almost completely superseded tubocurarine, gallamine and decamethonium as muscle relaxants in electroplexy. The literature now contains a number of reports of prolonged respiratory arrest associated with the use of these new relaxants. In publishing the results of early experience at Long Grove with three of the new compounds, Monro *et al.* (1953), tended to favour Scoline with thiopentone in a body-weight dosage using a one-syringe technique. The infrequent occurrence of excessive apnoea proved to be no great problem and was easily dealt with. However, during subsequent work in the same hospital, we were impressed by the markedly more abrupt action of suxethonium (Brevidil "E") and felt that further investigations into its clinical properties might yield some reward.

Our aim was to devise a method of protection in E.C.T. that would enable us to treat every patient in need of it with the assurance that the procedure was virtually without danger or discomfort. In a hospital of 2,400 beds, with a large and rapidly increasing turnover, it was thought desirable that the method used should, as far as possible, comply with the following conditions:

(*a*) The time of each treatment should not be unduly increased beyond that required for unmodified E.C.T.

(*b*) The technique should be simple and strictly accurate individual dosage unnecessary.

(*c*) As little extra strain as possible should be put on the nursing staff in the way of preparation, sterilizing syringes and the like.

(*d*) The patient should have no memory of distress associated with the procedure.

With these criteria in view, we tried various modifications of technique and dosage and, as a result, arrived at the following general conclusions regarding the properties of suxethonium:

(*a*) In all patients in sound bodily condition, increase of dosage up to 50 per cent. above the optimal relaxant dose caused no corresponding prolongation of the period of apnoea.

(*b*) It was markedly quicker in onset and briefer in duration of action than the suxamethonium compounds and, in adequate amounts, equally reliable.

(*c*) Concentrated solutions acted more rapidly than dilute and, similarly, rapid injection produced quicker and more profound results than slow injection. This may help to explain why we found that, when mixed with thiopentone,

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Brevidil "E" exhibited a slower, less abrupt onset than when administered alone. The mixture, too, tended to have a more prolonged action than the relaxant by itself. It may be relevant here to point out that the drug is destroyed by hydrolysis in alkaline solutions and may lose 25 per cent. of its potency in 5 minutes when mixed with thiopentone. This process is accelerated by a rise in temperature.

(*d*) In most cases where the combined injection was used, the effects of the relaxant became evident before those of the barbiturate, so that patients frequently showed signs of respiratory distress, attempting clutching movements at the throat as though to remove a constricting agent. In approximately 1 per cent. of treatments there was some ill-defined memory of suffocation. A possible explanation is that the time between the injection and the shock was longer than the associated retrograde amnesia. We shall return to this important point later.

Our findings outlined above do not materially conflict with those of Malone and Blayney (1952) and Wolfers (1953).

Techniques

Early in a series of 2,002 treatments on 341 patients, we evolved the following procedure which, we hoped, might go far towards meeting our requirements:

1/100 gr. atropine was given subcutaneously ¾ to 1 hour before treatment. Suxethonium is supplied as a white, crystalline, readily water-soluble powder in glass ampoules containing 100 mgm. active cation which we dissolved in 2 ml. sterile water. The required number of ampoules of the relaxant and of thiopentone sodium were prepared immediately before commencement of treatment and placed on a trolley together with syringes, No. 14 needles, swabs, spirit, at least two airways, suitable gags, and a tourniquet. Nikethamide was available. Anticholinesterases such as neostigmine are of no value as antidotes to the effects of this group of compounds, and may in fact potentiate them.

The patient lay supine in bed, thorax and abdomen exposed so that respiration could be observed; the head was kept low. 1·5 ml. (75 mgm.) for women, 2 ml. (100 mgm.) for men, were drawn into a syringe followed by 3 ml. 5 per cent. thiopentone and the mixture injected into the selected vein in from 2 to 5 seconds. Muscle fasciculation commenced in from 5 to 10 seconds and was evident first round the mouth and in the neck. Respiratory arrest took place early and was not, we found, a reliable indication of complete peripheral relaxation which, we assumed, was established with the cessation of muscle twitching. With a fast injection this normally occurred in from 10 to 20 seconds. The electrodes were placed in position and a gag put between the relaxed jaws, care being taken that the lips were not pinched between it and the teeth. We found this precaution to be extremely important because direct stimulation of the temporalis causes a short but powerful contraction of that muscle sufficient to damage the unprotected teeth or lips.

No preliminary oxygenation was necessary though we carried it out as an added precaution in the treatment of four patients in poor physical condition. The shock was given 15 to 20 seconds after the injection. The result could only rarely be described as a convulsion and was manifest often by the faintest peri-oral and -orbital tremor. In our experience, the most reliable means of knowing whether an adequate shock had been administered was to feel the patient's fingertips with one's own, when a tremor was evident. We prefer this

to possibly more dramatic and certainly more time-consuming methods. The gag could be removed safely and slow, gentle, rhythmic inflation started at the end of clonus. Apnoea was rarely shorter than 1½ and longer than 3 minutes. Recovery was gratifyingly uneventful and most infrequently accompanied by the noisy restlessness so often following "straight" E.C.T. Using this procedure, one doctor, assisted by three well drilled nurses, can carry out 16 treatments in one hour.

Prolonged respiratory arrest was the only troublesome complication encountered in this series and occurred only in four patients, all of whom were in a state of dehydration and semi-starvation due to their refusal to take adequate nourishment. In these cases, apnoea, on the usual dosage, lasted from 4 to 7 minutes. This matter will be considered later. We did not use an airway routinely but found it necessary in a few cases—usually obese, middle-aged or elderly patients. No bony injuries occurred in this series and complaints of muscle pain, headache and malaise were no more common than after unmodified electroplexy. Four patients said they remembered a feeling of suffocation before losing consciousness on a total of seven occasions. Only one of them showed any marked distaste for subsequent treatments.

We have already pointed out that dilution of suxethonium tends to retard and prolong its action. Thiopentone has a central respiratory action which might well potentiate the relaxant's effect on the muscles of respiration. It seemed possible to us that concentrated suxethonium alone with its very rapid onset of action might enable us to administer the shock so soon after the injection that the initial paralysing effect would come within the period of retrograde amnesia associated with electroplexy. Thus memory of the feeling of suffocation might be abolished. And omitting the barbiturate, we hoped, might reduce the possibility of prolonged respiratory arrest. We decided to put this hypothesis to the test and carried out a further series of 1,602 treatments on 267 patients using the following procedure.

100 mgm. suxethonium in 2 mls. of water was, we found, a convenient dilution. Within the comparatively rough limits of dosage required of this drug it is easy to measure the required amount in a 5 or even 10 ml. syringe. This concentration, too, produces optimal results. 1½ ml. (75 mgm.) for females, 2 ml. (100 mgm.) for males, were injected quickly into a suitable vein. In rarely more than 5 seconds muscle fasciculation became apparent and frequently the patient would attempt grasping motions at the throat but, quite dramatically, with the onset of total paralysis, the hands would drop, their purpose unaccomplished. At this juncture, between 5 and 10 seconds after the injection, the gag was inserted, the electrodes placed in position and the shock administered. As was the case in the previous series, clonus was minimal. In a few cases spontaneous breathing started at the end of clonus; in the majority assisted respiration was required for periods up to one and a half minutes. If excessive cyanosis developed, oxygen was administered during clonus but we carefully avoided over-ventilation, which we found sometimes lengthened both clonus and apnoea. In one case, a man of 77 in poor senile health, apnoea lasted for three and a half minutes, the longest period recorded in this series; subsequent doses of 60 mgm. provided adequate protection in his case with no further excessive respiratory arrest. Apart from the above exception, none of these patients was seriously cachectic.

All sufficiently accessible patients were asked what their last memory was before treatment. A few recalled having the injection but only one remembered a feeling of suffocation. She was an involutional depressive and well in touch.

Although she experienced this presumably distressing phenomenon on eight occasions and benefited considerably, at no time did she show any dread of the treatment. Recovery generally was quieter than after unmodified E.C.T.

It has been suggested that after the administration of this type of relaxant, muscular pain may occur, severe enough to incapacitate the patient for a day or so and that it is advisable to keep the patient in bed during treatment. This has not been our experience and in 1,602 treatments we have had complaints of muscle pain in only two and these not severe enough to interfere with the course of treatment.

Very rarely the depolarizing effect of Brevidil "E" did not manifest itself for up to 15 seconds after injection although the dose given was adequate, as shown by eventual full relaxation. We considered it possible that in such cases circulation time played a part. According to Best and Taylor (1950), some of the causes of lengthened circulatory time are hypertension, myxoedema, polycythemia, and heart failure. Secondary polycythemia may be associated with chronic pulmonary disease, congenital cardiac abnormalities, some forms of heart disease, chronic poisoning with a number of chemicals, and adaptation to the rarified atmosphere of high altitudes. Haemoconcentration due to shock or dehydration could also delay the passage of blood. All our patients who showed a delayed response to the relaxant came within the age group in which hypertension, chronic bronchitis and emphysema and some degree of cardiac decompensation are commonly found. In our first group the four cachectic patients who were most subject to excessive apnoea showed this delayed response to Brevidil "E". Perhaps their apnoea was related to the same mechanism. The drug is said to have a selective action at the skeletal neuro-myal junction and to be rapidly destroyed mainly by serum pseudocholinesterases. A slow circulation time could be associated with a relative stasis at the sites of action of suxethonium. Consequently the slow "turnover" of pseudocholinesterases could delay the inactivation of the relaxant and thus prolong paralysis.

These observations and speculations may help to explain occasional unexpected variations in response to the drug and suggest other lines of investigation.

Summary and Conclusions

Two methods of protection in E.C.T. are described. In the first, fixed doses of Brevidil "E" with thiopentone were used; in the second, Brevidil "E" alone. Perhaps it is too early to dogmatize but, nevertheless we are confident that the second method of treatment is safe, rapid, uncomplicated and significantly reduces the risk of prolonged apnoea associated with the use of the newer relaxant drugs. We had none in our series of 1,602 treatments. Because of its simplicity it is as nearly foolproof as possible and demands little extra time and effort from the staff concerned. Complications peculiar to barbiturates such as sensitivity, central respiratory depression, perivenous and intra-arterial injection are avoided. It appears therefore to be a suitable method for a large hospital or out-patient department where E.C.T. has to be given promptly to all patients in need of it, regardless of their bodily state, with the minimum of danger and discomfort. Finally we would like to emphasize three points culled from our experience:

(*a*) Over-enthusiastic ventilation may prolong apnoea.

(*b*) Too early oxygenation during the convulsion in some cases lengthens quite markedly the duration of the convulsion, possibly by reducing cerebral CO_2 tension and thus interfering with the self-limiting action of the fit.

(*c*) A cachectic patient who has initially required a lower than standard dose of relaxant, may, after two or three treatments, when his appetite, and consequently his physical state, have improved, require a larger dose if full relaxation is aimed at.

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