REPORT ON SHORT-ACTION MUSCLE RELAXANT RO/3/0386 IN E.C.T.

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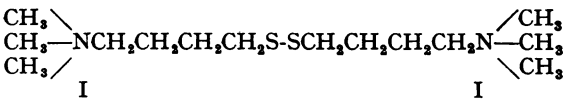
THE use of muscle relaxants as a help in minimizing the hazards of E.C.T. has been reported by a number of workers (Hobson and Prescott, 1947; Davies and Lewis, 1949; Shepherd and Watts, 1949; Smith and Thomas, 1951; and Thompson and Norton, 1951). From these observations the value of such substances in reducing the muscular force of electrically-induced convulsions is clear. Nevertheless the trial of a new substance was embarked upon in order to establish whether it approaches more closely the ideal drug for the purpose.

The trial about to be described was carried out with RO/3/0386 which is 5 : 6 Dithiadecane 1 : 10-bis (trimethylammonium iodide) (monohydrate) :



Its general properties and pharmacology have already been described by Hunter (1952), who suggested that certain special attributes might make it the drug of choice as a muscle relaxant in E.C.T. The drug was used on more than 250 occasions.

Dosage.

With doses of 3·5 mgm. of RO/3/0386 the relaxant effect obtained was very little; with 4 mgm. quite good modification of the fit occurred in many patients, but the results were erratic and unpredictable. On some occasions the results were minimal, and the modification of the fit insufficient.

With doses of 5 mgm. satisfactory modification was obtained in every patient except one. Dosage for this patient was gradually raised to 9 mgm. RO/3/0386 plus 5 c.c. of 5 per cent. thiopentone before a satisfactory degree of relaxation was obtained. With this higher dosage there was no additional interference with respiration and no ill effects or difficulties were encountered.

In a few other patients doses of 6 and 7 mgm. were tried. The degree of relaxation obtained was no greater than that of many patients on doses of 5 mgm. and the depressant effect on respiration appeared to be increased.

Effective dosage appears to have little relation to the weight of the patient, and individual patients vary somewhat from day to day in their response to the same dosage. Except in resistant cases, therefore, it was felt that any increase over a 5 mgm. dose was unnecessary and valueless. No case of hypersensitivity was observed.

Mode of Administration.

The drug was first administered alone, by intravenous injection. It was later decided to add 3 c.c. of 5 per cent. thiopentone, which was drawn into the same syringe as the relaxant. If atropine was required this also was drawn into the syringe.

Effects.

(*a*) Given alone, about 20 seconds after injection the patients appeared to gasp slightly. There was seldom a complaint of difficulty in breathing, and although the depth of respiration was lessened it did not cease nor did it increase in rate. Most patients complained of unpleasant, sometimes frightening feelings, but not of difficulty in breathing. Cyanosis occurred in one patient to whom three drachms of paraldehyde had been given shortly before the injection. Muscle tone decreased rapidly and patients were usually unable to move or speak after 45 seconds. It was found that the fit could be given with satisfactory relaxation after 60 to 90 seconds. No alteration in heart-rate or blood-pressure before the convulsion was observed. Respiration returned to normal about three minutes after the injection was completed and all effect on muscular tone seemed to have gone after six or seven minutes.

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(*b*) Given with thiopentone (because patients complained when the drug was given alone,) there was no obvious difference in the effects except a more marked diminution in respiration and a greater incidence of cyanosis after the fit. This was overcome without difficulty by routine administration of oxygen.

Modification of Fit.

This ranged from a slight but sufficient modification, which was enough to obviate the risk of fractures, to a state in which the patient hardly moved. The effect varied in the same patients from day to day with the same dosage. The apparent extent of the decrease in muscular tone before the convulsion was not always a guide to the degree of modification obtained during the convulsion, a patient sometimes being able to move a limb slightly and yet having a very much modified fit. When patients had recovered from the effects of the convulsion they were able to walk back to the ward.

Comparison with Succinylcholine.

For comparison 18 patients were treated with succinylcholine and thiopentone. As these drugs are not miscible the thiopentone was given first from a separate syringe. Dosage of both drugs was calculated on a weight basis and no case of hypersensitivity was observed.

1. Thiopentone 5 per cent. solution . $\frac{\text{Body weight in pounds} \times 1 \text{ c.c.}}{40}$

2. Succinylcholine 5 per cent. solution . $\frac{\text{Body weight in pounds} \times 1 \text{ c.c.}}{200}$

Effects.

The first sign, a fine twitching of the face, appeared in 10 to 15 seconds after completion of the injection; it was soon followed by loss of muscular tone and cessation of respiration. The convulsions could be given in about 45 seconds and oxygen was given immediately to prevent cyanosis. Breathing returned in two to four minutes and complete recovery of muscle tone in about five minutes.

Results.

No modification occurred in one patient on the first occasion, but good modification was obtained with the same dose on the next occasion. In another patient extra-systoles occurred, and a fairly deep cyanosis developed which was controlled by administration of oxygen. On all other occasions good relaxation (on the whole rather more marked than with RO/3/0386) was obtained and there were no untoward incidents. When patients had recovered from the effects of the convulsion they were able to walk back to the ward.

Conclusions.

RO/3/0386 appears to be a reliable, useful and safe relaxant for reducing the muscular force of electrically-induced convulsions which does not cause complete respiratory arrest. It has the advantage of being compatible with both thiopentone and atropine and mixed injections can therefore be given from the same syringe. From a small number of observations succinylcholine appears to be a reliable relaxant, but has the disadvantage that respiration ceases for a short time and that, succinylcholine being incompatible with thiopentone, it is necessary to use two syringes for the injection.

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