THE EFFECTS OF PRECURARIZATION WITH A PROTECTIVE DOSE OF d-TUBOCURARINE IN THE CONSCIOUS PATIENT

RAYNALD DÉRY, M.D., F.R.C.P.(C)*

THE ADMINISTRATION OF MYORELAXANTS in conscious human beings has always been considered a distressing experience. In the early 1940s some anaesthesiologists had minimal to large doses of curare injected into themselves or to volunteers in order to assess the pharmacological properties of the drug.^{1,2} These heroic experiments were crucial for the pioneers who, after Griffith, promoted the use of curare on a large scale, thus opening the door to modern anaesthesia.³ In connection with these recollections, the more recent work by Vandewater and his collaborators is worth mentioning. In 1963, he administered succinylcholine to alcoholic patients as part of a conditioned aversion therapy against alcohol. In every instance these experiments were described as extremely frightening.⁴

During the last five years the list of untoward reactions following the administration of succinylcholine has become longer.⁵⁻¹⁵ Fortunately, in the meantime, pretreatment with a subparalysing dose of curare has been widely used as an effective means of preventing or attenuating these difficulties.¹⁶ This protective dose is currently administered after the induction of narcosis.

An increasing number of anaesthetists are now injecting the protective dose of curare in the conscious subject, a few minutes before anaesthesia. The purpose of our study was to assess the effects of this clinical practice from both subjective and objective points of view, as they concern the patient.

METHODS

Our study included 200 patients, of whom 100 received d-tubocurarine before anaesthesia while the others served as controls, receiving the usual thiopentone, d-tubocurarine, succinylcholine sequence. The subjects were unselected, uninformed surgical patients, with a wide distribution of age (Figure 1), physical status and surgical conditions. As premedication both groups received meperidine, 1 mg per kilogram of body weight, with atropine in usual doses. Once in the operating room and lying in the supine position, they were instructed to deliver a forced vital capacity into the Collins expirometer. As the reliable testing of respiratory mechanics requires cooperation, patients were told that this procedure would provide their anaesthetist with guidelines for better monitoring of their respiration throughout the anaesthesia and surgery. The measurements were repeated two or three times until duplicate readings were obtained. Then, in the

*Department of Anaesthesia and Resuscitation, L'Hôtel-Dieu de Québec and Laval University.

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FIGURE 1. Frequency distribution of the subjects according to their age.

first group of patients, 6 mg of d-tubocurarine in the male and 4 mg in the female, were rapidly injected into the perfusion tubing. The patients were left unaware of having received any drug. Timing was started at this point. At one minute and a half, the patients were asked how they felt and had their expiratory measured once again. They were also asked to lift the head, count fingers, swallow, and press their fingers on a hand-grip ergometer. Pulse rate and arterial blood pressure were recorded. The same measurements were repeated at three minutes, after which the patients were put to sleep with a thiopentone-succinylcholine sequence.

The control patients had the same study conducted with the same timing but received the myorelaxants after they were put to sleep.

Before we display our results, a brief comment on the Collins expirometer seems appropriate. The unit is a small, portable, electronically operated device for the measurement of vital capacity, forced vital capacity, forced expiratory volume at one second, and peak flow. The data appear on a digital display already corrected B.T.P.S. The sensing head is a finely finned turbine blade which spins in jewelled bearings at over 100,000 rpm when exhalation is at its peak flow. The air moving through the sensing head causes the turbine to spin. As the turbine spins, it cuts through a light beam. The number of interruptions of the

FIGURE 2. Principle of operation and data display of the Collins Expirometer.

light beam are counted and finally displayed on the meters. Because of the extremely low mass of the turbine, it stops spinning almost immediately at the end of expiration (Figure 2).

Calibration of the expirometer was effected repeatedly with a super-syringe and with constant flow rate air blowers. The reproducibility of the readings was confirmed in a series of measurements obtained from nurses, residents in anaesthesia, and patients.

RESULTS

The subjective feelings in patients of group 1, who received d-tubocurarine in the conscious state, are listed in Figure 3. The first effects occurred between one and one and a half minutes after injection and were connoted by the patient as drowsiness and a peculiar sensation of heaviness of the eyelids. One patient reported that his eyelids were as heavy as if they were loaded with one hundred pound weights. Paradoxically, one patient could not close his eyes.

Ten per cent complained of various degrees of diplopia, some in a vivid style: one patient had the impression that the small holes in the ceiling tiles were dancing. Another reported that the lights seemed paler.

One patient, in the denutrition stage of Hodgkin's disease, had some difficulty in raising his head from the pillow. Another, a late cancer patient, felt short of

FIGURE 3. Subjective responses following a protective dose of d-tubocurarine in the conscious state (n: 100 patients).

breath and had a rash. Two young females, obviously distressed by the repeated measurements of their breathing, just dissolved in tears.

Finally, 34 per cent of our patients had no subjective response at all, and simply did not feel the drug.

On the whole, patients were comfortable and relaxed, most of them with a sensation of going to sleep. They could swallow, smile, sit on the operating table and move their limbs freely.

The mechanical properties of the respiratory system, as influenced by precurarization, were compared with the values obtained in our control series. No significant differences were noted between the two groups, either for Forced Vital Capacity (Figure 4), Forced Expiratory Volume at one second (Figure 5) or Expiratory Peak Flow rates (Figure 6). However, the initial readings were lower than the predicted values by a mean of 20 per cent, both before and after curarization, obviously because the measurements were achieved in premedicated subjects lying in the supine position.

In assessing the strength of the superior limbs in patients with precurarization, the relatively crude estimate possible with the use of a hand-grip ergometer indicated a mean decrease of 10 per cent at one and a half and at three minutes after injection.

FIGURE 4. Comparative measurements of Forced Vital Capacity (FVC) between precurarized patients (●, n: 100) and the control group (▲, n: 100).

No visible fasciculations were observed in either group. Tracheal intubation was easier to perform in the first group of patients, and was attended with very slight autonomic responses, as opposed to the control group, in which a few patients moved during this procedure and disclosed a tremendous adrenergic reaction.

DISCUSSION

If we refer to the classification of the stages and depths of myorelaxation (Figure 7), it is most likely that the protective dose of d-tubocurarine induced a slight degree of muscular weakness in our conscious patients, especially in the muscle groups with a fast chronaxie.¹⁷ These include the head and neck muscles, among which the extrinsic musculature of the eye is the most sensitive. Muscles with longer chronaxies, albeit partially impregnated with curare, did not show evidence of functional disability. The relationship between the dose of curare, the chronaxie and the degree of myorelaxation is again illustrated in Figure 8, in which we can predict that the smaller the dose of curare and the longer the chronaxie of a muscle group, the lesser will be the subsequent paresis. With the

FIGURE 5. Comparative measurements of Forced Expiratory Volume (FEV₁) between precurarized patients (●, n: 100) and the control group (▲, n: 100).

standard doses of curare we used for precurarization in the conscious state, the curves correlating dose/chronaxie are shifted to the upper part of the figure. This results in minimal asthenia of the small, discriminative muscles of the face, with almost no significant effect on the limbs and the respiratory muscles.¹⁸

The rationale for precurarization in the conscious state, rather than postcurarization in a patient already asleep, rests on two bases. Firstly, precurarization with a protective dose is mandatory in some clinical cases, namely in patients with a full stomach and in subjects with penetrating eye injuries, in which postcurarization carries the definite hazards of a delayed onset of full paralysis and late endotracheal intubation.

Secondly, the pharmacokinetic profile of induction benefits with precurarization in the conscious patient in such a way that endotracheal intubation can be performed at peak activity of the three drugs involved, d-tubocurarine, ultra-short acting barbiturate and succinylcholine. This is illustrated in Figure 9, in which the kinetics of distribution of the drugs are compared for two induction techniques, d-tubocurarine 4 to 6 mg followed 3 minutes later by thiopentone and succinylcholine, and the thiopentone-tubocurarine-succinylcholine sequence. With precurarization, the endotracheal intubation occurs at a plasma and brain thiopentone level equivalent to 75 per cent of the initial dose, near the peak of

FIGURE 6. Comparative measurements of Peak Flow between precurarized patients (●, n: 100) and the control group (▲, n: 100).

central depression.¹⁹⁻²⁰ On the contrary, with postcurarization, the endotracheal tube is inserted when the brain concentration of thiopentone has already fallen to 25 per cent of the maximal depressive activity of this drug. This means a fully reactive autonomic system and moreover, increased defense reflexes travelling down the motor pyramidal tract. These phenomena may provide an explanation of the need for higher doses of succinylcholine with postcurarization.²¹

If we sum up the advantages of precurarization with a protective dose of d-tubocurarine in the conscious patient against its disadvantages, we are inclined to think of this technique as permissible, attended with very few unpleasant side-effects, mandatory in some particular cases and, eventually, acceptable as a routine procedure.

SUMMARY AND CONCLUSION

Precurarization with a protective dose of d-tubocurarine, 6 mg in the adult male, 4 mg in the female, was achieved in a series of 100 patients three minutes before the induction of anaesthesia. This procedure was well tolerated on both psychological and physiological bases. The patients displayed no modification of their respiratory mechanics and could exhibit normal coordinated movements of their hands, legs and head. Slight diplopia and a sensation of drowsiness occurred frequently.

Precurarization in the conscious patient affords effective protection against the untoward side-effects of succinylcholine and provides a more harmonious pattern to the pharmacokinetic profile of induction. With appropriate timing, endotra-

FIGURE 7. The Stages and depth of myorelaxation. The progression of myorelaxation is from the normal state to increased fatigability. Bremer's atony is characterized by suppression of muscle tone at rest, with conservation of both reflex and voluntary movements. Vulpian's paralysis is defined by the absence of voluntary or reflex muscular activity and tone, with preserved response to electrical stimulation. Claude Bernard's paralysis is total paralysis, unresponsive even to electrical stimulation.

**THE EFFECTS OF A "CLINICAL" FULL CURARIZING DOSE OF A
MYORELAXANT IN RELATIONSHIP WITH CHRONAXIE VALUES**

FIGURE 8. The effect of a "clinical" full curarizing dose of a myo-relaxant in relationship with chronaxie values.

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**PHARMACOKINETIC PROFILES OF TWO DIFFERENT
 DRUG SEQUENCES AT INDUCTION**

FIGURE 9. Pharmacokinetic profiles of two different drug sequences at induction. The first sequence, with postcurarization, illustrates how improper timing may lead to endotracheal intubation of a full curarized, poorly anaesthetized patient. The sequence shown at the lower part of the figure, with precurarization, provides with better conditions. Note that the half life of thiopentone in the brain and plasma is about four minutes.

cheal intubation can be performed at the peak of pharmacological activity of the involved drugs, d-tubocurarine, ultra-short acting barbiturate and succinylcholine.

This technique appears not only quite harmless, comfortable and permissible, but also mandatory in some cases. Our orientation is toward its use as a routine procedure.

RÉSUMÉ

La majorité des effets secondaires indésirables de la succinylcholine peut être contrée par l'administration préalable d'une dose protectrice d'un pachycurare, en

l'occurrence la d-tubocurarine. Cette dose protectrice s'administre généralement chez le sujet déjà anesthésié à l'aide d'un agent d'induction. Cependant, un certain nombre d'anesthésistes ont commencé à injecter cette dose protectrice chez l'individu conscient, quelques minutes avant l'induction de l'état anesthésique. Nous avons voulu, dans cette étude, évaluer certains aspects psychologiques et physiologiques d'une telle pratique.

L'administration de 6 mg de d-tubocurarine chez l'adulte mâle et de 4 mg chez la femme, trois minutes avant l'induction de la narcose, n'a pas entraîné, chez les 100 sujets soumis à cette expérience, de manifestations désagréables. La plupart des patients ont l'impression qu'on a commencé à les endormir et ressentent une certaine lourdeur des paupières. Dix pour cent accusent une diplopie d'intensité variable, voire quelques ennuis d'accommodation. Un fort pourcentage de patients n'ont ressenti aucun effet subjectif d'une telle précurarisation.

Des déterminations sériees de la mécanique respiratoire (Capacité vitale forcée, Capacité vitale chronométrée à 1 seconde, débit expiratoire maximal,) n'ont montré aucune détérioration attribuable à une telle conduite. Par contre, l'impact de la prémédication et de la position dorsale sur le rendement mécanique du système respiratoire de nos patients a été nettement perçu par des diminutions allant jusqu'à 20 pour cent de la normale prédite.

L'administration préalable d'une dose protectrice de d-tubocurarine trois minutes avant l'induction de l'anesthésie nous est apparue non seulement permise, mais recommandable. En plus de s'imposer dans quelques cas (estomac plein, plaies pénétrantes du globe oculaire) cette manoeuvre nous a paru conférer à l'induction de l'anesthésie un profil pharmacokinétique plus opportun, en ce sens qu'elle permet à l'intubation endotrachéale de s'effectuer au moment du pic d'action des agents d'induction, myorelaxants et éléments de narcose. Les réponses motrices et neurovégétatives à la mise en place de la canule trachéale sont moindres.

Fort bien tolérée par nos patients, cette technique de précurarization avec une dose protectrice de d-tubocurarine présente tellement peu d'inconvénients subjectifs et objectifs que nous sommes en voie de l'adopter comme mesure de routine.

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