Prolonged Curarization in a Patient with Renal Failure

Case Report

By D. D. Riordan and A. A. Gilbertson

Summary

A patient with chronic renal failure received tubocurarine to provide relaxation during surgery and neuromuscular block was successfully reversed at the end of the operation. However, the continued use of the drug to facilitate intermittent positive pressure ventilation for the treatment of pulmonary oedema resulted in prolonged interruption of myoneural transmission. It is considered that the absence of renal excretion of tubocurarine resulted in the saturation of depot sites.

Tubocurarine is frequently used to provide relaxation for surgery in patients with renal failure. Churchill-Davidson, Way and de Jong (1967) found that recovery from paralysis by tubocurarine was normal after bilateral nephrectomy. In the case to be described the use of this drug during surgery was uncomplicated but its subsequent use in large doses to facilitate prolonged intermittent positive pressure ventilation resulted in grossly prolonged paralysis.

Case Report

The patient was a man aged 31 years who had suffered from chronic glomerulonephritis for 10 years. He was recently admitted to the Liverpool Regional Urological Centre because his uraemia required treatment by dialysis. He was dyspnoeic, and he had pulmonary and ankle oedema. The blood pressure was 190/120 mm Hg and triple rhythm was present. The blood urea was 282 mg/100 ml. Serum electrolytes were: sodium 129 m.equiv/1, chloride 91 m.equiv/1, and potassium 4.2 m.equiv/1. The haemoglobin was 6.5 g/100 ml. Peritoneal dialysis was commenced but after some weeks was complicated by the formation of intraperitoneal adhesions. Laparotomy and division of the adhesions was performed under general anaesthesia.

Anaesthesia was induced with thiopentone 250 mg and tubocurarine (45 mg) was given for relaxation. Nitrous oxide (6 l./min) and oxygen (2 l./min) were administered by intermittent positive pressure ventilation (IPPV). No incremental dose of relaxant was required, and at the end of the operation reversal of curarization, using neostigmine (5 mg) and atropine (1.2 mg) appeared satisfactory.

However, in the following 2 hours the patient developed pulmonary oedema and became severely hypoxic. He was re-anæsthetized using nitrous oxide, oxygen and halothane. The trachea was intubated without the use of a relaxant and IPPV resumed. Attempts to suppress spontaneous respiration by injection of phenoperidine were unsuccessful, and tubocurarine (45 mg) was given intravenously to allow continued positive pressure ventilation. Incremental doses of 10 mg were given as required to suppress spontaneous respiratory movements. The total dose of tubocurarine was 125 mg in 20 hours. Left ventricular failure was treated with digoxin and guanethidine and peritoneal dialysis (using hypertonic fluid to reduce the blood volume) was resumed.

Thirty hours after operation no relaxant had been given for 10 hours but the patient remained apnoeic and completely unresponsive to any stimuli. Electrical stimulation of the ulnar nerve, using a portable peripheral nerve stimulator* (Churchill-Davidson, 1965) showed complete myoneural block. As the pulmonary oedema had now improved as judged on clinical and radiological grounds, and the blood gases were within normal limits, neostigmine (5 mg) and atropine (1.2 mg) were injected intravenously.

Spontaneous respiration returned almost immediately and the patient was able to confirm that he had, in fact, been conscious but paralyzed, in spite of the long interval (10 hours) since the last incremental dose of tubocurarine. He now had strong limb movements and he could confirm that he had, in fact, been conscious but paralyzed, in spite of the long interval (10 hours) since the last incremental dose of tubocurarine. He now had strong limb movements and was able to confirm that he had, in fact, been conscious but paralyzed, in spite of the long interval (10 hours) since the last incremental dose of tubocurarine.

Fifteen to 20 minutes later ptosis and limb weakness indicated recurrence of the myoneural block. This was confirmed by demonstration of fading of the response to repeated single stimuli to the ulnar nerve, and post-tetanic facilitation. Improvement followed a further dose of neostigmine (2.5 mg) and atropine. A further similar dose was required 40 minutes later. Some weakness remained for a further 24 hours but recovered without specific treatment.

Pulmonary oedema recurred several times subsequently until eventually haemodialysis controlled the renal failure. Pulmonary ventilation was maintained during these episodes by patient-triggered assisted ventilation via a tracheostomy. This was allowed to close 10 days after the operation and there have been no further episodes of pulmonary oedema. The patient's renal failure is now managed by intermittent haemodialysis in his own home.


* R. G. Wakeling & Co. Ltd.
The intravenous administration of tubocurarine produces an initial high concentration of the drug in the plasma associated with the development of myoneural block. The concentration of the alkaloid falls rapidly at first, and during this phase recovery from the paralysis occurs.

This rapid decline is followed by a second phase in which the plasma level falls more slowly. Marsh (1952), Mahfouz (1949), Kalow (1953) and Cohen, Corbascio and Fleischli (1965) have interpreted this biphasic decay in plasma levels of tubocurarine as follows:

1. The initial rapid decline is due to redistribution of the alkaloid to non-active tissue depots.

2. The slower phase is due to depletion of the plasma as the drug is excreted, mainly unchanged in the urine. Fleischli and Cohen (1966) recovered 60–70 per cent of the injected dose of the drug in the urine, and a further fraction is excreted in the bile. These authors considered that metabolism of curare is unlikely to be a significant factor in its disappearance from the plasma.

Churchill-Davidson, Way and de Jong (1967) have stated that the response to tubocurarine is normal in the absence of renal function. As the activity of the drug appears to be related to its concentration in the plasma (Cohen, 1959) and as that concentration is reduced to non-paralytic levels by redistribution rather than by excretion, this finding is not unexpected. However, Marsh (1952) has pointed out that the inactive depot may be progressively filled by repeated doses of the relaxant, and the rate of decay of the plasma level will then be primarily related to the rate of excretion of the drug. It appears possible that saturation of the inactive depot occurred in our patient, and in the absence of renal excretion diffusion from the depot was able to maintain a plasma level of tubocurarine sufficiently high to produce grossly prolonged paralysis.

The possibility that an abnormal plasma protein pattern (Baraka and Gabali, 1968) might have been responsible for the prolonged paralysis was considered, but both total proteins and the electrophoretic pattern were shown to be normal. Cohen (1959) demonstrated that the decline in plasma level of tubocurarine may be delayed in dehydrated patients. Although it is possible to remove large volumes of fluid from patients by peritoneal dialysis using hypertonic dialysis solutions, this is unlikely to have been the case in the patient described, because dialysis had been rendered relatively ineffective by the peritoneal adhesions which had formed.

Although the cause of the prolonged curarisation described must remain speculative, the most probable explanation is that doses of tubocurarine of the order of 40–60 mg can be removed from the myoneural junctions by redistribution to non-active sites, but that larger doses (in this case 125 mg in 20 hours) may saturate these sites unless they in their turn can be cleared of the drug by renal excretion. Clearance by excretion of tubocurarine in the bile has been shown to occur, but it is probably relatively slow.

REFERENCES


CURARISATION PROLONGEE CHEZ UN MALADE ATTEINT D'INSUFFISANCE RENALE: OBSERVATION D'UN CAS

SOMMAIRE

Chez un malade atteint d'insuffisance rénale chronique, les effets de l'administration de tubocurarine en vue de parvenir à un blocage neuromusculaire et à une myoréparation au cours d'une intervention, ont pu être inversés avec succès à la fin de celle-ci. L'administration continue de la médication afin de faciliter une ventilation intermittente sous hyperpression dans le but de s'opposer à l'oedème pulmonaire a néanmoins abouti à une interruption prolongée de la transmission neuromusculaire. On considère que l'absence d'excrétion rénale de la tubocurarine a provoqué une saturation des zones où cette substance s'accumule.
VERLÄNGERTE CURARISATION BEI EINEM PATIENTEN MIT NIEREN-VERSAGEN: FALL-BERICHT

ZUSAMMENFASSUNG


CURARIZACION PROLONGADA EN PACIENTES CON INSUFICIENCIA RENAL: COMUNICACIÓN DE UN CASO

RESUMEN

Un paciente con insuficiencia renal crónica recibió tubocurarina para obtener relajación durante la operación y el bloqueo neuromuscular fue anulado satisfactoriamente al final de la intervención quirúrgica. Sin embargo, el uso continuado del medicamento para facilitar la ventilación con presión positiva intermitente para el tratamiento de edema pulmonar resultó en una interrupción prolongada de la transmisión mioneural. Se considera que la ausencia de excreción renal de la tubocurarina dio lugar a una saturación de los lugares de depósito.

PRACTICAL ANAESTHESIA IN THE SEVENTIES

A Refresher Course for Consultant Anaesthetists will be held at

The Postgraduate Medical Centre, Royal Victoria Hospital, Bournemouth, Hants.

from Wednesday, October 27 to Friday, October 29, 1971

Registration fee £10. Number of places limited to twenty.

It is intended for those Consultants who have not had an opportunity of attending courses or departments where the more recent developments are practised. It is not intended, therefore, for anaesthetists in training or for newly-appointed Consultants.

Applications to:

Dr R. A. L. Leatherdale, Royal Victoria Hospital, Bournemouth

COURSE IN PAEDIATRIC ANAESTHESIA AND INTENSIVE CARE

A short course for Consultants and Senior Registrars in paediatric anaesthesia and intensive care will be held at the Royal Liverpool Children's Hospital and Alder Hey Children's Hospital from September 13 to 17, 1971. The numbers participating will be limited to 20. The Course will consist of lectures and demonstrations. Some accommodation will be available in University Halls of Residence. Fees: £22.

Apply before June 30 to: Director of Paediatric Anaesthetic Studies, Department of Anaesthesia, University of Liverpool.