PROLONGED PARESIS FOLLOWING GALLAMINE

A Case Report

BY

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SUMMARY

A case of prolonged muscular paresis is reported following the administration of 120 mg of gallamine triethiodide to a patient who developed anuria. The muscular weakness continued for five days, necessitating artificial ventilation; it was finally reversed by haemodialysis. It is probable that the neuromuscular weakness was accentuated by the effects of a low extracellular potassium concentration and by streptomycin.

The duration of action of the muscle relaxants depends upon the efficacy of redistribution, excretion and metabolic destruction in lowering the circulating concentration of the drug below that level required to produce a clinical effect. The plasma level of muscle relaxant required to cause a neuromuscular block is influenced by many factors including patient sensitivity, potassium depletion and the presence of synergistic drugs.

The patient described in this case report developed muscular paresis postoperatively, requiring assisted ventilation for five days following a single dose of 120 mg gallamine triethiodide. It is probable that the prolonged action of the muscle relaxant was due to a combination of factors:

1. A failure to excrete the drug.
2. A low extracellular potassium.
3. The synergistic effect of an accumulation of streptomycin.
4. A possible altered response by the patient to gallamine.

CASE REPORT

The patient was a 37-year-old female Spanish domestic worker who had recently arrived in this country and who spoke no English.

April 29.

The patient presented at Kingston General Hospital with a 24-hour history of abdominal pain. Examination revealed evidence of generalized peritonitis and it was decided to perform a laparotomy. The patient's general condition did not cause any anxiety; her blood pressure was 100/80 mm Hg and her pulse 100 beats/min. She was clinically dehydrated and she was anaemic (haemoglobin 54 per cent). Morphine 15 mg had been given following the examination and she was therefore premedicated with atropine 0.6 mg.

Anaesthesia was induced with thiopentone 220 mg followed by suxamethonium 50 mg to facilitate tracheal intubation. Gallamine 120 mg was administered to provide muscular relaxation for the operation. A mixture of nitrous oxide 5 l/min and oxygen 2 l/min was used to maintain anaesthesia. The patient was ventilated through a circle absorber with a minute volume in excess of 8 l. The laparotomy revealed a perforated gastric ulcer with gross peritoneal soiling, compatible with a 24 to 36-hour perforation. The ulcer was oversewn and the peritoneal cavity aspirated. An ovarian cyst, an incidental finding, was removed. The operation lasted 35 minutes and was completely uneventful. At the closure of the peritoneum, atropine 0.6 mg and neostigmine 2.5 mg were injected and the soda lime was excluded from the circuit. Spontaneous respiration returned in about 3 minutes; however, the tidal volume appeared to be inadequate clinically although the rate of respiration and the character of the breathing was normal. A further 0.6 mg of atropine and 2.5 mg of neostigmine were administered and the patient was allowed to breathe oxygen. The patient opened her eyes and strained on the endotracheal tube, the endotracheal tube was removed and she was returned to the ward. Within an hour the patient's respiration became inadequate, resulting in cyanosis and carbon dioxide retention. The trachea was intubated and hyperventilation using room air was started. Her colour improved and she regained consciousness although her generalized muscular weakness remained. She had the appearance of a patient suffering from severe myasthenia gravis, although she was conscious and co-operative. The only abnormality on clinical examination was diminished muscle tone and power. Her hand grip was very feeble, her voice was weak, she used her frontalis muscle to assist in opening her eyes and she appeared to have some difficulty in swallowing saliva. Her reflexes were depressed and her plantar reflex, which had been extensor immediately postoperatively, became normal later. Edrophonium 10 mg was administered without any improvement in her muscle power.

In view of her good physical condition it was felt inadvisable to confuse the clinical picture by the indiscriminate administration of drugs. The patient was started on a course of streptomycin 1 g daily with penicillin. The streptomycin injections were continued...
for four days. Following the transfusion of two bottles of stored blood the patient's serum potassium was 2.6 m.equiv/l., the standard bicarbonate of 23.5 m.equiv/l. and a blood urea 118 mg per cent.

April 30.

Twelve hours later the patient's condition was unchanged and a tracheostomy was performed. The electrolyte examination revealed a serum potassium concentration of 2.4 m.equiv/l. The blood urea was 148 mg per cent. In view of the low serum potassium an e.c.g. was performed but this did not reveal evidence of hypokalaemia. Sixteen milliequivalents of potassium was administered intravenously in an hour. This produced some improvement in muscle tone. Following the infusion 10 mg of edrophonium was injected with insufficient improvement in muscle power to allow the patient to breathe spontaneously. Unfortunately this improvement was only temporary and was not prolonged by 2.5 mg of prostigmine and a return to artificial ventilation was necessary. A blood sample at this time showed a serum potassium of 3.2 m.equiv/l. A further 16 milliequivalents of potassium produced no further clinical improvement.

It was noticed that the patient had only passed 60 ml of urine since the operation in spite of receiving some 4 litres of fluid.

May 1.

The patient's condition remained unchanged. The volume of urine passed in the day was less than 100 ml and it was decided to treat the patient as one with oliguric renal failure. In spite of a serum potassium of 2.8 m.equiv/l. it was considered inadvisable to administer potassium in the absence of renal function. The patient remained paretic and was unable to maintain an adequate tidal volume spontaneously.

May 2.

Patient's condition unchanged.

May 3.

The patient's muscle power was slowly improving although she still required artificial ventilation and appeared myasthenic. She could manage to feed herself with ice. In view of the rising blood urea it was thought advisable to transfer her to the care of Professor Milne at Westminster Hospital. Her plasma potassium had risen to 3.4 m.equiv/l. At Professor Milne's suggestion preparation was made for haemodialysis. Before this was carried out it was confirmed that a non-depolarizing block was present, using a Medelec stimulator. Sixty milliequivalents of potassium was infused and 10 mg of edrophonium injected. This produced a considerable improvement in muscle power. Following the administration of 2.5 mg neostigmine the patient was able to breathe spontaneously with a minute volume of 10 l. In spite of this the patient retained her myasthenic appearance. It was only after the haemodialysis that the patient's muscle power returned to normal and she was able to breathe spontaneously with ease. Throughout the remainder of the patient's stay in hospital her motor power remained normal.

Further course in hospital.

Unfortunately the patient's renal function did not improve; she remained anuric. Repeated haemodialyses were required for the rising blood urea. Two days after the second dialysis she suffered a subarachnoid haemorrhage and later started to bleed from her stomach. The haemorrhagic tendency continued in spite of further dialysis using regional heparinization. She finally died almost four weeks after her operation in spite of being dialyzed six times and receiving a total of sixty bottles of blood for her gastro-intestinal haemorrhage. Autopsy revealed healing renal tubular necrosis and three chronic gastric ulcers, one of them oversewn following perforation.

DISCUSSION

Gallamine triethiodide is largely excreted in the urine. Mushin and his colleagues (1949) recovered 30 to 100 per cent of the original dose from the urine of rabbits in the two hours following its administration. Prolonged action of the drug consequent upon delayed renal excretion has been reported (Fairley, 1950; Montgomery and Bennett-Jones, 1956). In neither of these cases did the duration of the muscular weakness exceed 36 hours. The present case is most unusual in that the paralysis exceeded five days following a total dose of 120 mg of the drug. This dose of gallamine is usually expected to last under 1 hour. It is most unlikely that even in a person with normal renal function the drug is completely excreted in this time. It is more probable that the combination of redistribution and tissue binding produce a fall in plasma concentration which is maintained by renal excretion. It is therefore likely that other factors contributed to the prolonged effect of gallamine in this patient. This is also suggested by the incomplete response to neostigmine, for if the paralysis has been entirely due to residual gallamine, it should have been completely reversed by neostigmine.

The low extracellular potassium that was demonstrated in this patient and the improvement that followed the infusion of potassium, suggest that a disturbance of the ratio of the intracellular:extracellular potassium contributed to the increased susceptibility of the patient to gallamine (Wilson and Wright, 1937).

Streptomycin has a mild neuromuscular blocking effect (Brazil and Corrado, 1957). This effect summates with the non-depolarizing muscle relaxants and is incompletely reversed by neostigmine. In this patient 4 g of streptomycin were administered in four days. In the absence of renal function it would be expected that a very high plasma con-
centration would have developed by the fourth day. As the streptomycin treatment was not instituted until after the establishment of the paresis, it can only have played a secondary role by continuing the patient's susceptibility to the muscle relaxant.

The failure of neostigmine to reverse the effect of the gallamine is difficult to explain unless one postulates a possible alteration in the effect of gallamine in this patient or an unusual sensitivity.

The ultimate complete reversal of the muscular weakness by haemodialysis proves that the basic cause was an agent that was dialyzable. It is probable that this was gallamine.

ACKNOWLEDGMENTS

We acknowledge our indebtedness to Professor Milne for his most helpful advice with this patient. We are also indebted to the surgeons, pathologists and anaesthetists of Kingston and Westminster Hospitals and to the Department of Clinical Measurement of Westminster Hospital for their willing co-operation.

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REFERENCES


PARÉSIE PROLONGÉE APRÈS GALLAMINE

SOMMAIRE

Compte-rendu d'un cas de parésie musculaire prolongée après administration de 120 mg de triéthiodide de gallamine à un patient devenu anurique. — La faiblesse musculaire continua pendant cinq jours, elle nécessita la respiration artificielle — mais fut finalement ramenée à l'état normal par hémodialyse. L'atonie neuro-musculaire fut probablement renforcée par les effets d'une concentration trop basse du potassium extra-cellulaire et par l'administration de Streptomycine.

VERLÄNGERTE MUSKELLÄHMGUNG NACH VERABFOLGUNG VON GALLAMIN

ZUSAMMENFASSUNG

Es wird über einen Fall von verlängerter Muskellähmung nach Verabfolgung von 120 mg Gallamin bei einem Patienten mit einer sich entwickelnden Anurie berichtet. Die Muskelschwäche hielt fünf Tage an und nachte eine künstliche Beatmung notwendig, sie wurde letztlich durch eine Hämodialyse rückgängig gemacht. Es ist möglich, daß die neuromuskuläre Schwäche durch die Auswirkungen einer niedrigen extrazellulären Kaliumkonzentration und durch Streptomycin verstärkt wurde.