Summary

A clinical comparison is presented of the use of an opium derivative, codeine, and an antispasmodic, tricyclamol, in the treatment of chronic non-specific diarrhoea.

The antispasmodic failed to control the symptoms and in a number of subjects exaggerated them.

Codeine is an effective symptomatic remedy for chronic non-specific diarrhoea.

We are grateful to Dr. F. Avery Jones for helpful advice in preparing this paper.

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Medical Memorandum

Dequalinium in Myasthenia Gravis

During the course of treatment of a severe case of myasthenia gravis the patient developed a pharyngitis and was given decamethylenebis-4-aminoquinaldinium chloride (dequalinium chloride; "dequadin"). This compound was discovered to have antimicrobial activity by Babbs *et al.* (1956). They also found that, like other heterocyclic polymethylene bis-quaternary ammonium salts, there was a neuromuscular blocking activity, and that mice receiving it intravenously were paralysed. Clinically this drug is used as an oral antiseptic, and whilst being given on this account marked improvement was noted in the patient's myasthenia. The following case is reported because the problem may be worthy of further specialized study. The initial diagnosis in this instance was reached after marked resistance to suxamethonium ("scoline").

CASE HISTORY

A woman aged 62 was admitted to hospital on March 10, 1957, with a three-days history suggestive of a bulbar palsy. She had first developed difficulty in speaking. Progression of this disability with the onset, the previous day, of inability to swallow had made special care necessary. A vascular cause was at first suspected in view of the acute onset and the finding of a blood pressure of 230/120 mm. Hg. Her previous health had been good apart from some weakness in the left leg of six to eight months' duration on climbing stairs.

During her first day in hospital laryngeal stridor with difficulty in breathing led to anxiety. Preparations were made for a tracheotomy under general anaesthesia. Suxamethonium up to 9 ml. (450 mg.) did not paralyse the vocal cords, and, myasthenia gravis being suspected, she was allowed to come out of the anaesthetic and given intravenous neostigmine, 2 ml., which produced immediate relief of all symptoms.

The full-blown syndrome of myasthenia became obvious during the first week, with ocular palsy, drooping of the lids, and weakness of the neck and arms in addition to the initial symptoms. These were relieved by neostigmine and pyridostigmine bromide ("mestinon") for about two hours. After 11 weeks she was discharged on neostigmine, 30 mg. every three hours by mouth. She was able to get around quietly, although weakness became obvious two hours after her neostigmine.

One month after discharge the patient complained of a sore throat and, associated with this, a deterioration of her

voice. Examination showed some inflammation of the fauces, and dequalinium, one tablet (0.25 mg.) every three hours, to be sucked, was prescribed. In 24 hours there was marked improvement in her condition, and for the first time since the onset she felt almost normal. Before this she had felt herself needing head support even 20 minutes after neostigmine. Her voice, swallow, and general strength also improved and she felt able to go for short walks. After three days the dequalinium was stopped and immediately her condition deteriorated, to cause concern.

As a result of this, a trial was begun as follows. (1) Dequalinium, 0.25 mg., was given four-hourly for one week and then withdrawn the next week. This was repeated five times. It appeared that whilst on the drug the patient was considerably improved and had no symptoms. It was in fact possible to reduce the dosage of neostigmine to every four instead of three hours, and between doses of this drug she was much stronger. When off dequalinium she felt tired within half an hour after neostigmine, and before each dose was due felt very weak, unable to talk or swallow, and had double vision. (2) A blind trial with dummy tablets was performed on three separate occasions. Three days on dequalinium were alternated with three days on dummy tablets. Whilst on dequalinium there was considerable improvement and a relapse during the control periods. In fact, the relapse was enough to require almost three days on dequalinium before a return to normal.

The patient has been on dequalinium continuously for six months without ill effect and is asymptomatic on all counts with a steadily reducing dosage of neostigmine. At present she is having dequalinium, 1 tablet six-hourly, and neostigmine, 30 mg. six-hourly.

COMMENT

The basic pathology of myasthenia gravis is still far from clear. It is difficult, therefore, to give a simple explanation of the findings in the case reported above. The present position regarding the physiological action of neuromuscular blocking agents has been reviewed by Burn (1957). It would seem in myasthenia that there is a competitive block and the muscle and plate respond abnormally. Grob, Johns, and Harvey (1956) suggest the possibility that the defect could be due to choline or an abnormal product of acetylcholine. Potassium is known to be of great importance in the production of the end-plate potential, and Bülbring and Burn (1942) have investigated how sensitivity may be increased by adrenaline.

It is known that myasthenia gravis may remit spontaneously. However, there was sufficient immediate benefit in this case to suggest that dequadin might be responsible. It could act as a mild depolarizer or anticholinesterase potentiating the action of acetylcholine, or it might resensitize the plate.

The marked resistance to suxamethonium in myasthenia gravis is also not fully understood, but it too may be affected by the competitive block reaction. An adequate explanation is still required.

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