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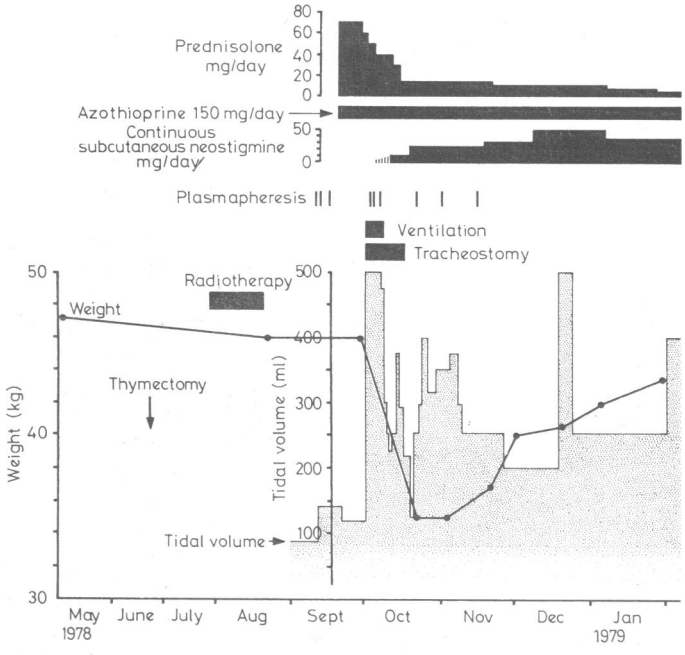
Continuous subcutaneous neostigmine in the management of severe myasthenia gravis

Oral anticholinesterase drugs are variably and incompletely absorbed and sometimes fail to maintain patients with myasthenia gravis independent of hospital care, even when combined with steroids and immunosuppressive agents. We describe such a patient and suggest a novel addition to the management of this problem.

Case report

In May 1978 a 27-year-old woman presented with an 18-month history of dysphagia and dysarthria. Examination showed that she had myasthenia gravis, which was confirmed by a Tensilon test, and investigation showed a thymic tumour. In June 1978 a thymic carcinoma affecting pleura and pericardium was removed as completely as possible; radiotherapy was given in July and August 1978 (see figure).

Before and after operation the myasthenia was controlled with neostigmine and pyridostigmine. After radiotherapy the patient's myasthenia worsened and affected her eyes, limbs, and respiratory muscles as well as swallowing. Because of severe weakness she was readmitted to hospital on 22 August 1978. Over the next month various combinations of neostigmine up to 300 mg/day, pyridostigmine up to 600 mg/day, and ambenonium 30 mg/day were given. A mild cholinergic crisis occurred once, but muscle weakness was often severe, causing problems with speech, breathing, and swallowing. The patient could not move far from her bed.



Course of myasthenia and treatment.

By 10 September 1978 breathing and swallowing were difficult and the tidal volume was only 90 ml. The patient could not lift her arms above her shoulders. Plasmapheresis was started, and after three exchanges over four days the tidal volume doubled, swallowing improved, and the patient could get out of bed. Within a few days she deteriorated, and prednisolone 75 mg/day and azothioprine 150 mg/day were added to the treatment. The patient's general condition did not improve over 12 days and her muscle weakness increased. Intubation and ventilation were started, followed by a tracheostomy. Three further plasmaphereses were done.

While the patient was being maintained on the ventilator and because we failed to control the myasthenia with oral neostigmine, we gave intermittent subcutaneous and intravenous injections of neostigmine in doses (up to 2 mg) recommended in *National Formulary*.

Ventilation was discontinued after a week, and as tidal volume was maintained at about 250 ml we increased the dose of subcutaneous neostigmine. The dose of prednisolone was slowly reduced to 15 mg/day as she showed no response to high doses and because of the severe catabolic state and repeated infection.

On 9 October 1978 we changed the subcutaneous neostigmine from intermittent to continuous administration, using an infusion pump. The daily dose was increased from 10 mg to 25 mg to control the muscle weakness as judged by tidal volume, speech, and power in the limbs. Swallowing, however, did not improve and nasogastric feeding was continued.

Two attempts to reduce the dose of neostigmine led immediately to severe myasthenia with respiratory embarrassment and inability to sit up. The patient's general condition then began to improve and for the first time in three months we considered discharging her.

In early December 1978, to increase the patient's mobility, we obtained a small battery-operated infusion pump (Syringe Driver Type MS-Pye Dynamics Ltd) to administer the contents of a 10 ml syringe; this was connected to the patient with 90 cm of fine plastic tubing and a butterfly cannula inserted into a subcutaneous site on the abdomen. The pump was carried in a shoulder holster and permitted full activity. The rate of infusion could be varied by the doctor or patient. Since then she has taken 36 to 60 mg of neostigmine daily. The cannula site has been changed every two weeks. The syringe has to be filled twice daily because of the strength of neostigmine solution (2·5 g/l) available. The patient manages the syringe herself.

With continuous subcutaneous neostigmine the patient has been able to go home and to do light housework, go shopping, and drive a car. Her weight has slowly increased towards normal (see figure), and swallowing has recently improved so that she can now eat normally. Steroids and azathioprine are gradually being withdrawn.

Comment

Continuous subcutaneous neostigmine may have a place in the management of severe myasthenia gravis in the short or medium term. Subcutaneous absorption seems to be reliable and there have so far been no local reactions to continuous subcutaneous administration. The dose, up to 50 mg/day, differs considerably from that normally recommended. The syringe driver seems to be reliable, needing new batteries every six weeks, and can be managed by the patient with infrequent visits to her doctor or the hospital.

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Monocyte maturation and prognosis in primary breast cancer

Patients with cancer show many functional abnormalities in the mononuclear phagocyte system. Dizon and Southam[1] found that patients with malignant disease have an impaired ability to mobilise macrophages. Studies in malignant melanoma[2] show that monocytes from patients with disseminated disease are unable to differentiate into macrophages in tissue culture.