MEPHENESIN CARBAMATE IN THE TREATMENT OF SPASTIC PARALYSIS

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Mephenesin was introduced in 1951 as a muscle relaxant. It was found to act mainly on the spinal cord, but also on the basal ganglia and the brain stem. Favourable comments on its action have been published in cases of rheumatoid arthritis, fibrositis, spastic paralysis, disseminated sclerosis, and other conditions.

Since 1954 mephenesin (Tolserol, Squibb) has been replaced by mephenesin carbamate (Tolseram) as being more efficacious and less toxic. Reports of its value have appeared from Engler[1,2] in severe spastic disorders present from birth, from Larkin[3] in fibrositis, and from Marshall[4] in disseminated sclerosis. On the other hand Fasser[5] has stated that 'Tolserol and other related drugs have been found to possess no value or very little indeed' in cerebral palsy.

It was therefore decided to test its efficacy on 10 spastic patients in this Institution. All are certified mental defectives of various grades, and all suffer from severe spastic disorders of various types.

Dosage. The drug is available as 0·5 g. tablets and was administered in a little milk immediately after meals. In adults the initial daily (divided) dose was 6 g., and this dosage was maintained for 4 weeks if the patient responded. Where no response was obtained the daily dose was raised to 9 g. In children the initial dose was 1·5-3 g. daily, according to age, which was increased to 4·5 g. and later to 6 g. where no initial response was obtained. Where no response was obtained at the end of 3 weeks treatment was stopped. In the other cases tailing off was begun at the end of the 4th week, when the dosage was halved. The following week it was halved again, and this reduction continued until adults were getting 1 g. per day and children 0·5 g. per day as maintenance doses.

Side-effects. These were mild and transient. One patient vomited, two showed drowsiness, one showed marked pallor, and one had a sense of weakness and loss of power in the spastic limbs. One patient complained of pains in the affected muscle-groups, and another of giddiness of short duration shortly after swallowing his tablets. Two patients showed a marked increase in appetite during treatment. In no case did

treatment have to be suspended because of undesirable side-effects.

PATIENTS

The patients were selected entirely on the basis of suffering from severe forms of spastic paralysis without taking into account the cause of the paralysis. Their spasticity was due to such varied conditions as cerebral palsy, localized upper-motor-neurone lesions, and encephalitis. Their mental states varied from idiocy to high-grade feeblemindedness.

All patients were given a careful neurological examination before treatment was begun, and were re-examined at weekly intervals during the period of treatment. One of the difficulties encountered was the assessment of the amount of spasticity present. Engler[2] measured the range of movement in the joints of his patients before treatment, and was thus able to record any subsequent improvement. After consultation with an orthopaedic surgeon and a physiotherapist we decided that there was no truly reliable objective method of measuring the amount of spasticity, and we decided to rely on our own subjective impressions of the amount of spasticity present. We recorded this in our notes as absent (—), minimal (±), mild (+), severe (++), or very severe (+++).

None of the cases had had any form of physiotherapy in the institution before Tolseram was administered, although simple forms of this were initiated in several cases once a noticeable improvement had been demonstrated.

A brief description of the individual cases and their responses will now be given:

1. *Male aged* 19 *years*

Spasticity was first noticed at 6 months. At 4 years he could no longer stand or walk, and was treated for a short time at Uplands Orthopaedic Home, Pietermaritzburg.

Before Tolseram treatment was begun he showed severe spasticity of all the limbs and neck, he grimaced continually, his speech was quite unintelligible, he had difficulty in swallowing, and salivation was marked. He could only move around by sliding on his buttocks on a piece of leather.

At the end of the 1st week of treatment spasticity was no longer present in the neck, and it was markedly diminished in the limbs. He could now feed himself, and swallowed with less difficulty. Grimacing and salivation were noticeably diminished.

At the end of the 2nd week grimacing and salivation were absent, and spasticity in the arms and legs had further diminished. He was now able to walk a few steps with assistance—something he had not done for many years. At the end of the 3rd week he could walk fairly well while pushing a wheel-chair. His appetite had increased prodigiously and his general physical condition had improved noticeably. By the end of the 4th week he was generally happier and more cheerful, and was easier to manage. His speech was clearer and more intelligible. This improvement has been sustained on the lowered maintenance dose after 4 weeks.

2. *Male aged* 10 *years*

Had encephalitis at 2 years. Three months later he developed numerous attacks of petit-mal and signs of Parkinsonism.

Before treatment he showed severe spasticity of all the limbs, marked tremor in the arms, and gross incoordination. Patellar and ankle clonus were present and his plantar reflexes were extensor. Speech was markedly slurred and indistinct, and salivation was severe. He could not sit up without assistance, could not walk and had to be fed, and his personal habits were faulty.

At the end of the 1st week of treatment rigidity in the arms and legs was considerably diminished, tremor of the arms had ceased, and salivation was noticeably less. The ankle clonus had disappeared, although knee clonus was still present.

At the end of the 3rd week spasticity in all limbs was minimal, and knee clonus was absent. He could now sit up unassisted, and could feed himself reasonably well. When he wished to urinate he asked for the bottle. At the end of the 4th week his speech was much more distinct and he asked to be taken to the lavatory to defaecate, i.e. his personal habits were now clean. He could walk the length of the ward with minimal support. This improvement has persisted after 4 weeks on a low maintenance dose.

3. *Male aged* 24 *years*

At 10 years of age he suddenly lost the use of his left arm and leg and by the time he was 15 he showed the typical features of a spastic hemiplegia. In 1955 all the toes on his left foot were amputated because of a plantar flexion deformity which hindered walking.

Before treatment was begun he showed marked spastic rigidity of the left arm and leg. The arm was kept fully flexed at the elbow and showed severe athetotic movements. Coordination was poor and he could perform the grossest movements only, with difficulty.

At the end of the 1st week of treatment there was no change apparent on physical examination, but the patient (a high-grade defective) stated his left arm felt more relaxed. At the end of the 2nd week the arm was noticeably less spastic and was not kept fully flexed any longer. He could open his left hand voluntarily, and could pick up a small pin off the table without undue difficulty. The leg showed diminished spasticity, and he stated he now walked better and with less discomfort.

At the end of the 3rd week the athetoid movements in the arm were hardly noticeable, while spasticity had decreased still further. He stated he could now walk 'a hundred times better', and the leg showed no spasticity on examination. At this stage simple physiotherapy for the left arm was begun. At the end of the 4th week the arm was carried practically fully extended, and he had good control over it. He felt his walking was still improving. After 4 more weeks on only a maintenance dose improvement was sustained.

4. *Male aged* 47 *years*

His condition set in at 3 years after a febrile illness.

Before treatment he showed moderate spasticity of arms, legs and neck. He walked with difficulty, ate slowly and spilt a good deal of his food. Salivation was marked. At the end of 2 weeks of treatment there was some diminution in spasticity. At the end of the 3rd week there was no further improvement despite increased dosage, and treatment was discontinued.

5. *Male aged* 53 *years*

He was normal till 14, when he developed epileptic seizures followed by spastic paralysis of both legs. For the last 18 years he has been confined to a wheel-chair. Before treatment his legs showed moderate spasticity, with bilateral patellar clonus and a positive Babinski. He had bilateral club-foot. At the end of the 2nd week of treatment spasticity had disappeared and clonus was absent. At the end of another week the patient stated that his legs felt more relaxed. During the 4th week of treatment he made an attempt to walk which was unsuccessful largely owing to the gross fixed deformity of his feet. He is more placid and happier, and is now adjusting well to vocational training, though still confined to his wheel-chair.

6. *Male aged* 23 *years*

No previous history is available. Before treatment was begun he showed a right-sided hemiplegia, with moderate spasticity of the arm and leg, patellar clonus and a positive Babinski. At the end of the 1st week of treatment the patellar clonus was absent, but there was no further improvement in spite of increased dosage of Tolseram. Treatment was discontinued at the end of the 3rd week.

7. *Male aged* 4 *years*

A case of apparently congenital spastic quadriplegia. Before treatment he showed severe spasticity of all the limbs and was completely helpless. There was marked salivation, which diminished after one week of treatment. As no further change occurred the dosage was increased at the end of the 2nd week. No further improvement was noted on examination, but the nursing staff reported that he moved around more freely in his cot. The dosage was increased again but with no further improvement, and treatment was discontinued.

8. *Male aged 6 years*

He had basal meningitis at 2 months, followed by hydrocephalus and spastic paralysis. A craniotomy was performed by a neurosurgeon in Johannesburg with no improvement.

Before treatment was begun he showed spasticity of arms, legs and neck, and was completely helpless. At the end of the 1st week there was diminished spasticity but no further improvement resulted even after the dose had been increased twice. Treatment was then discontinued.

9. *Female aged 5 years*

Spastic quadriplegia and epilepsy present since birth. Before treatment she showed moderate spasticity of arms, legs and neck, and she was completely helpless. As treatment brought about no change in spite of 2 increases in dosage, it was discontinued in the 4th week.

10. *Male aged 5 years*

A boy who developed normally until he was 18 months old, when he suddenly became comatose and remained unconscious for a week. When he regained consciousness he was unable to walk or talk and showed spastic paralysis. An air-encephalogram showed right fronto-parietal cortical atrophy.

Before treatment was begun he showed spasticity of arms and legs, most marked on the left, and neck rigidity. He used only his right hand, was unable to walk, and grimaced continually. At the end of a week's treatment the grimacing was less marked and the spasticity of the neck and limbs had diminished. At the end of the 2nd week there was no further improvement on examination, but he could now stand and take a few steps with assistance. At the end of the 3rd week spasticity in the left leg and arm had diminished still further. He could now kneel in his cot unassisted. Further treatment produced no other improvement, but the improvement gained has been sustained after 4 weeks on a maintenance dose.

CONCLUSIONS

Of the 10 cases treated with Tolseram, in only one case (no. 9) could it be said that there was no response at all, although in 4 others (nos. 4, 6, 7, and 8) improvement was only transient and the treatment was ultimately discontinued.

The other 5 cases showed sufficient improvement to warrant continuation of maintenance doses of the drug, while in 3 cases (Nos. 1, 2 and 3) improvement can fairly be described as striking. One therefore feels justified in stating that Tolseram is worthy of a trial in all forms of spastic paralysis, more especially as it appears to be quite safe and unaccompanied by any serious side-effects.

SUMMARY

Mephenesin carbamate has been administered to 10 cases of spastic paralysis for a period of 8 weeks. Five cases showed some improvement and, of these, 3 showed a striking improvement.

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