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Effect of Mydeton in the rehabilitation of hemiparetic patients

Dr Miklós FEHÉR, Dr Péter JUVANCZ and Dr Melinda SZONTAGH

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Summary: The authors compared the muscular tension relaxing effect of Mydeton and Baclofen on 48 spastic hemiparetic patients by a double-blind method. The Rivermead scale and the Barthel index were used as test parameters. On the basis of their results, Mydeton proved to be more effective in the rehabilitation of spastic hemiparetic patients.

Irrespective of their cause, injuries of the motor tract and of the pyramidal tract originating from the former lead to hemiparesis, which is usually associated with increased muscular tension and spasticity. In its distribution, the increased muscular tonus shows a typical predilection for the anti-gravitational muscles. Thus, the lower extremities are characterised by increased muscular tonus in extension while the upper extremities exhibit flexion hypermyotonia. From the above it is easy to understand that spasm is a Janus-faced phenomenon in the rehabilitation of hemiparetic patients. Extension spasm of the lower extremities enables these extremities to bear weight even when this would not be possible because of the reduced muscular strength. At the same time, the flexion spasm of the upper extremities can prevent the expedient use of the hands even when this would be made possible by the restored muscular power.

While in a certain proportion of cases the development of spasm can be prevented by the use of special physiotherapeutic methods (e.g. Bobath), once spasm has developed, it can no longer be fully eliminated. This means that, with our help, patients have to fight against their spasm day by day. In addition to different physiotherapeutic treatments (curative gymnastics, use of ice packs, bio-feed-back), hypomyotonic drugs are also needed in that fight. We need agents that decrease muscular tension while affecting muscular strength only slightly or not at all. These agents should also be free of side effects in order to be suitable for prolonged use. One of the drugs meeting these requirements is Mydeton, an agent that we are also using in the rehabilitation of hemiparetic patients with cerebral damage on the basis of the favourable experience gained with it by others.

Mydeton, the chemical composition of which is 1-piperidion-2-Methyl-3-p-Tolyl-Propanone-3-Hydrochloricum, was synthesised by Nádor et al. in the laboratory of Gedeon Richter Chemical Works in 1955.¹⁰ The detailed pharmacological study of the agent was reported by Pórszász et al. in 1960.¹¹ By animal experiments they demonstrated that Mydeton acted mainly on the central nervous system, inhibited the multisynaptic spinal reflexes, alleviated electroshock-induced convulsions, and had pronounced anti-

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nicotinic as well as tremor-inhibiting effects. Its principal point of attack is the bulbar facilitation system. The findings of Pórszász were later confirmed by Japanese researchers.

In 1965, Kato et al.⁵ also observed the inhibitory effect of the drug on the spinal polysynaptic reflexes (e.g. on the crossed extension reflex). In addition, they found that in a large dose the drug inhibited the monosynaptic reflexes as well. The reflex-inhibiting effect of Mydeton surpassed that of Mephenesin.

In 1970, Fukuda et al.³ recorded the peripheral effect of the drug: when used in high concentrations *in vitro*, Mydeton diminished twitching caused by indirect stimulation of isolated rat diaphragm. Thus, the pharmacological studies have demonstrated that the low-toxicity Mydeton is suitable for alleviating hypermyotonia and muscular spasm of central origin and that it may also be effective in the treatment of spasm of peripheral origin.

Clinical trials of the drug were first reported in 1961 by Lehoczki¹⁰, who observed marked spasm reduction in patients with spastic paralysis of spinal and cerebral type after the administration of Mydeton. Dobí² observed the decrease of muscular rigidity in parkinsonian patients having taken Mydeton. Boudouresque et al.¹ and Szobor¹² achieved good results with Mydeton primarily in patients with spastic paralysis of spinal origin, thus especially in those suffering from multiple sclerosis. In addition to the above, several other papers have reported the good therapeutic effect of Mydeton in patients with diseases of the peripheral arteries.⁶

Baclofen is one of the drugs most commonly used in the treatment of spastic hemiparetic patients. In order to demonstrate the efficacy of Mydeton in an objective manner, we have performed a double-blind study, using Baclofen as reference drug.

The patients to be included in the study were selected very carefully. Only such hemiparetic patients were included in the study who had already developed spasm, whose predicted duration of hospital treatment exceeded six weeks, who were not suffering from severe concomitant diseases, whose cognitive abilities were not substantially impaired (IQ over 70), and who appeared to be co-operative and, thus, there was hope of their more or less successful medical rehabilitation.

The patients selected for the study were assigned serial numbers and received tablets of the same size and colour three times a day, at predetermined times. Each of these tablets contained either 150 mg Mydeton or 25 mg Baclofen according to a code unknown to both the physician and the patient. In addition, patients suffering from vascular disease usually received Cavinton as vasodilator while trauma patients were given Enerbol to improve their cerebral metabolism. The administration of other drugs was avoided as far as possible, and medicines potentially influencing muscular tonus were absolutely not given. All patients equally participated in individual and group curative gymnastic exercises. For the passive mobilisation of shoulders affected by contracture ice packs were regularly used.

Like several other researchers, we also encountered difficulties in measuring the magnitude and changes of muscular spasm. Objective instrumental recording by EMG is very complicated and only provides information on the severity of spasm existing at the time of the examination. The semi-objective methods, such as scoring of the estimated magnitude of resistance perceived by the examiner during passive movement of the limb on an artificial numerical scale, are burdened by a high margin of error. From the aspect of successful rehabilitation, isolated measurement of the spasm is much less important than judging the types of movements that the patient can carry out and estimating the extent to which their self-supporting functions have been restored. We used two functional scales for testing these parameters. The first was a hierarchical scale elaborated at Rivermead Rehabilitation Centre (UK) by Lincoln and Leadbitter⁸. This scale allows us to study the global functions (such as sitting, standing, walking), the movement of the lower extremities and the trunk, as well as the movements of the upper extremities in an integrated man-

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ner, according to their complexity and degree of difficulty. In the evaluation of certain movements there are only two possibilities: namely, whether or not the patient can carry them out as instructed, and accordingly receives a score of either 1 or 0. The maximum total score that can be achieved is 38. The second scale that we used was the well-known Barthel index, by the use of which the patient's self-supporting ability can be measured (eating, dressing, washing, toilet use, use of vehicles). Depending on their relative importance, the individual activities can be given 5, 10 or 15 points, and the maximum score that can be achieved is 100. These two functional tests were performed before the patients started taking the drugs and after they had stopped taking them.

The patients took the drugs for a period of six weeks. If during drug-taking the patients exhibited any severe sign that could be interpreted as a side effect, treatment was suspended immediately. If milder symptoms occurred, the administration of the drug was suspended for two days and it was terminated finally only if the clinical signs had re-occurred. We did not have to open the envelope containing the code in any case. The data were analysed by a statistical method. The means and the standard deviations were calculated. Changes in the value of parameters within groups were compared by a one-sample while the differences between the groups by a two-sample *t*-test. The non-parametric data were evaluated by the chi-squared test. Only the values of patients completing the study were taken into consideration in evaluating the efficacy of the drugs tested. A total of 48 patients participated in the study. Ten of the patients had to be excluded from the study for different reasons. Thus, the efficacy of the drugs could be tested on a total of 38 patients.

Table I

	Male patients		Female patients		Total	
	Mydeton	Baclofen	Mydeton	Baclofen	Mydeton	Baclofen
Vascular disease	11	9	2	7	13	16
Trauma	7	5	1	–	8	5
Tumour	1	3	2	–	3	3
Total	19	17	5	7	24	24

The distribution of patients included in the study according to sex and the type of cerebral injury was comparable. The same can be said of the average age of patients, which was 43.96 ± 2.91 years and 46.33 ± 2.91 years in the Mydeton-treated group and the Baclofen-treated group, respectively.

The results of the study are summarised in the following table.

Table II

	Baclofen		Differ- ence	Mydeton		Differ- ence	Com- parison of dif- ferences
	B. T.	A. T.		B. T.	A. T.		
Barthel	50.56 ± 7.14	72.78 ± 6.39	$p < 0.001$	47.25 ± 4.95	82.00 ± 5.60	$p < 0.001$	$t = -1.95$ N. S.
River- mead	10.11 ± 2.53	16.78 ± 2.80	$p < 0.001$	6.90 ± 1.34	20.25 ± 2.35	$p < 0.001$	$p < 0.01$

B. T. = before treatment; A. T. = after treatment

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The measured values of both the Barthel index and the Rivermead scale demonstrate that the severity of the condition of the two groups of patients was nearly identical at the start of the study. As a result of the rehabilitation treatments, the performance of the patients improved substantially in terms of both functional indices in the group treated with Baclofen as well as in the group treated with Mydeton. The improvement observed on the Rivermead and the Barthel scales was higher in the group treated with Mydeton than in the Baclofen-treated group. The difference between the two groups was statistically significant in the case of the Rivermead scale and was at the borderline of statistical significance in the case of the Barthel index.

In addition, we analysed the cases of those 10 patients who interrupted the taking of drugs. There was no substantial difference between the two groups in the total number of patients whose medication was interrupted.

Table III

	Baclofen	Mydeton	Difference
Vascular disease	6	1	
Trauma	–	1	$X^2=0.51$
Tumour	–	2	N. S.
Total	6	4	
<i>Baclofen</i>		<i>Mydeton</i>	
Dizziness, nausea	5	Operation	1
Epileptiform convulsion, urticaria	1	Left voluntarily	1
		Lack of efficacy	1
		Vomiting	1

If, however, the reasons for suspending drug administration were analysed separately, it was discovered that while in the Baclofen group all interruptions of treatment were due to adverse effects, in the Mydeton-treated group only a single interruption was attributable to adverse effects.

DISCUSSION

The detailed pharmacological study of Mydeton was carried out almost 30 years ago. Soon after that the clinical trial of the drug was performed in numerous nervous disorders and other diseases associated with increased muscular spasticity. All publications reported good efficacy of the drug. Despite this fact, recently the use of Mydeton has become limited to an ever narrower field. Thus, in several countries including Hungary Baclofen has become the drug most often selected for the medicinal relaxation of hypermyotonia in spastic hemiparetic patients. This was partially due to the incorrectly selected dose range (3×50–100 mg daily) and also to the lack of controlled double-blind studies performed by an adequate method. Of the two functional tests selected by us, the Rivermead scale proved to be suitable for the indirect measurement of spasm. Namely, this scale expresses the movement performance of paretic extremities, which performance depends on the muscular strength, the muscular tonus (and its distribution) and the coordination. Under the conditions of our study, hemiparetic patients of the same age and

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suffering from hemiparesis of the same severity received identical treatment, with the only difference that they received either of two different muscular tension relaxing drugs in two groups formed at random. With high certainty, the statistically significant difference observed in the movement performance of the patients can be explained by the efficacy difference between the two drugs. There was no statistically significant difference between the two groups in the measured values of the Barthel index. We attribute this to the fact that the Barthel index measures the total performance of the individual examined, irrespective of which hand of the patient and what appliances are used for performing the self-supporting functions in question.

In conformity with the results of the functional tests, Mydeton proved to be more effective than Baclofen also on the basis of the semi-subjective opinion of the examining physician and the subjective opinion of the patients. However, we must emphasise that this higher efficacy was achieved with Mydeton administered in a dose higher than usual, i.e. in a total daily dose of 450 mg. Another argument for the future use of Mydeton is that, at the doses tested, Mydeton causes far fewer side effects than Baclofen.

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