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Tetrabenazine (Nitoman) Therapy of Chronic Spontaneous Oral Dyskinesia

A Video- and EMG-Controlled Study

M. Bartels and E. Zeller

Department of Psychiatry (Director: Prof. Dr. H. Heimann), Osianderstrasse 22, D-7400 Tübingen, Federal Republic of Germany

Summary. Therapeutic results achieved with tetrabenazine in six patients with spontaneous oral dyskinesia were evaluated by clinical rating as well as time-blind video and EMG assessment. Dramatic improvement of symptoms was observed in five of our six patients and good to satisfactory improvement in the remaining patient. The correspondance among clinical findings, EMG data, and video analysis was good. Medication was started at low doses and slowly increased. Adverse reactions (i.e., rigidity, akinesia, vasodepression) were minimal.

Key words: Tetrabenazine – Spontaneous oral dyskinesia – Therapeutic results – EMG

Introduction

Spontaneous oral dyskinesia, also referred to as buccolinguofacial dyskinesia (Delwaide et al. 1977, 1980) is characterized by involuntary, irregular movements of the pharyngeal, masticatory, and oral muscles. In contrast to neuroleptic-induced tardive dyskinesia in which dyskinetic-like movements of the extremities and trunk are present in approximately half the cases (Bartels and Themelis 1983) or L-dopa-induced hyperkinesia in which dyskinesia occurs primarily in the extremities (Gerlach 1977), this movement disorder is almost always limited to the orofacial region. While the etiology of most movement disorders in elderly patients is unclear, it is assumed that a functional shifting of the dopamine-acetylcholine relationship in the striate bodies in favor of dopamine, due to vascular-induced degenerative processes, plays an essential role (Rüther et al. 1978).

The results of clinical trials with classic neuroleptic agents such as perphenazine and haloperidol or cholinomimetic substances such as deanol acetamidobenzoate (Casey 1977) have not been convincing.

As early as 1973, Kazamatsuri reported satisfactory results with tetrabenazine therapy in neuroleptic-induced tardive dyskinesia. Based on a previous study (Schumm et al. 1981) with excellent results, but which was an open trial, we attempted better quantification and objectivity of the therapeutic findings.

Offprint requests to: M. Bartels at the above address

Method

The individual data for our six patients are presented in Table 1. Disturbed cerebral circulation was diagnosed in all of the patients. The mean duration of the disorder was 12.2 (±7.4) months. The various drugs administered prior to Nitoman therapy are also included in Table 1. The tetrabenazine dosage was gradually increased over a 3-day period to 50 mg. When this dosage proved ineffective and when the patient's condition permitted, it was increased to a maximum of 100 mg/day. Rigidity was clinically and anamnestically estimated by questioning the patient and his or her family, and then rated according to the following degrees of severity: 0 = absent, 1 = normal to minimal, 2 = mild, 3 = moderate, 4 = severe. Severity was initially estimated clinically once a day and then at 14-day intervals.

Video Analysis

A standardized video interview was carried out at the same time each day and recorded with a semiprofessional stereosound video recorder (Panasonic NV 8200), using one channel as a sound channel and the other to record electrical activity arising from the upper part of the orbicularis oris muscle. The electrical potentials were amplified with a standard electromyograph (EMG) unit (DISA 13 A 69), and EMG was performed with bipolar leads, using small surface electrodes (amplification 500 μ volt/division). The 20-min interview included two 1-min relaxation phases, one sensomotor provocation phase (simple writing, drawing, and speech tasks) and one emotional stress phase.

The Data were Evaluated as Follows: Sound and EMG signals were recorded from the video cassette to a recorder with a paper speed of 10 mm/s, and the interview was transcribed verbatim. EMG discharges preceeding dyskinesia were counted and, for purposes of comparability, extrapolated to 5 min. The provocation phase potentials during the EMG burst were measured (Figs. 1 and 2). Videotapes were evaluated by two time-blind experienced neuropsychiatrists.

The extent of orofacial dyskinesia was assessed with a modification of the abnormal involuntary movement scale; buccolinguofacial movements were rated according to the following degrees of severity: 0 = absent, 1 = normal to minimal, 2 = mild, 3 = moderate, 4 = severe.

Table 1. Age, sex, neurologic and pharmacotherapeutic patient data

Patient	Age	Sex	Topographic distribution	Mean daily dosage of tetrabenazine (in mg)	Primary disease	Therapy	Duration (in months)	Observation time (in months)
KB	74	M	BLM	100	DCC	Piracetam	24	18
FR	73	F	BLM	50	DCC	Meclofenoxat	12	8
MU	77	F	BLM	50	DCC	Biperiden	12	36
MZ	81	F	BLM	75	OP	Thioridazine	6	24
ML	72	F	BLM	50	DCC	Piracetam	16	24
ES	47	F	L[a]	50	DCC	Biperiden	3	12
Mean ± SD							12.2 ± 7.4	20.3 ± 9.9

DCC = disturbed cerebral circulation
OP = organic psychosyndrome
[a] EMG lead from mylohyoideus muscle

Table 2. EMG bursts in 5-min interval, EMG baseline, tonus, clinical and video rating of sample

Patient	Without specific medication	Tetrabenazine	EMG baseline activity	Tonus	Clinical rating pre – post	Video rating pre – post
KB	124	32	(+)[a]	0[b]	3 1 (−2)	4 2 (−2)
FR	710	10	+	+	4 1 (−3)	4 1 (−3)
MU	187	20	+	+	4 2 (−2)	4 1 (−3)
MZ	188	24	(+)	0	4 2 (−2)	3 1 (−2)
ML	720	65	+	++	4 0 (−4)	4 1 (−3)
ES	280	31	+	+	4 1 (−3)	4 2 (−2)

[a] (+) = slight increase
+ = marked increase
[b] 0 = unchanged
+ = increased
++ = rigidity with cogwheel sign

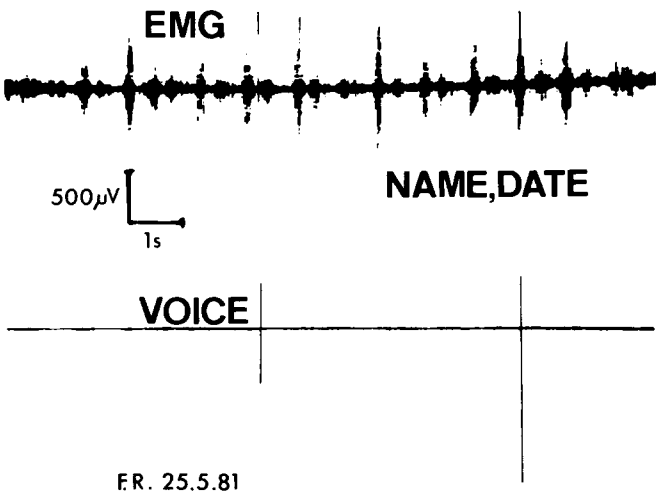

Fig. 1. EMG activity and sound channel during one phase of sensomotor provocation in a female patient before Nitoman therapy

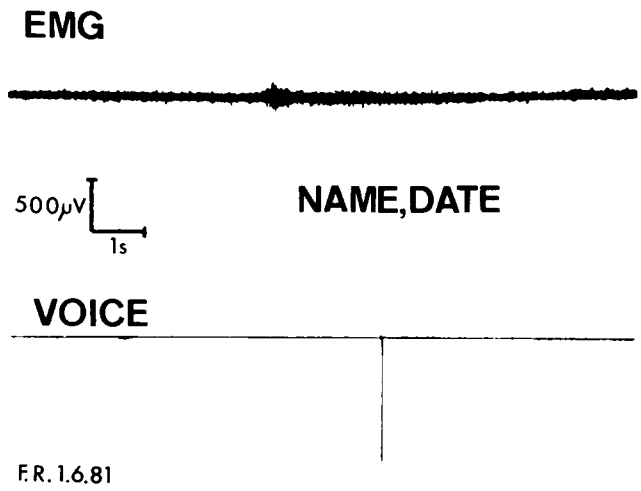

Fig. 2. EMG activity and sound channel during one phase of sensomotor provocation in a female patient with Nitoman therapy. Note increased EMG baseline activity

Results

Assessment of clinical improvement based on interviews of patients and their family as well as on clinical impression revealed marked improvement in five of our six patients, and good improvement in the remaining patient (for individual values, see Table 2). The frequency of dyskinetic movement on time-blind video analysis dropped dramatically in three patients and markedly in the other three. The EMG burst count decreased dramatically in all patients. Residual dyskinetic

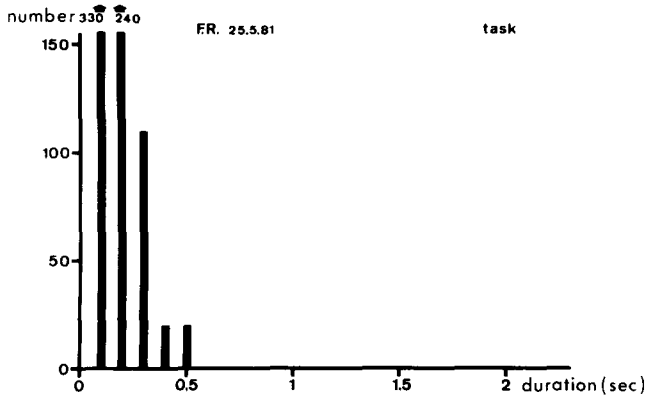

Fig. 3. Number and duration of EMG bursts before Nitoman therapy and with provocation (extrapolated to 5 min)

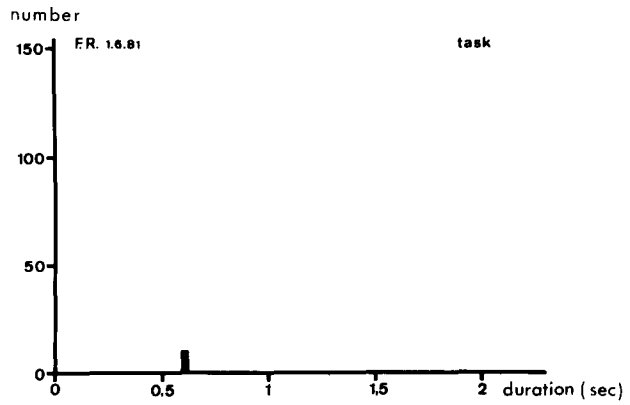

Fig. 4. Number and duration of EMG bursts with Nitoman therapy and provocation (extrapolated to 5 min)

movements with pharmacotherapy ranged between 5% and 25% of the initial values. Tonus was unchanged on clinical tests in two patients, slightly increased in three patients, and moderately increased in one patient; EMG analysis additionally revealed increased baseline activity in those patients with increased tonus. One representative example of decreased dyskinetic movement and increased baseline activity is shown in Figs. 1–4.

Discussion

Our clinical trial showed an impressive reduction of movement disorders in some patients after 3 days, but usually after 1 week. A maximum dosage of 50 mg/day was generally sufficient; in two cases, however, 75 and 100 mg/day were necessary. The initial adverse reactions were tiredness, disturbed orthostatic regulation, and, in four patients, mild rigidity. The tiredness and mild orthostatic dysregulation disappeared in all patients after 1 to 3 weeks. While the mild rigidity persisted, both the patients and their relatives accepted it far better than the hyperkinetic syndrome. Interestingly enough, rigidity demonstrated on clinical tests was also detectable in the increased EMG baseline activity. Contrary to Marsden (1973), none of our patients were depressive. Instead, we observed pronounced improvement in the mood of most patients. This change in mood could have been an emotional reaction to the dramatic improvement in motor impairment experienced by the patient.

The favorable therapeutic results reported in this study correspond to the good symptomatic results achieved in tardive dyskinesia (Brandrup 1961; Godwin-Austin and Clark 1971; Kazamatsuri et al. 1973) and spontaneous oral dyskinesias (Pakkenberg et al. 1968, 1974). In contrast to Fog and Pakkenberg (1970) (see also Kazamatsuri et al. 1973), dyskinesia did not recur in our patients, who have now been followed for more than 2 years. Patient compliance, which is easily controlled since Nitoman is not commercially available in the Federal Republic and therefore must be obtained by special order, is excellent. We attribute the favorable therapeutic results to our tailoring of the dosage to the needs of the individual patient at initiation of and during therapy. We are aware of the fact that Nitoman, like reserpine, which, however, can be better regulated, lowers the concentration of dopamine (and also serotonin and norepinephrine) in the striate bodies via release of the presynaptic nerve terminals and therefore is a purely symtomatic therapy. Our EMG results also clearly indicate that a pronounced hypotonic-hyperkinetic picture is replaced by a variously pronounced hypertonic-hypokinetic picture. The good patient compliance, however, shows that Nitoman has a favorable and long-term effect on this extrapyramidal movement disorder.

In summary, we conclude that Nitoman considerably enriches the possibilities of treating spontaneous oral dyskinesia, a disorder which up to now has not responded satisfactorily to therapy. Moreover, therapeutic success in disorders of the extrapyramidal system, which are otherwise extremely difficult to quantify, can be reliably evaluated with the lead method introduced in our study.

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