

Ipertermia Maligna e Morte nella Malattia di Parkinson

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[Akinetic crisis--a possible form of parkinsonism]

[Article in German]

Gehlen W.

Publication Types:

- Letter

PMID: 836388 [PubMed - indexed for MEDLINE]

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[Akinetic crisis--a possible manifestation of Parkinson's disease]

[Article in Norwegian]

Sundal E.

PMID: 635862 [PubMed - indexed for MEDLINE]

Gehlen W. Akinetic crises-a possible form of parkinsonism. Dtsch Med Wochenschr 1977; 18:102.

Sundal E. Akinetic crises-a possible manifestation of Parkinson's Disease. Tidsskr Nor Laegeforen 1978;28:98.

Bachli E, Albani C. Akinetic crisis in Parkinson's disease. Schweiz Med Wochenschr 1984;11:124.

Fortschr Med 1982 Sep 16;100(35):1583-5

[3 crises in Parkinson disease]

[Article in German]

Danielczyk W.

Three dangerous crises have great influence on the social relations of the Parkinson-patient and his life. Two of the three crises show the importance of the psychical component of the disease: In the beginning of the disease we often see a phase of "masked Parkinsonism" with serious depression. A hard break takes place in the patient's way of life. The second crisis is a phase of psychotic symptoms such as halucinations, paranoid ideas and mental confusion. This phase is a reaction between the disease and the antiparkinsonian medication. In the third, the akinetic crisis at last an extinction of physical mobility and psychic-reaction ability place takes. It is very important to start immediately with specific therapy in every one of the three crises.

The profile of hospitalised patients with Parkinson's disease.

chest infections	22%
falls	13%
PD symptoms	10%
general medical problems	9%
urinary dysfunction	8%

Postoperative complications in Parkinson's disease. Pepper PV, Goldstein MK, *J Am Geriatr Soc* 1999 Aug;47(8):967-72, Dept. of General Internal Medicine, Naval Medical Center San Diego, California 92134-5000,USA.

.....longer acute hospital stays than non-Parkinson's patients (11.4 +/- 15.9 days vs 8.8 +/- 9.0 days, $P < .001$). In addition, Parkinson's patients had a higher in-hospital mortality than non-Parkinson's patients (7.3% vs 3.8%, $P = .006$). Parkinson's patients had significantly increased incidences of urinary-tract infection (odds ratio 2.045, $P < .001$), aspiration pneumonia (odds ratio 3.825, $P < .001$), and bacterial infections (odds ratio 1.682, $P < .001$).

Neuroleptic Malignant Syndrome

**Ipertermia maligna e Sindrome Acinetica da
sospensione della dopamino-stimolazione**

Coscienza Alterata

Ipertermia

Disfunzione Autonoma

Rigidità Muscolare

DSM IV

Ipertermia

2 o più dei seguenti

Rigidità muscolare

Diaforesi

Disfagia

Tremore

Incontinenza

Alterazione della coscienza

Tachicardia

Iper/ipo tensione

Leucocitosi

↑CPK

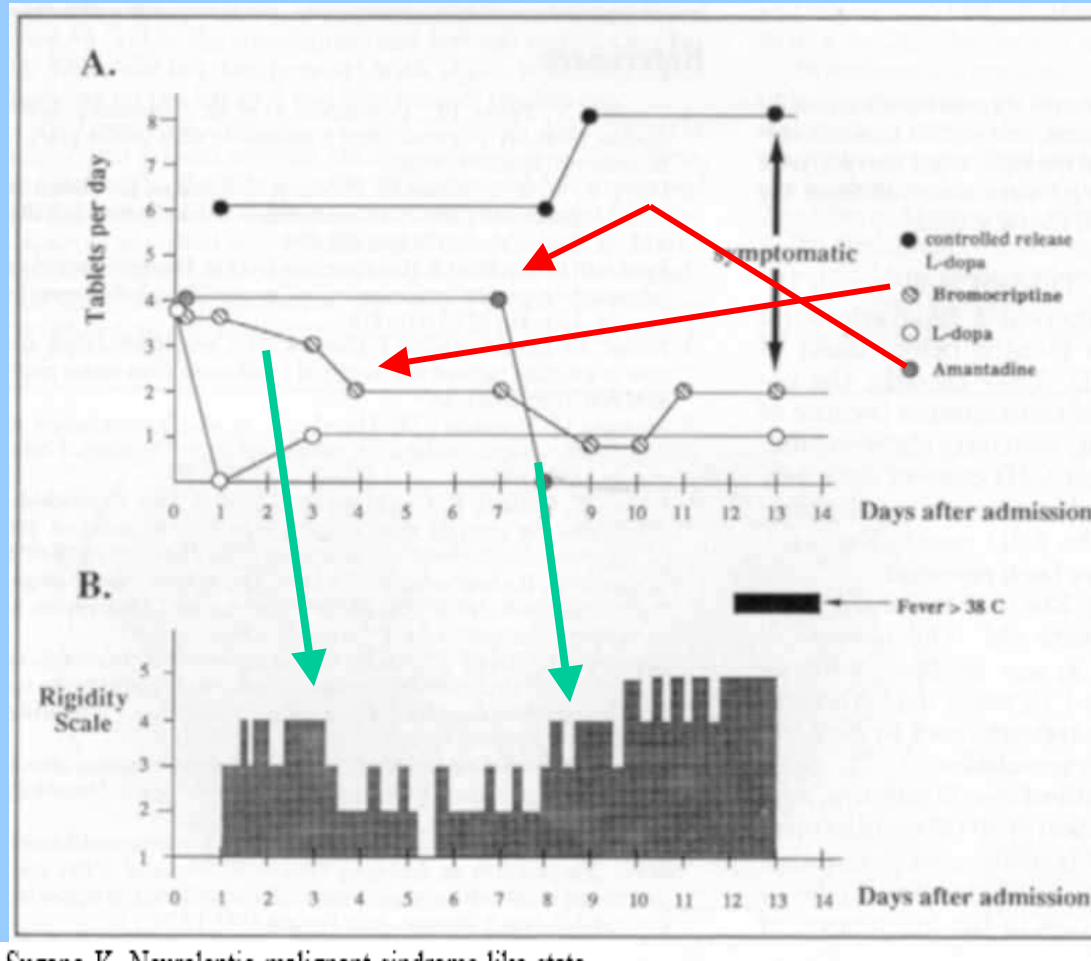
NMS nella Malattia di Parkinson

- **Sospensione improvvisa di L-DOPA** ^{1,2}
- **Sospensione di L-DOPA e Bromocriptina** ³
- **periodo “off”**⁴
- **cambiamenti nella terapia**⁵
- **neurolettici atipici** ^{6, 7}

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Controlled-release delivery of L-Dopa associated with nonfatal hyperthermia, rigidity, and autonomic dysfunction

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following withdrawal of antiparkinsonian drugs. J Nerv Ment Dis 1981;168:324-327.

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NEUROLOGY/2004/044529

Acute Akinesia in Parkinson's Disease

Marco Onofrj and Astrid Thomas

Group I										Acute Akinesia								Recovery				
Pt.n°/sex	age	DD	H/Y	L-Dopa	other:	III	I	PF	H/Y	III	I	therapy	Temp.	CPK	MYO	days	H/Y	III	I			
			on/off	mg/day	mg/day	on / off						mg/day	°C/days									
1/m	42	2	2	-	0	C 12	28	-	0	F	3	64	1	-	38,8	5	315	201	12	2,0	32	0
2/m	66	1	1	-	0	B 8	13	-	0	F	4	72	4	L-D + 375	39,2	6	412	218	16	1,5	26	0
3/m	39	2	2	-	600	R 15	18	-	2	F	4	40	2	L-D +300	38,1	2	985	398	7	2,0	18	2
4/m	71	8	3	4	725	Br 15	36	10	1	F	4	79	1	A 100	40,1	5	801	670	18	3,0	38	1
5/w	74	11	3	3	1200	-	42	56	1	F	5	86	4	A 100-200	40,0	18	2870	1430	-	-	-	-
6/m	67	4	2	-	725	R 6	51	-	1	F	5	84	5	A 100-200	38,5	5	1004	820	9	2,0	52	2
7/m	69	9	2	-	600	Pg 3	36	-	2	BP	5	62	2	A 200	39,8	7	801	772	21	3,0	41	2
8/m	74	9	3	3	600	Br 15	49	62	2	BP	5	96	5	A 200	40,5	18	1205	898	-	-	-	-
9/m	65	3	2	-	500	R 15	34	-	0	BP	4	57	0	L-D +400	38,7	3	220	99	10	2,0	33	0
10/w	76	11	3	4	925	-	42	54	3	BF	5	90	3	A 100	36,6	0	140	102	26	3,0	46	3
11/m	73	12	2	3	900	-	40	52	1	BF	4	62	1	A 50	36,6	0	35	25	5	2,5	42	1
12/m	75	9	2	-	725	Br 30	48	-	1	BF	4	84	1	L-D +200	36,7	0	85	46	4	2,5	48	1
13/m	72	10	2	3	600	P 2,1	54	65	1	BF	4	79	1	L-D +400	36,8	0	65	32	9	2,5	56	1
14/w	71	14	2	-	600	Pg 3	46	-	0	BF	4	77	4	A 150	38,0	4	1012	356	12	2,5	46	1
15/w	67	6	2	-	625	P 2,1	41	-	0	BF	4	61	4	A 200	39,0	10	828	415	21	3,0	50	1
16/w	77	13	3	4	1200	-	62	75	4	BF	5	91	7	A 75-100	38,9	13	1028	820	-	-	-	-
17/m	68	9	2	3	725	-	51	64	0	BF	5	82	0	A 100	38,8	4	870	512	6	2,5	51	0

Group II										Acute Akinesia								Recovery				
Pt.n°/sex	age	DD	H/Y	L-Dopa	other:	III	I	PF	H/Y	III	I	therapy	Temp.	CPK	MYO	days	H/Y	III	I			
			on/off	mg/day	mg/day	on / off						mg/day	°C/days									
18/m	72	9	3	4	900	-	36	62	0	GI	4	57	4	A 150	38,1	2	2502	1340	4	3,0	36	1
19/w	69	8	3	4	725	R 15	41	58	0	GI	5	78	4	A 100-200	38,8	7	1205	998	14	3,0	46	0
20/m	76	5	2	-	900	R 21	36	-	0	GI	4	67	4	A 150	39,9	6	600	420	14	3,0	35	1
21/w	73	13	3	-	800	C 6	46	-	2	dw	5	87	2	A 150-200	39,0	7	1660	998	-	-	-	-
22/m	76	11	3	4	850	Br 30	42	57	5	dw	5	76	5	-	40,1	2	2109	998	6	3,0	42	5
23/w	68	8	2	-	650	R 24	36	-	1	dw	4	57	1	L-D +350	36,7	0	344	230	6	2,5	36	1
24/w	82	6	2	-	500	-	39	-	0	dw	4	68	1	A 100	36,5	0	75	56	12	2,0	42	0
25/m	68	4	2	-	600	Pg 3	28	-	4	Ia	4	49	3	A 75-100	40,9	2	356	225	3	2,0	28	2
26/m	75	16	3	4	900	-	56	69	2	Ia	5	91	2	A 150	38,5	4	629	560	10	3,0	68	1



Malignant syndrome in Parkinson's disease: concept and review of the literature

Yoshikuni Mizuno^{a,*}, Hideki Takubo^b, Eiji Mizuta^c, Sadako Kuno^c

Table 1
Clinical features of levodopa withdrawal malignant syndrome

Elevation of body temperature (up to 40 °C)
Marked rigidity
Altered consciousness
Autonomic disturbance
Tachycardia
Perspiration
Anhidrosis
Non-obstructive ileus
Fluctuation of the blood pressure
Vocal cord paralysis
Elevation in serum creatine kinase
Rhabdomyolysis
DIC
Acute renal failure (myoglobin plugging)

	Levodopa withdrawal malignant syndrome	Neuroleptic malignant syndrome	Malignant hyperthermia
Underlying disease	Parkinson's disease Secondary parkinsonism	Schizophrenia Manic depressive psychosis	Central core disease in some cases
Genetics	Sporadic	Sporadic	Autosomal dominant and sporadic
Triggering event	Withdrawal of anti-parkinsonian drugs, particularly levodopa	Neuroleptic drugs	Inhalation anesthesia
Muscle rigidity	Marked	Marked	Marked
Body temperature	Marked elevation	Marked elevation	Marked elevation
Consciousness	May be disturbed	May be disturbed	May be disturbed
Autonomic dysfunction	Present	Present	
Serum CK	Marked elevation	Marked elevation	Marked elevation
Rhabdomyolysis	May occur	May occur	May occur



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 Parkinsonism &
 Related Disorders

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A collaborative study on the malignant syndrome in Parkinson's disease and related disorders

Hideki Takubo^a, Toshihide Harada^b, Takao Hashimoto^c, Yutaka Inaba^d, Ichiro Kanazawa^e,
 Sadako Kuno^f, Yoshikuni Mizuno^{g,*}, Eiji Mizuta^f, Miho Murata^h, Toshiharu Nagatsuⁱ,
 Shigenobu Nakamura^b, Nobuo Yanagisawa^j, Hirotarō Narabayashi^k

UPDRS and Hoehn & Yahr stage scores

	Before MS	During MS	After MS
Hoehn & Yahr stage	3.4 ± 0.6	4.7 ± 0.6**	3.8 ± 0.8**
Dementia	1.0 ± 1.2	1.2 ± 1.4*	1.1 ± 1.4*
<i>Tremor</i>			
Upper extremity	0.54 ± 0.8	0.57 ± 0.9	0.45 ± 0.7
Lower extremity	0.27 ± 0.7	0.34 ± 0.7	0.29 ± 0.6
<i>Rigidity</i>			
Upper extremity	1.4 ± 0.9	1.9 ± 1.1**	1.3 ± 0.9
Lower extremity	1.3 ± 0.9	2.0 ± 1.2**	1.5 ± 1.0
Axial	1.3 ± 0.9	2.0 ± 1.2**	1.5 ± 1.0
Akinesia	2.2 ± 0.9	3.6 ± 0.8**	2.5 ± 1.0**
Speech disturbance	1.8 ± 0.8	2.8 ± 1.0**	2.0 ± 1.0**
Finger tap	1.8 ± 0.9	2.7 ± 1.1**	2.1 ± 1.1**
Stooped posture	1.8 ± 0.9	3.2 ± 1.1**	2.0 ± 1.1*
Gait	2.1 ± 1.0	3.7 ± 0.7**	2.4 ± 1.1**
Retropulsion	2.1 ± 0.9	3.6 ± 0.9**	2.4 ± 1.1**

Precipitating events for MS

Causes	PD	Other Parkinsonism	Total
Number of episodes	77	22	99
Withdrawal or reduction of drugs	24	5	29
Because of hallucination	21	4	25
Other reasons	3	1	4
Infectious diseases	12	7	19
Respiratory tract	5	4	9
Urinary tract	5	2	7
Others	2	1	3
Anorexia/poor food intake	13	0	13
Dysphagia	2	5	7
Poor medication compliance	6	0	6
Fall/fracture	4	2	6
Wearing off alone (no other triggers)	5	0	5
Hot weather	3	0	3
Cerebral infarction	2	1	3
Ileus	2	0	2
Strenuous physical activity	1	0	1
Unknown	3	2	5

Clinical features of recovered and non recovered patients (mean \pm SD)

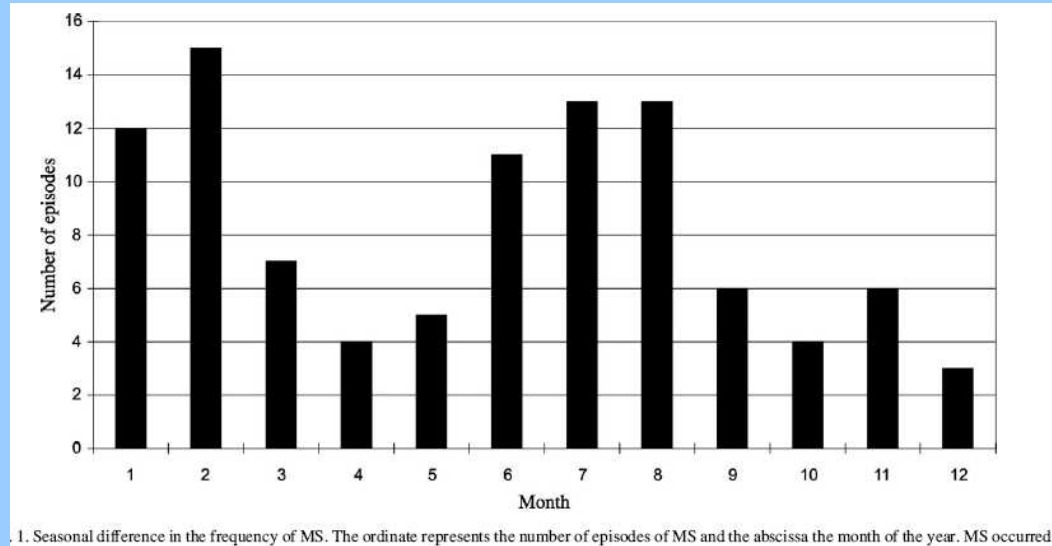
	Recovered	Non- recovered
Number of episodes	68	31
Age	67.6 \pm 8.8	73.9 \pm 9.2**
<i>Sex</i>		
Male	40	20
Female	28	11
Duration of the disease (years)	9.4 \pm 7.3	7.5 \pm 4.7
<i>Primary disease</i>		
PD	56	21
Other parkinsonism	12	10
<i>Hoehn & Yahr stage</i>		
Before MS	3.4 \pm 0.5	3.5 \pm 0.7
During MS	4.6 \pm 0.6	4.9 \pm 0.4*
After MS	3.4 \pm 0.6	4.6 \pm 0.6**
<i>Problems prior to the development of MS</i>		
Hallucination	33	14
Wearing off	26	5*
Dementia	17	8
Dyskinesia	12	4
Autonomic disturbance	11	2
<i>UPDRS scores prior to the development of MS</i>		
Arm rigidity	1.2 \pm 0.8	1.9 \pm 1.0*
Axial rigidity	1.6 \pm 0.9	2.1 \pm 0.9*
Akinesia	2.2 \pm 0.8	3.3 \pm 1.0**

Treatment of MS

	Number of episodes
Intravenous fluid infusion	97
Cooling	78
Antibiotics	59
Dantrolene sodium	57
Addition or increase of anti-parkinsonian drugs	42
Addition of bromocriptine	20
Intravenous levodopa infusion	32
Antipyretics	11
Treatment of DIC	10
Gamma-globulin	8
Hemodialysis	2
Corticosteroid	2
Diazepam	2

Majority of patients received multiple modalities of treatment as needed. The total number of patients was 93. One patient had four recurrences and three patients had two recurrences of MS.

Seasonal differences



Malignant syndrome in Parkinson's disease: Presentation of three cases occurring during the 2003 heat wave

C. Gaig, M. Gomez-Choco, S. Amaro, M. Marti, E. Tolosa (Barcelona, Spain)

Objective: To present three patients with Parkinson's disease (PD) who developed Malignant syndrome (MS) during summer heat wave of 2003 in Barcelona

Background: Malignant syndrome (MS) is an infrequent complication that can occur in patients with PD following sudden dopaminergic treatment withdrawal. Other known precipitating factors of MS include intercurrent infection, dehydration or hot weather. It is a serious and potentially lethal disorder. Early diagnosis and treatment are essential for a favourable prognosis.

Patients: Three patients with advanced PD (H&Y stage IV; mean age 73.6 years; mean disease duration 10years) presented a subacute worsening of parkinsonism, associated with hyperthermia, altered consciousness, autonomic dysfunction and increased serum creatine kinase (CK) levels. Other abnormal laboratory test were leukocytosis, hypernatremia and increased transaminases. None of them had stopped or reduced their anti-parkinsonian drugs and no other triggers for MS except for warm weather were detected. Diagnosis was delayed because in all three cases infection was initially suspected. Treatment with intravenous fluid infusion, external body cooling, bromocriptine and dantrolene was applied. Two patients recovered quickly, but the third died of respiratory failure.

Congress of Parkinson's Disease and Movement Disorders June 14-17 Rome, Italy, p420

AA appearing during respiratory tract infections, trauma or bone surgery

6 patients (pt. 1-6) had AA 3-4 days after the onset of a flu-like syndrome

2 patients (pt. 7, 8) had AA two days after the onset of fever in the course of bronchopneumonia

1 patient (pt 9) had AA and confusion during a gallbladder inflammation

8 patients (pt. 10-17) presented AA 3-4 days after hip-joint surgery or bone fractures

AA akin to NMLS

3 patients (pt. 18-20) had AA during acute GI disturbances (duodenal ulcers,intestinal volvulus)

1 patient (pt. 21) had AA during pneumonia-dysphagia (discontinuation of anti-PD therapy

1 patient (pt 22) had AA because of amantadine withdrawal

1 patient (pt. 23) had AA 12 hrs after switch from ropinirole 24 mg/day to pramipexole 2.1 mg/day

1 patient (pt. 24) had AA because of treatment withdrawal for 4 days for a colonoscopy

2 patients (pt 25-26) presented AA and hyperthermia, following risperidone administration

Table 2 Demographics and Follow-up evaluation

	Total Group (26 pts)	AA 1 st Group (17 pts)	AA 2 nd Group (9 pts)
Age	69.3±9.3	67.4±10.8	74.9±5.7
Sex (w/m)	9/17	5/12	4/5
Duration of disease	8.2±3.9	7.8±4.1	8.9±3.9
H/Y baseline	2.5±0.5	2.4±0.6	2.7 ±0.4
H/Y AA	4.4±0.6	4.3±0.6	4.4±0.5
H/Y recovery	2.5±0.5*	2.4±0.5***	2.7±0.5**
UPDRS III baseline	40.4±10.9	40.0±12.7	41.1±8.2
UPDRS III AA	72.98±14.5	74.0±15.1	70.5±14.8
UPDRS III recovery	41.5±11.0*	40.6±10.9***	42.7±11.7**
ADL baseline	70.4±13.4	70.0±15.0	71.3±10.5
ADL AA	12.7±13.7	15.9±15.4	6.7±7.1
ADL recovery	74.0±10.5*	72.1±12.5***	71.3±6.4**
Mentation baseline	1.3±1.4	1.1±1.2	1.6±1.8
Mentation AA	2.7±1.8	2.6±2.1	2.8±1.4
Mentation recovery	1.0±0.8*	1.1±0.9***	0.9±0.7**
T °C	38.6±1.3	38.5±1.3	38.7±1.4
CPK IU	852.9±744.3	745.4±700.3	1035.1±814.2
Myo ng/ml	524.7±414.8	456.4±406.4	634.0±425.2
Recovery in days	11.2±6.2*	13.1±6.8***	8.31±8.6**
Increment body temperature (days)	4.3±3.5	5.6±3.2	1.7±2.9
Mean L-DOPA dose baseline	695.2±273.7	661.8±320.6	758.3±147.9
Mean L-DOPA dose AA	852.8±272.5	813.9±311.1	926±171.4
Mean L-DOPA dose recovery	756.8±281.7*	704.4±294.9***	848.2±245.6**

* 22 surviving patients; ** 8 surviving patients; *** 14 surviving patients



cohort

VS

multicenter

Table 3 Prevalence of laboratory abnormalities, treatments and symptoms

	Patients n°
Fever	20/26
CPK	21/26
MYO	22/26
L-Dopa baseline	24/26
L-Dopa recovery	21/22
Dopamino agonist baseline	20/26
Dopamino agonist recovery	16/22
Amantadine baseline	1/26
Amantadine recovery	0/22
I- Comt baseline	5/26
I-Comt recovery	2/22
"on-off" baseline	14/26
"on-off" recovery	10/22
Mentation baseline	8/26
Mentation recovery	10/22

Laboratory findings before, during, and after developing MS

	Before MS	During MS	After MS
Total protein (g/dl)	6.9 ± 0.6	6.4 ± 0.9**	6.4 ± 0.6**
Total bilirubin (mg/dl)	0.67 ± 0.3	1.1 ± 0.9**	0.62 ± 0.3
Al-P (IU/l)	228 ± 88	221 ± 147	305 ± 330
GOT (IU/l)	23 ± 17	142 ± 497**	29 ± 28**
GPT (IU/l)	20 ± 18	89 ± 484**	28 ± 25**
γ-GTP (IU/l)	18 ± 16	21 ± 23	34 ± 37**
CK (IU/l)	118 ± 107	3196 ± 5758**	102 ± 206
LDH (IU/l)	359 ± 122	840 ± 1729**	401 ± 168
BUN (mg/dl)	17.4 ± 5.3	25 ± 16**	15 ± 8.7**
Creatinine (mg/dl)	0.77 ± 0.4	0.89 ± 0.54	0.71 ± 0.74**
Uric acid (mg/dl)	4.6 ± 1.4	4.5 ± 2.1	3.8 ± 1.3*
Na (mEq/l)	141 ± 2.9	139 ± 6.2*	140 ± 4.5*
K (mEq/l)	4.1 ± 0.3	4.0 ± 0.5	4.2 ± 0.4
Cl (mEq/l)	105 ± 3	103 ± 5.8	103 ± 4.5
RBC (× 10 ⁴) (cmm)	418 ± 47	414 ± 51	376 ± 62*
Hb (g/dl)	12.9 ± 1.4	12.9 ± 1.6	11.8 ± 1.6*
Ht (%)	38.7 ± 4.0	38.4 ± 4.6	35.5 ± 4.6*
WBC (cmm)	6673 ± 2087	10137 ± 5067**	6549 ± 2249
Platelet (× 10 ⁴) (cmm)	21.7 ± 4.6	19.2 ± 6.6**	26.8 ± 8.9**
CRP (mg/dl)	1.0 ± 1.7	8.3 ± 9.8**	1.5 ± 2.7
ESR (h)	12.3 ± 6.3	32.4 ± 26**	29.7 ± 24
FDP (mg/l)	nd	13.3 ± 19	7.9 ± 6.1
Serum myoglobin (ng/ml)	nd	372 ± 629	97 ± 136
Urinary myoglobin (ng/ml)	nd	20133 ± 89411 ^a	13.2 ± 18.3

cohort

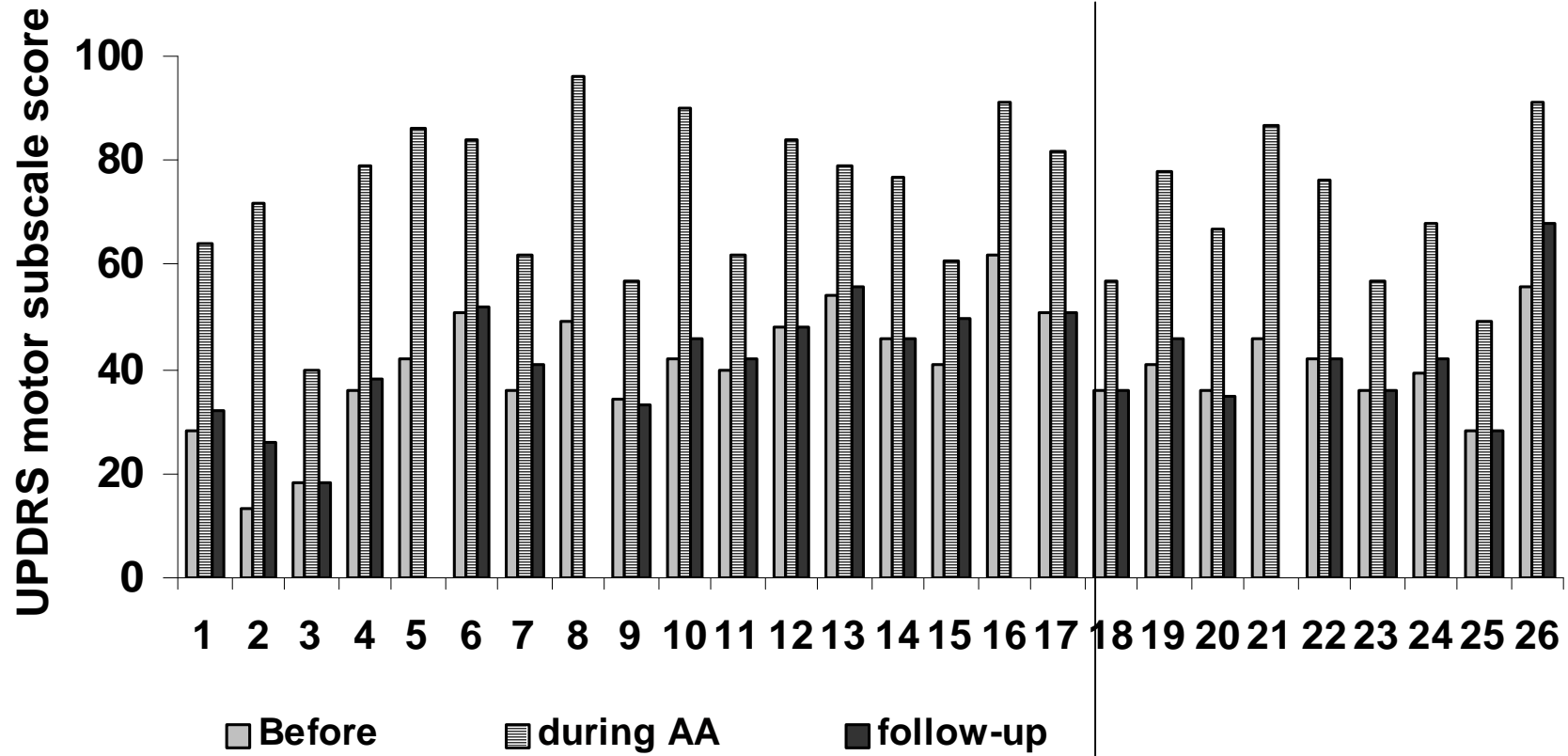
VS

multicenter

	Complete recovery	Partial recovery
	9.3±5.9 days	16.0±4.3days
	16 patients	6 patients
Age	67.8±11.5	70.3±4.2
Duration of disease	7.6±3.7	7.5±5.0
H/Y baseline	2.4±0.4	2.3±0.8
H/Y akinetic state	4.2±0.5	4.5±0.6
H/Y follow-up	2.4±0.4	2.8±0.6
UPDRS III baseline	39.3±9.7	37.2±13.9
UPDRS III akinetic state	68.6±14.4	71.8±11.3
UPDRS III follow-up	40.4±9.8	44.3±14.4
T °C	38.1±1.4	39.2±0.5
CPK IU/L	682.4±734.3	745.8±270.9
Myo ng/ml	382.0±391.4	563.3±281.1

Clinical features of recovered and non recovered patients (mean ± SD)		
	Recovered	Non- recovered
Number of episodes	68	31
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Hoehn & Yahr stage		
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During MS	4.6 ± 0.6	4.9 ± 0.4*
After MS	3.4 ± 0.6	4.6 ± 0.6**
<i>Problems prior to the development of MS</i>		
Hallucination	33	14
Wearing off	26	5*
Dementia	17	8
Dyskinesia	12	4
Autonomic disturbance	11	2
<i>UPDRS scores prior to the development of MS</i>		
Arm rigidity	1.2 ± 0.8	1.9 ± 1.0*
Axial rigidity	1.6 ± 0.9	2.1 ± 0.9*
Akinesia	2.2 ± 0.8	3.3 ± 1.0**

UPDRS before, during, after AA



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Danielczyk

Behandlung von akinetischen Krisen

Forschung und Praxis

Die Behandlung von akinetischen Krisen

W. Danielczyk

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(Vorstand: Univ. Prof. Dr. W. Jankovics)

In den letzten Jahren hat die Beschäftigung mit dem Biochemismus des Hirnstammes positive Auswirkungen auf die Behandlung des Parkinsonpatienten gezeigt. Die Therapie von Erkrankungen des Nervensystems, die scheinbar hoffnungslos weit hinter den Behandlungserfolgen bei Krankheiten anderer Organsysteme zurückgeblieben war, hat durch die zunehmende Erkenntnis der Wichtigkeit eines funktionierenden Zusammenspiels von Neurotransmittern und Neurorezeptoren einen entscheidenden Aufstoß bekommen. Es kann heute bereits als gesichert angenommen werden, daß die Balance der biogenen Amine (3) der entscheidende Faktor für die Aufrechterhaltung von motorischen und psychischen Funktionen ist, die im Hirnstammbereich ihre Schaltstellen haben. Der Weg vom Tierexperiment und den biochemischen Untersuchungen in vitro und in vivo bis zur Praxis des neurologischen Alltags ist lang. Ein allzu schematisches Denken, ein Sichergehen bei Konzeptionen von einem Forschungsprozess, der ständig weitergeht, ist für die Anwendung der neu

gefundenen Erkenntnisse keine erfolgversprechende Basis. Nur unter Berücksichtigung der differenzierten Eigenart des Patienten ist eine optimale medikamentöse Einstellung möglich, die dem Patienten ein Maximum an motorischer und psychischer Freiheit bei einem Minimum an unerwünschten Nebenwirkungen garantiert. Wesentlich ist dabei ein Anpassen der Therapie an die jeweilige Krankheitsphase.

Es gibt Patienten, die jahrelang auf L-Dopa allein oder unterstützt von einem Decarboxylasemmer und Anticholinergika sehr gut eingestellt sind und die auf Amantadin allein unbefriedigend ansprechen.

Bei einer anderen Gruppe erzielt man durch den Dopasparenden Amantadin-Effekt mit der Kombination L-Dopa + A. (7, 23) die günstigste Wirkung und es gibt wieder eine andere Gruppe, die auch auf geringe L-Dopa-Gaben mit Unverträglichkeitserscheinungen wie involuntary movements, Magenbeschwerden oder Kreislaufstörungen reagieren und für die nur A. allein — eventuell mit sehr geringen Beigaben von

J Neural Transm Suppl 1995;46:399-405

Twenty-five years of amantadine therapy in Parkinson's disease.

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Until a few years ago, the anti-parkinsonian effect of amantadine hydrochloride (AHC) and amantadine sulfate (AS) could not be explained. The beneficial effect of amantadine, which has been observed for a long time, may be connected with its site of action at the glutamatergic excitatory transmitter system, i.e. the N-methyl-D-aspartate receptor. A clear distinction can be made between AHC and AS with regard to this pharmacokinetic profile. Therefore, AS can be administered in higher doses than AHC and is thus more effective. A major advantage of AS is that it can also be given intravenously. Yet so far it is marketed only in twelve countries of the world. Intravenous infusions of AS permit the treatment of patients with aphagia during akinetic crises and when L-dopa and dopaminergic agonists are not tolerated in the akinetic terminal stage. Amantadine has the best ratio of therapeutic effects to side effects when compared with the other anti-parkinsonian drugs currently used. Long-term treatment with amantadine may have a considerable L-dopa saving effect. Given in higher doses, amantadine may permit a drastic reduction of L-dopa dosis and dopaminergic agonists so that the well known side effects of such drugs disappear. In addition, some authors assume a neuroprotective action of amantadine. Unlike L-dopa and dopaminergic agonists, AS does not produce hemiballism or dystonia.

Die Amantadinsulfat-Infusion in der Akut-Behandlung des Morbus Parkinson

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Neben der peroralen Amantadin-Therapie, überwiegend in Kombination mit L-Dopa-Präparaten und Anticholinergika, hat die Anwendung der Amantadinsulfat-Infusionslösung in der Akut-Behandlung des dekompensierten Parkinson gute Erfolge gebracht. Es wird von teilweise dramatischen Überreaktionen berichtet (1, 2). Doch liegen bisher nur wenige systematische Untersuchungen vor (2, 5). Über die eigenen Ergebnisse der letzten 5 Jahre wird berichtet.

53 Patienten mit unterschiedlichen Voraussetzungen wurden behandelt

Vom 1. 1. 1975 bis zum 31. 12. 1979 wurden 53 Patienten, die mit einem

* Amantadinsulfat, Produkt der Firma Merz, Frankfurt.

Leitlinien: Parkinson-Syndrome

4.3.4 Spezielle Behandlungsprobleme

Identifizierung des Auslösers:

- Dehydrierung
- Infekt
- Einnahmefehler
- Gabe von Neuroleptika
- Störungen der Resorption
Ileus, Diarrhö, Gastroenteritis
Antibiotikagabe

Allgemeine Maßnahmen:

- Flüssigkeits- und Elektrolytausgleich
- Ausreichende Kalorienzufuhr
- Thromboseprophylaxe
- Pneumonieprophylaxe
- Dekubitusprophylaxe
- Behandlung internistischer Grunderkrankungen und Komplikationen
- Fiebersenkung

Durchbrechung der akinetischen Krise

Amantadin i.v.

Dosis: 1 - 2 x 200 mg (über je 3 Stunden)

Maximal: 3 x 200 mg/d

L-Dopa per Magensonde, wobei sich die tägliche Dosis an der vorherigen Dosis orientiert.
Auch bei Gaben über die Magensonde auf Interaktion mit Sondenkost achten.

Zusätzliche Option unter intensivmedizinischen Bedingungen:

Apomorphin s.c.

Einmalige Bolusinjektion 2 - 10 mg

Wirkungseintritt: 10 - 15 min

Wirkungsdauer: 30 - 60 min

Weiterführung mit s.c. Dauerinfusion

initiale Dosierung: 1 - 2 mg/h; 8 - 12 h Pause in der Nacht

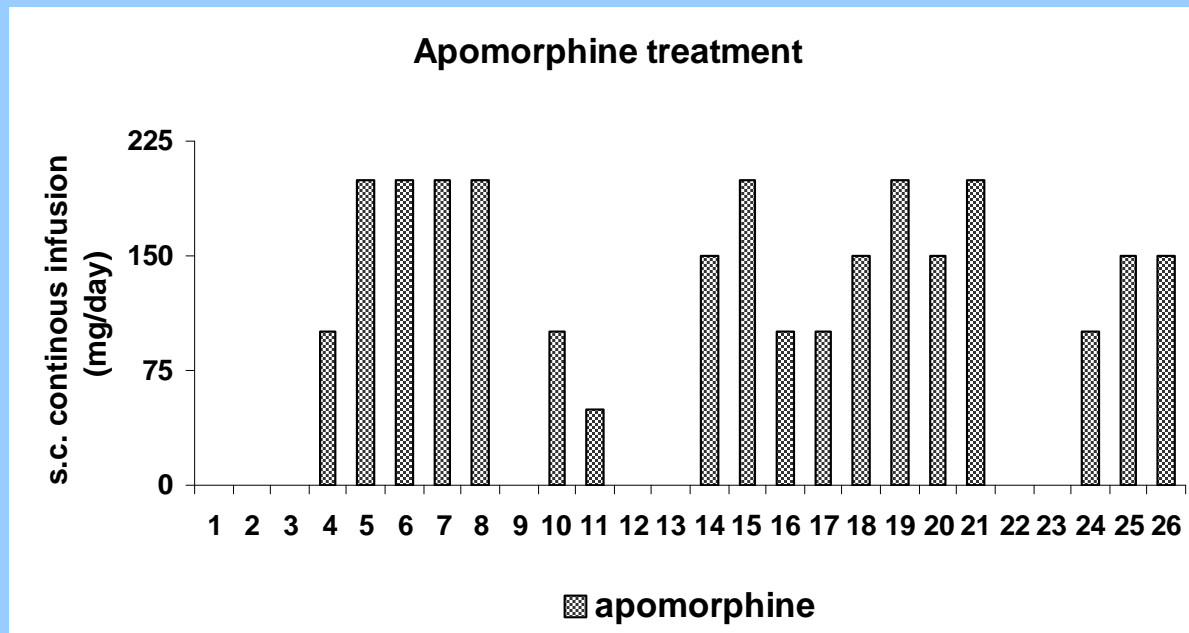
Steigerung: 0,5 - 1 mg/h alle 12 h

maximalen Rate: 10 mg/h (=170 - 240mg/d)

Gleichzeitige Gabe von Domperidon:

nicht notwendig, wenn dopaminerge Langzeittherapie.

Pre-treated with Ondansetron (antiemetic, 4-8mg e.v.)



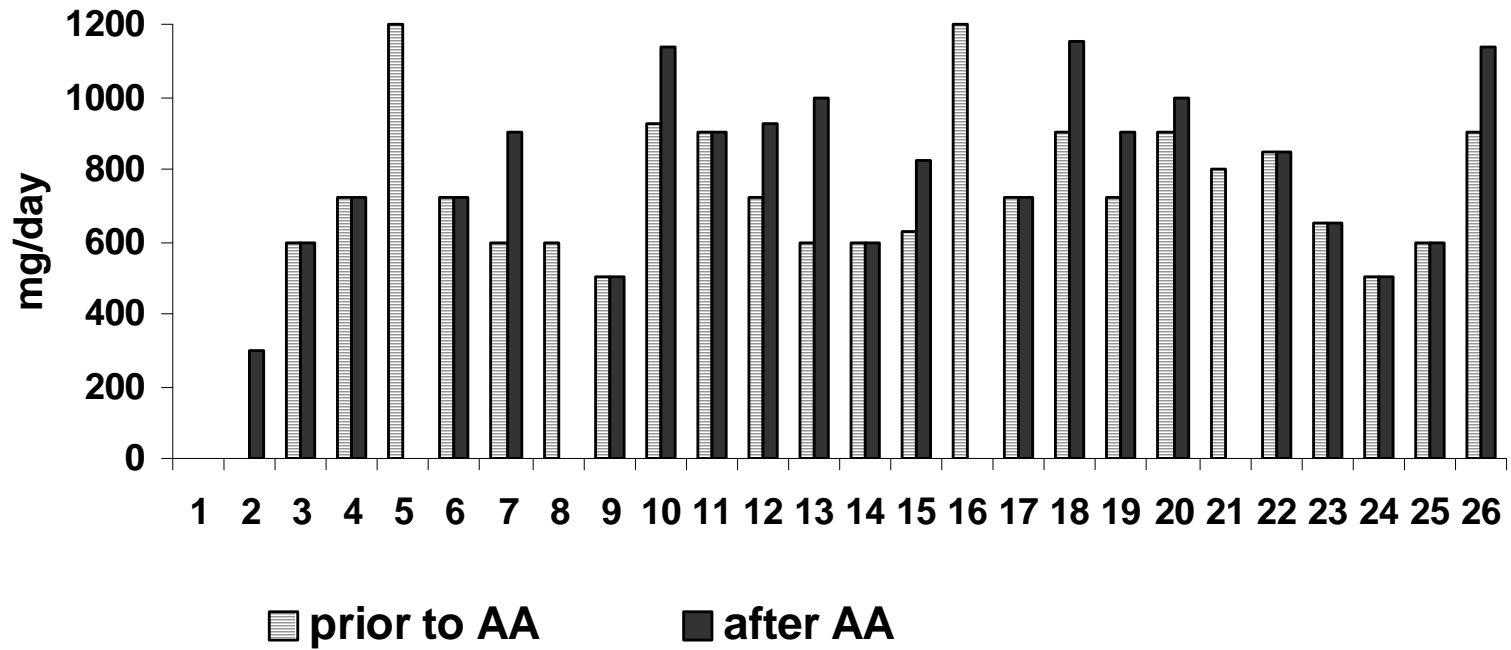
+

Dantriolene (50-200mg/day)

↑ CPK

Broussolle E Marion MH, Pollak P. Continuous subcutaneous apomorphine as replacement for levodopa in severe parkinsonian patients after surgery. Lancet 1992;340:851-852.

L-Dopa dose



Efficacy of methylprednisolone pulse therapy on neuroleptic malignant syndrome in Parkinson's disease

Y Sato, T Asoh, N Metoki, K Satoh

J Neurol Neurosurg Psychiatry 2003;74:574-576

Background: Neuroleptic malignant syndrome (NMS) is a dangerous complication in patients with Parkinson's disease (PD).

Aims: To evaluate the efficacy of methylprednisolone pulse therapy compared to placebo in PD patients with NMS.

Methods: In a double blind, placebo controlled study, 20 PD patients with NMS received steroid pulse therapy for three days, and 20 PD patients received placebo. Both groups received levodopa, bromocriptine, and dantrolene.

Results: NMS in the steroid group healed within 10 days in 17 patients; median value of duration of illness of NMS in this group was 7 days (range 4-20). NMS in the placebo group healed within 10 days in five patients; in the remaining 15, it persisted for 12-27 days after the onset of NMS; median value of duration illness of NMS in this group was 18 days. Hyperthermia, rigidity, and consciousness improved within 10 days in many patients in the steroid group; these signs persisted more than 10 days in many patients in the placebo group.

Conclusions: Steroid pulse therapy is useful in NMS for reducing the illness duration and improving symptoms.

Incidence of AA

26 cases in 12 Years in 675 patients

3‰ ← The Japanese Study
2% in 7 years = 3 ‰

Refractoriness to Apomorphin

11±2.2 days (4-26 days) 16 patients

not treated

7±2.2 days (4-11 days) 8 patients

Mortality

T°/CPK/MYO/Treatment/PD duration n.s

AA duration p<0.002

The definition of AA

“ An acute motor complication of PD, coincident with infectious disease, surgery, treatment manipulations, consisting of acute worsening of parkinsonian symptoms and transient unresponsiveness to current treatments or to increase of dopaminergic treatments. AA might recover completely or leave residual motor worsening, or, in the most severe forms, might lead to untreatable complications”

The final recommendation is that AA should be promptly recognized, in order to intensively treat the patients with :

- rehydration,
- reduction of body temperature
- removal of comorbid factors

Le 3 crisi durante la Malattia di Parkinson

- 1. Crisi : inizio della malattia,
depressione**
- 2. Crisi: disturbi psicotici, allucinazioni,
idee paranoidee, decadimento
cognitivo**
- 3. Crisi: crisi acinetic- estinzione della
mobilità fisica ed acinesia psichica**