Neurol Sci (2003) 24:219–220
DOI 10.1007/s10072-003-0139-6

Acute akinesia or akinetic crisis in Parkinson's disease

A. Thomas · D. Iacono · A.L. Luciano · K. Armellino M. Onofrj (✉)
Department of Neurophysiopathology, Movement Disorder Center, Department of Oncology and Neuroscience, University "G. D'Annunzio", Chieti-Pescara, Italy

Abstract In 22 patients with idiopathic Parkinson's disease we observed a sudden worsening of motor symptoms and severe akinesia during hospitalization because of infectious diseases, bone fractures, surgery for gastrointestinal tract diseases, and iatrogenic causes. Of these patients, 12 recovered completely, 6 had a partial recovery, and 4 died. Treatments included subcutaneous apomorphine/lisuride infusion and dantreolene (with a creatine phosphokinase level higher than 200 IU). In all patients a definite refractoriness to therapy was shown with a transient lack of response to apomorphine.

Introduction

Acute akinesia or akinetic crisis [1, 2] is an ill-defined complication occurring during the course of Parkinson's disease (PD) with infectious diseases, bone fractures, and gastrointestinal tract diseases. There is acute worsening of parkinsonian symptoms and transient unresponsiveness to current treatments or to increments of dopaminomimetic treatments. The major clinical symptoms are represented by a severe akinetic state with frequent cognitive and/or psychotic disturbances, and dysphagia and aphonia, with opportunistic infections in the most-severe forms. We report our experience with 22 patients who were being followed in our Movement Disorder Unit.

Patients and methods

In order to simplify descriptions we divided our patients into three categories.

Category 1: probable absorption deficit-akinetic crisis
This included 3 patients, 2 men and 1 woman , with a disease duration of 9, 8, and 5 years, Hoehn/Yahr stage (H/Y) 4, 4, and 2.5 [3] who were hospitalized because of acute akinesia, with UPDRS score increment (+) of 21, 37, and 27 points, confusioned state, incontinence, pyrexia (37.5–39.9°C), raised creatine phosphokinase (CPK, 628–2,502 IU), and increased myoglobinuria (Myo) 420-1,310 ng/ml, due to acute disturbances of the gastrointestinal tract (2 gastric stasis because of duodenal ulcers and jejunal volvulus). All patients were treated with 150-200 mg/day apomorphine (apo) subcutaneously for 6–3 days and pre-treated with ondansetron (4–8 mg/day, in 1 60 mg/day); dantreolene was added for 3 days. In 2 patients the recovery was slow, 14 days, and not complete; 1 patient recovered completely in 13 days.

A 73-year-old women, with a disease duration of 13 years and H/Y stage3, had pneumonia with pyrexia and dysphagia [CPK 1,660 IU, Myo 99.80 ng/ml, white blood cell count (WBC) 17,000/mm^3] with acute akinesia (UPDRS increased by 41 points) and mental confusion. She was treated with 150-200 mg/day apo subcutaneously and dantreolene 50 mg/day. After 5 days the motor score improved by only 7 points and on day 7 she died because of pulmonary embolism.

Category 2: without deficit of absorption—pure akinetic crisis
Three patients presented with acute akinesia (UPDRS increased by 26–34 points) with increased body temperature up to 40.5°C (CPK 801–2,870 IU, Myo up to 1,430 ng/ml, WBC 15,000–18,500/mm^3) 3–4 days after the onset of a flu-like syndrome. Two patients (a 71-year-old male, with a disease duration of 8 years, H/Y stage 3 and a 74-year-old women, with a disease duration of 11 years, H/Y stage 4) were treated with 100-200 mg/day apo subcutaneously. One patient partially recovered after 10 days, 1 died after 18 days with pneumonia. In the 3rd (a 75-year-old male, with a disease duration of 9 years, H/Y stage 3) the total L-dopa dosage was increased by 25%; recovery was complete in 7 days.

Two patients had acute akinesia (UPDRS increased by 22–26 points) in the course of broncho-pneumonia with pyrexia (38.9°C, 39.0°C, CPK 772 IU, 1,200 IU, Myo 423.80 ng/ml, 693.30 ng/ml, respectively). The 1st patient (a 74-year-old male, disease duration 9 years, H/Y stage 4, UPDRS increase 45), with altered consciousness, was treated with 75-200 mg/day apo; he died after 14 days. The 2nd patient (a 69-year-old male, disease duration 9 years, H/Y stage 2.5) recovered completely after 4 days on 75 mg/day apo therapy.

In 8 patients (67–74 years old, 3 male, disease duration 6–14 years, H/Y stage 2.5-4), acute akinesia (UPDRS increase 20–29) was observed 3–4 days after surgical treatment of femoral and/or hip fractures. Four had pyrexia (CPK 751-2,392 IU, Myo 339–1,023 ng/ml), 4 patients were apyretic, with CPK and Myo within normal ranges. Patients with pyrexia were treated with subcutaneous apo or lisuride [4, 5] One patient died after 13 days; in the 3 other patients UPDRS scores improved from day 12 to day 21, with complete recovery. The 4 afebrile patients recovered completely in 3–6 days; 2 patients were treated with L-dopa increases of 20%; 2 patients were given adjunct apo subcutaneously 50–100 mg/day.

One man (65 years old, disease duration 3 years, H/Y stage 2.0) had acute akinesia (UPDRS increase 21) during colecystitis. L-Dopa dosage was increased by 40%, with remission of symptoms in 8 days.

Category 3: iatrogenic akinetic crisis-neuroleptic malignant-like syndrome
A 76-year-old male, with a disease duration of 11 years and H/Y stage 4 had acute akinesia (UPDRS increase 26) with hyperthermia (40.1°C, CPK 2,109 IU, Myo 998.60 ng/ml), because of amantadine withdrawal. Amantadine was reintroduced; akinesia persisted for 6 days.

In a 68-year-old women (disease duration 8 years, H/Y stage 2.5), acute akinesia (UPDRS increase 21, CPK 344 IU, Myo 320.30 ng/ml) appeared 12 h after a rapid change from ropinirole 24 mg/day to pramipexole 2.1 mg/day. L-Dopa dosage was increased by 40%; recovery was observed after 6 days.

A 68-year-old male (disease duration 4 years, H/Y stage 2) had acute akinesia with hyperthermia (40.9°C, CPK 2,454 IU, Myo 1,233.80 ng/ml), because of administration of risperidone, 1 mg for 5 days. Risperidone was withdrawn and 70 mg/day apo was added to the therapy. He recovered in 2 days.

A 75-year-old male (disease duration 16 years, H/Y stage 4) had acute akinesia (UPDRS increase 25) with pyrexia (38.5°C, CPK 829 IU, Myo 560.00 ng/ml) due to risperidone (1.5 mg/day) for 1 week. Apo 50-150 mg/day was added to therapy; risperidone was withdrawn; partial recovery occurred in 10 days.

Statistics
Differences in continuous variables were evaluated with analysis of variance. Manthel-Haenzel and Fisher tests were used to assess categorical data. ANCOVA was used to verify differences in H/Y stage at follow-up between complete and partial recovery, adjusting for baseline and disease duration. Log-rank test was performed to identify survival variables (SAS 8.1).

Results

Table 1 summarizes the demographics, H/Y stage, and UPDRS motor scores before, during, and after the recovery from acute aki-

Table 1 Demographics and follow-up evaluation (*CPK* creatine phosphokinase, *Myo* myoglobinuria)

	Total group (22 patients)	Category 1 (4 patients)	Category 2 (14 patients)	Category 3 (4 patients)
Age (years)	73.86±1.1	72.5±2.5	74.9±1.3	71.8±2.2
Sex (F/M)	7/15	1/3	5/9	1/3
Duration of disease	11.81±0.9	13.5±1.9	11.9±1.1	9.7±2.5
H/Y baseline	3.2±0.2	2.7±0.9	3.1±0.3	3.1±0.3
H/Y akinetic state	4.5±0.2	4.6±0.3	4.3±0.2	4.8±0.3
H/Y recovery	3.1±0.2[a]	3.5±0.5[b]	3.0±0.3[c]	3.1±0.3
UPDRS III baseline	35.6±3.5	37.5±9.6	34.5±4.6	37.6±5.2
UPDRS III akinetic state	63.1±3.7	69.0±5.6	60.9±5.3	64.6±6.3
UPDRS III recovery	38.7±4.7[a]	50.0±17.3[b]	35.9±6.3[c]	37.8±5.3
Temperature (°C)	38.6±0.6	38.5±0.6	38.3±0.4	39.1±0.9
CPK	1,281.3±403.3	1,385±438	1,025±268	1434±504
Myo	704.7±186	793±218	543±133	778±207
Recovery in days	9.2±2.3	9.5±2.8	9.6±1.5	8.6±2.7

[a]Only 18 surviving patients; [b]Only 3 surviving patients; [c]Only 11 surviving patients

nesia, and duration of acute akinesia. All patients were on dopaminomimetic therapy and all had been visited 1–8 months before the occurrence of acute akinesia. Complete hematological parameters were monitored throughout acute akinesia, up to recovery or eventual complications. No correlations were observed with the acute akinesia course.

UPDRS motor scores and H/Y stage during acute akinesia compared with values obtained prior to acute akinesia and scores after recovery were statistically significant ($p<0.01$). H/Y stage and UPDRS score (baseline versus outcome $p=0.05$) indicated modest worsening after acute akinesia. Age, disease duration, and H/Y stage differentiated patients with partial from patients with complete recovery ($p=0.02$, $p<0.001$, $p=0.01$), with significant correlation between disease duration and H/Y stage ($t=23.1$, $p<0.001$) and outcome ($t=23.1$, $p=0.05$). None of the variables was able to predict the survival after acute akinesia.

Sixteen patients were treated with apo; 4 patients died because of complications without significant reductions of UPDRS scores, 12 improved from 2 to 21 days after the initiation of treatment. Six patients were treated with an increase of dopaminergic treatment and recovered in 2–6 days. The disease duration and UPDRS score before and after acute akinesia were significantly different ($p<0.05$) between patients treated or not with apo.

Discussion

Our report evidences a relevant heterogeneity of possible causes of acute akinesia, as in the few reports in the literature [1, 2, 6]. At least three precipitating factors could be defined. In 11 patients a possible common etiology could be identified in altered gastric absorption or inadvertent withdrawal of treatment or administration of antidopaminergic drugs. In 11 patients, however, there was no reason to suspect an abnormal absorption and acute akinesia appeared 2–3 days after flu-like symptoms, colecystitis, or bone fracture, when hematological parameters were within normal limits and alterations of fluid compartments could not be considered a causative factor. In all patients acute akinesia lasted for several days after tentative treatments, thus evidencing a transient unresponsiveness to dopaminomimetic agents.

We suggest that a sudden worsening of the UPDRS motor score by 20 or more points, accompanied by unresponsiveness to the same drug regimens that adequately corrected symptoms before the appearance of acute akinesia, could constitute a working definition of the akinetic crisis. Furthermore, the definition highlights the presence of transient unresponsiveness to dopaminomimetic treatment, which should constitute the fundamental element of the crisis.

German literature suggests [1, 6, 7] that amantadine sulfate (available in Austria, Germany, and Hungary) at an intravenous dose of 500 mg/day my resolve aphagia; some authors also hypothesized that apo might be useful in acute akinesia [5], but our studies indicate that acute akinesia outlasts the apo administration by several days (2–10 days before the reduction of UPDRS and H/Y stage was observed) and 4 patients died despite treatment. The patients treated with apo were significantly more ill then patients not treated with apo. Due to delayed recovery in 12 patients and the death of 4 patients, we hypothesized that apo was useful mostly in avoiding the possible complication of dopaminergic drug withdrawal.

References

1. Danielczyk W (1973) Die Behandlung von akinetischen Krisen. Med Welt 24:1278–1282
2. Danielczyk W (1982) 3 crises in Parkinson disease. Fortschr Med 100:1583–1585
3. Hoehn MM, Yahr MD (1967) Parkinsonism: onset, progression, and mortality. Neurology 17:427–442
4. Bittkau S, Przuntek H (1988) Chronic s.c. lisuride in Parkinson's disease motor-performance and avoidance of psychiatric side effects. J Neural Transm 27[Suppl]:35–54
5. Broussolle E, Marion MH, Pollak P (1992) Continuous subcutaneous apomorphine as replacement for levodopa in severe parkinsonian patients after surgery. Lancet 340:851–852
6. Oppel F, Klaes H (1981) Die Amantadin-Infusionen in der akuten Behandlung der Morbus Parkinson. Klinikarzt 10:559–565
7. Kornhuber J, Weller M, Riederer P (1993) Glutamate receptor antagonists for neuroleptic malignant syndrome and akinetic hyperthermic parkinsonian crisis. J Neural Transm Park Dis Dement Sect 6:63–72