

Levodopa

Levodopa Induced Dystonia in Parkinson's Disease

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Background : Various types of dystonia may be associated with Parkinson's disease (PD). This dystonic phenomenon is sometimes observed in untreated parkinsonian patients. However, it more commonly emerges as a side effect to long term levodopa (LD) therapy. We studied several factors which influence the risk of the occurrence of LD-induced dystonia (LID) in patients with PD. The types and involved sites in LID were also studied. **Methods :** Ninety-six patients diagnosed as PD were evaluated. We analyzed the contribution of several factors such as sex, age at onset of parkinsonian symptoms, disease durations, H & Y stages, average LD doses, LD durations, and types of initial symptoms (tremor vs non-tremor) to the occurrence of LID. The types of LID were divided into: wearing-off, morning-off, peak-dose, and diphasic groups. **Results :** LID was observed in 29 patients (30.2%). Among the 29 patients with LID, 11 were categorized as wearing-off dystonia, 10 as morning-off, 6 as peak-dose, and 2 as diphasic. LID occurred in the feet or toes of 23 patients, upper extremities of 3, and in the heads or necks of 3. Sixteen patients had dystonias on the same side of their initial symptoms, 4 on the opposite side, and 6 on both sides. Among the several factors, the types of initial symptoms, average LD doses, LD durations, age at onset of parkinsonian symptoms, and H & Y stages were found to significantly contribute to the occurrence of LID. **Conclusions :** Dystonia often appeared as a side effect to anti-parkinsonian medications. Wearing-off dystonia was the most common type of LID. LID was commonly seen on the same side of initial symptoms. Initial parkinsonian symptoms were thought to be the most important contributing factor of LID.

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Key Words : Parkinson's Disease, Levodopa, Dystonia, Risk Factors

1,2

가 (dystonia) .³
가

(levodopa) ,

(motor fluctuation)

가 (levodopa induced dystonia : LID).^{1,2} wearing-off, morning-off, peak-dose, diphasic 4

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1.

1990 4 1998 7

Calne 가 (neuroleptics) parkinsonism plus (multiple system atrophy) 가가 가 96 96 35 61 20 81 56 (56.09 ± 10.70) 6 15 60 (60.63 ± 38.99), 1 10 30 (30.08 ± 25.84) (Table 1).

(agonist) (bromocriptine) 5-10mg 가 wearing-off , morning-off , peak-dose , diphasic 4 morning-off wearing-off (H & Y stage), (bradykinesia)

2. modified Hoehn and Yahr stage (H & Y stage)

3. PC-SAS program version^{6,11} Chi-square test, Fisher's exact test, t-test multivariate logistic regression analysis

(). 가

1. 96 29 (30.2%) 가 23 , 가 , 가 3 가 3 26

Table 1. Characteristics of the patients

	Mean ± SD	Range
Age at onset(year)	56.09 ± 10.70	20-81
Men:Women	36:60	
Duration of disease(month)	60.63 ± 38.99	6-180
Duration of medication(month)	30.08 ± 25.84	1-120
Average daily dose(mg)	459.76 ± 228.64	103-1183
H & Y stage	2.5 ± 0.9	1-5
Initial symptom(NT:TR)	37:59	

SD : standard deviation

H & Y stage : modified Hoehn and Yahr stage

NT : non-tremor type, TR : tremor type

20

가 (p>0.05).

odds ratio

2. 가 H & Y stage, (Table 4).

Table 2

가

Table 3

Fig. 1

12

50

3.

가 (p=0.0154). wearing-off ,
 H & Y stage H & morning-off , peak-dose diphasic 11
 Y stage 3 (p=0.0476), 36 , 10 , 6 2
 (p=0.0468),
 500mg (p=0.0012), 가 4 .
 4 peak-dose 3 wearing-off 1
 가 . Peak-dose 3 2 wearing-off
 , 1 morning-off wear-
 ing-off 1 peak-dose .

Table 2. Comparison of contributing factors between LID(+) and LID(-) groups.

	LID(+)	LID(-)	p value
Age at onset(year)	50.27 ± 10.91	58.61 ± 9.65	0.0003
Men:Women	9:20	27:40	NS
Duration of disease(month)	59.48 ± 33.64	61.12 ± 41.33	NS
Duration of medication(month)	33.10 ± 27.24	28.78 ± 25.31	NS
Average daily dose(mg)	590.31 ± 261.44	403.25 ± 188.46	0.0012
H & Y stage	2.88 ± 0.91	2.34 ± 0.85	0.0066
Initial symptom(NT:TR)	20:9	17:50	0.0010

LID : levodopa induced dystonia

NS : not significant

H & Y stage : modified Hoehn and Yahr stage

NT : non-tremor type, TR : tremor type

Table 3. Multivariate logistic regression analysis of several contributing factors to LID

Variables	Variable coefficients	Adjusted odds ratio	95% Confidence limits		p value
			Lower	Upper	
Intercept	0.7557				
Age(year)	-0.1348	0.874	0.805	0.949	0.0014
Dose(mg)	0.00420	1.004	1.001	1.007	0.0078
H & Y stage	1.1744	3.236	1.322	7.922	0.0101
Duration of medication(months)	0.0495	1.051	1.012	1.091	0.0092
Initial symptom(TR=0, NT=1)	2.9339	18.801	3.569	99.029	0.0005

Logit P = -0.7557 + (degree of variables × variable coefficients)

LID : levodopa induced dystonia

H & Y stage : modified Hoehn and Yahr stage

TR : tremor type, NT : non-tremor type

Table 4. Adjusted odds ratio of several factors in LID

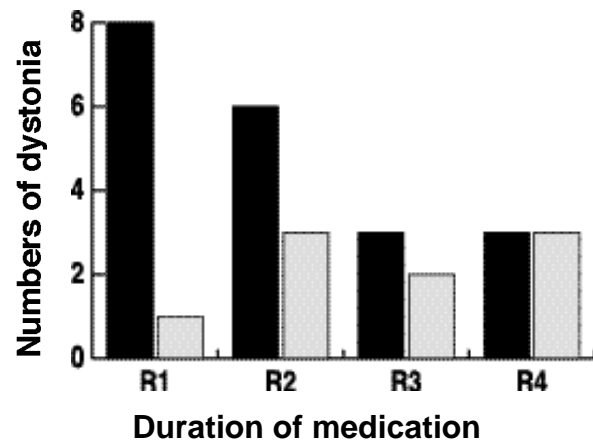
Factors for LID	Adjusted odds ratio	95% CI
Initial symptom of NT	16.885	3.702 - 77.019
Dose above 500mg	10.658	2.683 - 42.337
Duration of medication		
over 36 months	8.056	1.297 - 50.054
H & Y stage above 3	5.452	1.419 - 20.952
Age at onset of disease		
before 50 years	5.279	1.351 - 20.624
Women	2.730	0.772 - 10.324
Duration of disease		
over 60 months	0.304	0.061 - 1.526

LID : levodopa induced dystonia

CI : confidential interval

NT : non-tremor type

H & Y stage : modified Hoehn and Yahr stage



Dark bar : non-tremor group

Gray bar : tremor group

R1 : Less than 12 months

R2 : 12 to 36 months

R3 : 36 to 60 months

R4 : More than 60 months

Figure 1. Comparison of the types of initial parkinsonian symptoms according to the duration of medication in occurrence of LID

LID : levodopa induced dystonia

Table 5. Comparison of contributing factors in several types of LID

	MO	WO	PD	DP
Age at onset(year)	51.3 ± 11.8	51.9 ± 12.0	50.5 ± 5.5	35.5 ± 2.1
Men : Women	3:7	5:6	1:5	0:2
Duration of disease(month)	56.90 ± 21.59	65.36 ± 47.37	46.00 ± 22.31	80.50 ± 12.02
Duration of medication(month)	19.90 ± 17.92	37.91 ± 24.37	38.67 ± 41.68	56.00 ± 5.56
Average daily dose(mg)	661.10 ± 274.66	682.00 ± 257.63	364.33 ± 81.20	410.00 ± 155.56
H & Y stage	2.90 ± 1.02	3.18 ± 0.87	2.33 ± 0.82	2.75 ± 0.35
Initial symptom(NT : TR)	8:2	6:5	5:1	1:1

LID : levodopa induced dystonia

H & Y stage : modified Hoehn and Yahr stage

NT : non-tremor type, TR : tremor type

MO : morning-off , WO : wearing-off , PD : peak-dose , DP : diphasic

Levodopa

Morning-off , wearing-off , diphasic

peak-dose 6 3 가

(Table 5).

diphasic 2 30 가

wearing-off morning-off H & Y stage가 (p>0.05).

1960 Ehringer Hornykiewicz가

Barbeau Birkmayer 1967 Cotzias 가

5 가

7-10 , 8-11

wearing-off , morning-off , peak-dose diphasic 1,4,12 가

1,14,15 가 morning-off wearing-off

(odds ratio=8.056).

가

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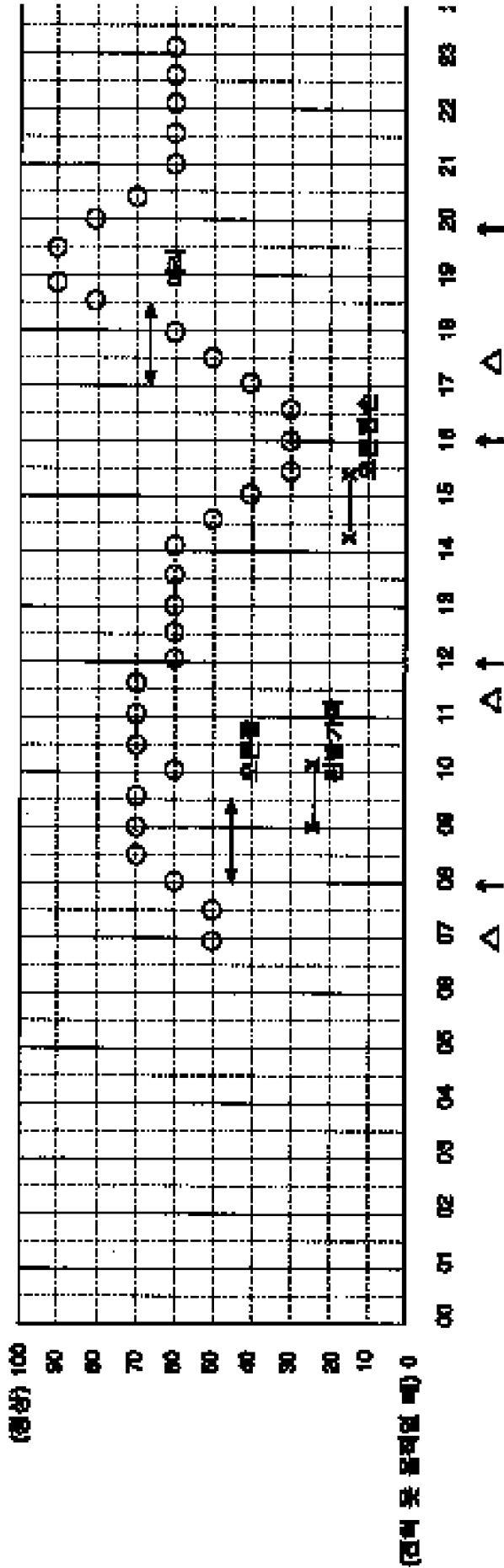
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파킨슨병 일기장

(199__년 __월 __일, __요일)

이상윤환 김티니

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- ; 몸의 상태를 30분마다 기록 (팔다리의 움직임이나 걸음걸이를 기준으로 작성, 표명되는 정도를 기준으로 하지 마세요.)
- ↔ ; 신체의 일부가 움직이지 않는데 움직이는 경우 (신체의 부위와 지속시간을 기록)
- x—x ; 팔다리이나 신체의 일부에 저절로 힘이 들어가거나 뒤틀리는 경우 (해당되는 신체의 부위의 지속시간을 기록)
- ↑ ; 파킨슨병의 치료제(시네렘브 혹은 마도파)를 복용한 시간 기록
- △ ; 식사시간 기록