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A study of 72 children with eyelid myoclonia precipitated by eye closure in Yogyakarta

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Abstract

This is a report of 72 children in Yogyakarta with predominant feature of eyelid myoclonia over a 10-year period from 1990-1999. The mean age of presentation was 7.4 years. Eighty-two percent were males. There were two siblings (4%) with similar illness. All the patients had absence. In 6% of the cases, the absence was mild. Other seizure manifestations such as head nod, head rotation, lateral or upward eye deviation, arm jerks, and automatism such as chewing, lip smacking, throat clearing, hand rubbing were seen in some of the patients. All patients also had hyperactivity behavior or inattentiveness. None had generalized tonic clonic seizure. Ictal and interictal EEG showed generalized discharges. Eye closure precipitated the eyelid myoclonia in all the cases. Photoconvulsive response was seen in 17%. All the patients with photoconvulsive response had generalized 3-6 Hz polyspike and slow wave, and higher proportion with other seizure manifestations including automatism when compared to patients without photoconvulsive response. There was good response to clonazepam. At 6 months of follow-up, 57% had excellent response with total absence of eyelid myoclonia and co-existent seizure, 26% had good response with occasional eyelid myoclonia and absence of co-existent seizure, and 17% had fair response with reduction of the eyelid myoclonia and the seizure. At 3 years of follow-up, 90% had excellent response and 10% had good response. *Conclusion:* The differences of our patients with previously reported cases of eyelid myoclonia with absence suggest that its manifestation is broader than previously described.

INTRODUCTION

Eyelid myoclonia is a nonspecific manifestation seen in various cryptogenic and symptomatic epilepsy conditions.[1] Eyelid myoclonia with absences however, is a discrete syndrome first described by Jeavons.[2] It characteristically affects young children with brief episodes of jerking of eyelids and upward deviation of the eyes, associated with generalized 4-6 cycle per second spike-wave discharges, and occurring on closure of the eyes. All patients are said to have photosensitivity. It is resistant to treatment and may be lifelong.[1,3,4] The ILAE however, is yet to recognize eyelid myoclonia as a distinct syndrome. In the proposed diagnostic scheme in 2001, eyelid myoclonia with or without absences is listed as epileptic seizure types.[3,5,6] The author first saw an 8-year-old boy who presented with 3 months history of paroxysmal attacks of eyelid fluttering. He was referred by Dr Wasisdi Gunawan, a senior ophthalmologist from Yogyakarta. There may be associated head nods, lateral ocular deviation and brief alteration of consciousness with amnesia. The patient also had hyperactive behavior, but no family history of epilepsy. Electroencephalography (EEG) showed generalized spike-waves complex. The patient responded to 0.5 mg of clonazepam. Since then, the author has seen numerous other similar patients. This is a description of 72 of the cases.

METHODS

The subjects consisted of patients with eyelid myoclonia, seen by the author over a 10-years period from January 1990 to December 1999. The main inclusion criteria in this study were predominant clinical feature of eyelid myoclonia without associated major neurological abnormalities. Only patients whose eyelid myoclonia was precipitated by eye closure was included in this study. Patients with childhood

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Table 1. Age and sex distribution of eyelid myoclonia precipitated by eye closure in Yogyakarta (N=72)

Age (years)	Male	Female	Total (%)
5	19	5	24 (33)
6	7	1	8 (11)
7	6	0	6 (8)
8	8	1	9 (13)
9	6	1	7 (9)
10	3	2	5 (7)
11	0	2	2 (3)
12	4	0	4 (6)
13	3	1	4 (6)
14	3	0	3 (4)
Total	59 (82)	13 (18)	72 (100)

absence epilepsy, or where eyelid myoclonia was part of generalized convulsion, and those with associated ophthalmologic or other neurological abnormalities were excluded from the study. Case history was obtained based on a structured questionnaire with information from the patients and eyewitnesses who were mostly parents of the patients. The details of the history included the description of eyelid myoclonia, the precipitants, birth, early development and medical past history, family history, behavior abnormalities, and drug treatment. Careful observations for alteration of consciousness, other evidence of seizure was made during eyelid myoclonia episodes. Absence was defined as the presence of one or more of the followings: cessation of ongoing activities such as speech, impaired responsiveness and automatism. Mild absence was defined as impaired consciousness demonstrable only with testing, such as failure to continue counting, and repetition error. All patients underwent EEG. Intermittent photic stimulation was performed with a strobe light at flash frequencies of 3, 5, 10, 15, 15, 10, 5, and 3 per second. CT brain scan was performed on some of the patients. Clonazepam was given as first choice based on the good responses in the earlier cases. The initial dose was 0.5 mg/day, given as single dose at bedtime. The dosage was adjusted according to clinical response or side effects. Follow up was conducted weekly for the first month, and monthly thereafter. *Fair* response was when there was reduction in the eyelid myoclonia and co-existent seizures. *Good* response was when there was occasional eyelid myoclonia and absence of co-existent seizures. *Excellent* response was when there was a total

Table 2. Co-existing seizure manifestations of eyelid myoclonia precipitated by eye closure in Yogyakarta (N=72)

Seizure manifestations	n	%
1. Lateral gaze	31	43
2. Arm jerks	23	32
3. Head rotation	18	25
4. Up rolling eyes	16	22
5. Head nods	9	13
6. Automatism		
a. Swallowing (throat clearing)	30	42
b. Lip smacking	15	21
c. Hand rubbing	13	18

absence of eyelid myoclonia and co-existent seizures.

RESULTS

Sex, age of onset, family history

Seventy-two patients fulfilled the inclusion criteria and were studied. The age of presentation ranged between 5-14 years, with a mean of 7.4 years. Fifty-nine patients (82%) were boys and 13 patients (18%) were girls (Table 1). The duration of symptom at first presentation was 4-12 weeks, a mean of 6 weeks. The pregnancy, birth and early developmental history were all normal. There was no previous history of febrile convulsion, head injury, or central nervous system infections. There was no history of seizure among the first and second-degree relatives except two patients who were brothers. The older boy of 8 year had seizures 6 months earlier than his younger brother of 5 year. Both the boys had similar clinical manifestations with eyelid myoclonia, brief lateral gaze, and head rotation. Both brothers also had inattentive behavior.

Eyelid myoclonia and other seizure manifestations

The eyelid myoclonia consisted of abnormal rapid blinking of both eyes, which progressively

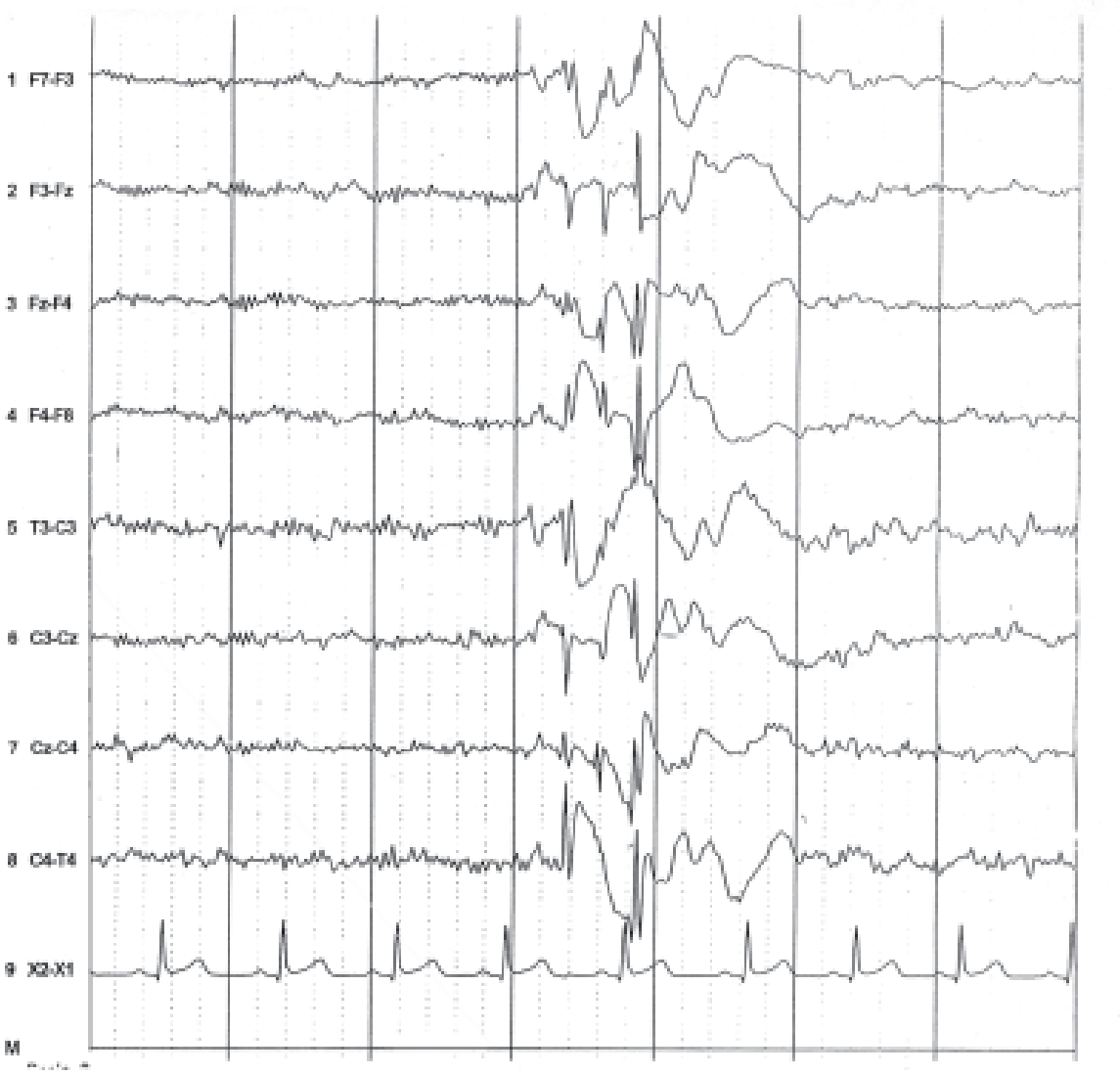

Figure 1a. A 6 years old boy with generalized 4 per second spike and slow wave.

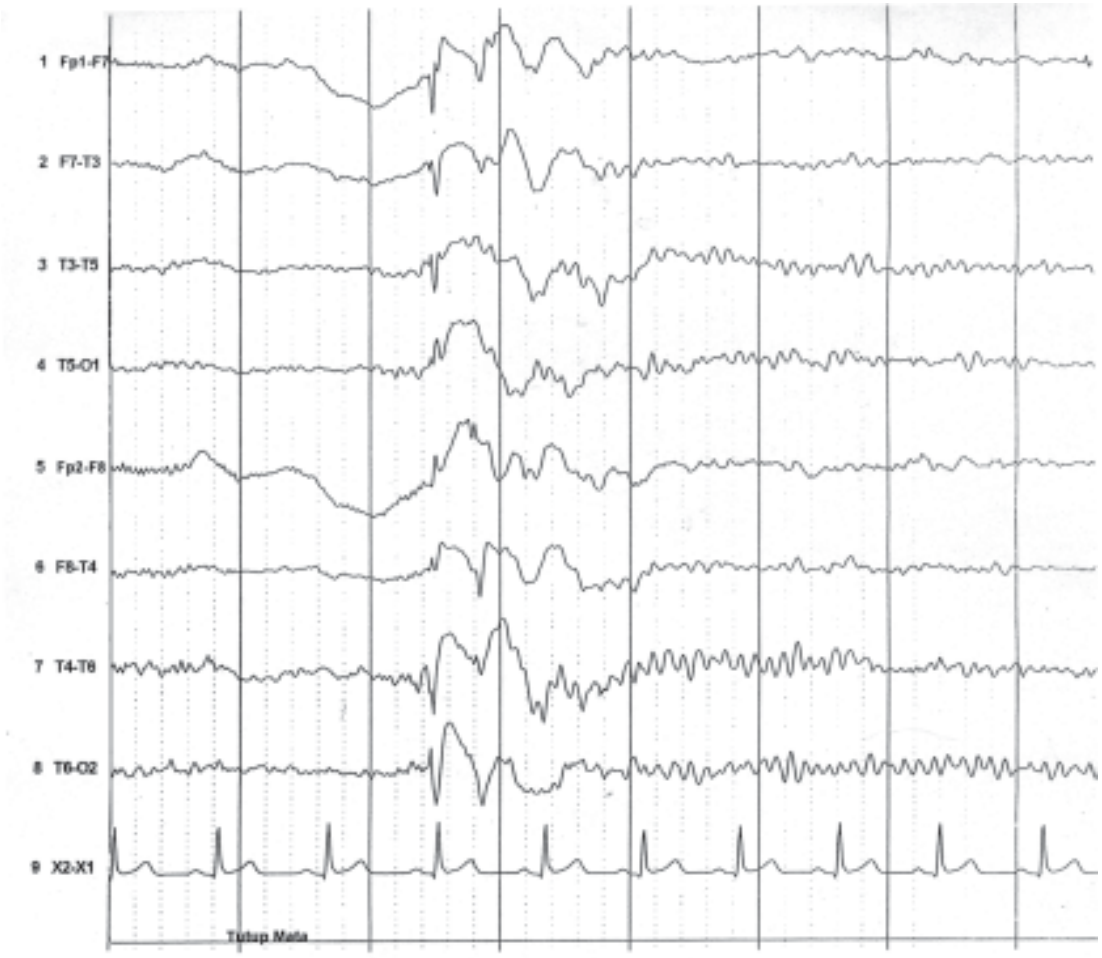

Figure 1b. Eye closure (tutup mata) precipitated the discharges.

became more frequent. On the first visit, typically the eyelid myoclonia occurred for 2-4 times over 15 minutes. The myoclonia typically lasted from 3-7 seconds. The co-existing seizure manifestations were as listed in Table 2. Sixty-eight patients (94%) had absence, consisting of impaired responsiveness and automatism in 61 patients, cessation of speech and impaired responsiveness in another 7 patients. Another 4 patients (6%) had mild absence demonstrable with failure to continue counting in 3 patients, and repetition error in one patient. The absence was concurrent rather than independent of the co-existing seizure manifestations. Other coexistent disturbances were: sudden and brief headache (26%), abdominal pain (20%), headache followed by vomiting (9%), epistaxis without nasal pathology (9%).

Other associated abnormalities

All patients also had hyperactivity behavior or inattentiveness. The descriptions frequently used by the parents were: “see but do not look, and hear but do not listen”, “never settle down to play, watch television, or sit at a meal table for more than a few minutes”, “always keep moving and talking”. Physical examination was otherwise normal with no other neurological deficit. Other than EEG, the investigations including CT brain scan done on 26 patients were all normal.

EEG

EEG was done in wakefulness. The interictal EEG showed various forms of bilateral synchronous generalized discharges. The discharges were: < 3Hz polyspike and wave (42%), >6 Hz polyspike and wave (17%), 3-6 Hz polyspike and wave (17%), repetitive sharp wave (24%). None of the patients had focal discharges. Ictal EEGs of 55 patients showed similar discharges but of higher amplitudes and longer duration of 1-2 seconds. Photoconvulsive response

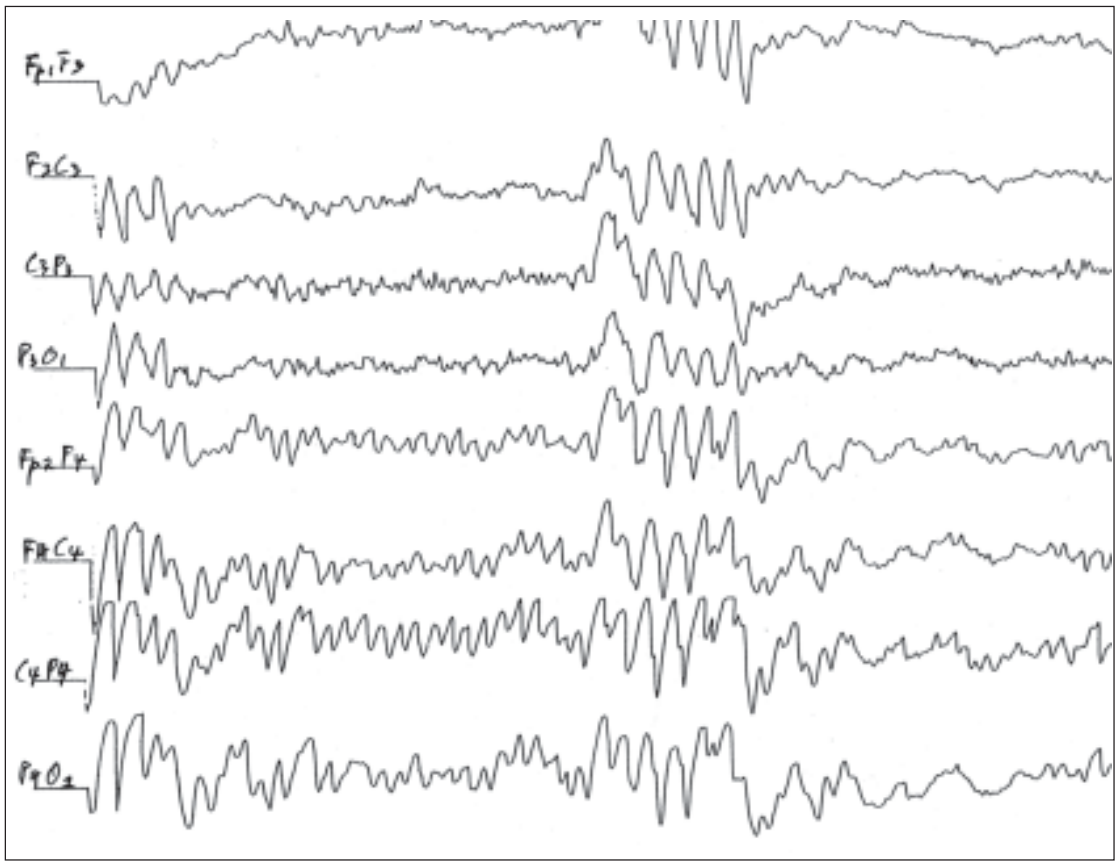

Figure 2. A 10 years old girl with generalized repetitive sharp wave.

was seen in 12 patients (17%). The eyelid myoclonia was precipitated by eye closure in all the patients. Figures 1 and 2 are examples of the interictal EEG.

Twelve patients (17%) had all the classical features of eyelid myoclonia with absence: eyelid myoclonia, 3-6 Hz polyspike and slow wave complexes in EEG, precipitation of the discharges by eye closure and photoconvulsive response. Table 3 is a comparison between the 12 patients with photoconvulsive response, and 60 patients without photoconvulsive response. As shown, co-existing seizure manifestation was seen in both groups of patients, but more common among the patients with photoconvulsive response. All the 12 patients with photoconvulsive response had absence. Of the 60 patients without photoconvulsive response, 56 patients had absence, 4 other patients had mild absence. The difference was not statistically significant. The 3-6 Hz polyspike and slow wave was only seen among patients with photoconvulsive response (Table 3).

Response to treatment

Clonazepam was given at initial dose of 0.5mg/day. After 2 weeks, the dose of clonazepam was adjusted according to the response, body weight, and adverse reactions. The response to clonazepam is as in Table 4. All patients had good compliance to treatment and there was no drop out in follow-up. As shown, with initial dose of 0.5 mg/day, at the end of 2 weeks, 90% of patients had *fair* response. At 6 months of follow-up, 57% had excellent response, 26% had good response and 17% had fair response. At 3 years of follow-up 90% had excellent response and 10% had good response. There was however no change in the hyperactive and inattentive behavior with clonazepam. With the increase of the dose of clonazepam after the first two weeks, 40% of patients had drowsiness and 8% had ataxia. The adverse reactions disappeared when clonazepam was given in divided doses, twice or three times per day. For the school children there was no disturbance in learning activities and achievement.

Table 3. Comparison between eyelid myoclonia patients with and without photoconvulsive response

	Patients with photoconvulsive response (N=12)	Patients without photoconvulsive response (N=60)	P value
Demography:			
Mean age (year)	6.5	8	
Male	8 (67%)	51 (85%)	NS
Female	4 (33%)	9 (15%)	
Co-existing seizure manifestations:			
Lateral gaze	10 (83%)	21 (48%)	0.002
Arm jerks	9 (75%)	14 (23%)	0.001
Head rotation	7 (58%)	11 (18%)	0.007
Up rolling eyes	2 (17%)	14 (23%)	NS
Head nods	5 (42%)	4 (7%)	0.0049
Automatism			
swallowing (throat clearing)	8 (67%)	22 (37%)	NS
lip smacking	6 (50%)	9 (15%)	0.013
hand rubbing	4 (33%)	9 (15%)	0.137
EEG:			
<3 Hz polyspike and slow wave	0 (0%)	30 (50%)	0.001
>6 Hz polyspike and slow wave	0 (0%)	12 (20%)	NS
3-6 Hz polyspike and slow wave	12 (100%)	0 (0%)	0.00
Repetitive sharp waves	0 (0%)	18 (30%)	0.022

The statistical methods used are chi-square or Fisher exact test,
NS = no significance, p>0.05

Replacement of clonazepam by other antiepileptic drugs, sodium valproate, lamotrigine, and carbamazepine in 7 patients were unsuccessful. There was recurrence of seizures or intolerable adverse reaction. The parents of the patients preferred to resume clonazepam at 2.0 mg/day. The response to clonazepam was good, whereas an increment of 0.5 mg/day resulted in intolerable drowsiness.

DISCUSSION

This is a description of a large group of children whose main complain was that of eyelid fluttering. Careful observation showed co-existence of other manifestations of seizure with transient absence and automatism. Ictal and interictal EEG showed generalized discharges. In all of the cases, the eyelid myoclonia was precipitated by eye closure. There was good response to clonazepam. Family history of similar seizure was only seen in a pair of siblings. There was no co-existent generalized tonic clonic seizure. The patients were all referred from ophthalmologist, as the parents were not aware that the abnormal blinking was part of a seizure disorder. In fact, most of the parents thought that the children's problem was due to infestation by round worms.

The absence of underlying disease and neurological abnormalities other than hyperactivity or inattentive behavior, the normal CT brain scan and other investigations, the EEG showing generalized discharges, and the co-existence of photoconvulsive abnormality in a proportion of cases, support that this is another example of idiopathic generalized epilepsy. On the other hand, head rotation and lateral gaze suggests a focal origin of the seizure. The relatively small proportion of patients with similar history among siblings is consistent with polygenic inheritance. The large number of patients in this series suggests that it may be more common in certain ethnic groups.

The characteristics of our patients is closest to that of eyelid myoclonia with absence first described by Jeavons.[2] Table 5 lists the

comparison between cases of eyelid myoclonia with absence from Giannakodimos & Panayiotopolos[4] and the present series. As shown, both have onset in childhood, eyelid myoclonia and absence as the predominant clinical features, eyelid myoclonia precipitated by eye closure, and other subtle manifestations of seizure such as hand jerks. On the other hand, the automatism seen in some of our patients suggests that the impairment of consciousness is more severe among our patients. The ictal EEG of Giannakodimos and Panayiotopolos' cases had polyspikes or polyspikes and slow wave of 3-6 Hz, and photoconvulsive response in all cases.[4] Photosensitivity and 3-6 Hz polyspikes and slow wave was only seen in less than a fifth of our patients. Further more, our patients was male predominant, have hyperactive behavior or inattentive, and had good response to clonazepam.

There appears to be two subgroups among our patients, those with photoconvulsive response and those without. The smaller group with photoconvulsive response has classical 3-6 Hz polyspike and slow wave, and higher proportions with co-existing seizure manifestations including automatism. The group without photoconvulsive response has other generalized abnormalities in EEG, and with less co-existing seizure manifestations including automatism.

The differences in clinical features and EEG of our patients with the previously reported cases of eyelid myoclonia with absence suggest that its manifestation is broader than previously described.

Clonazepam is effective in various disorders with myoclonic seizures and myoclonic jerks. In our patients, it was effective in ameliorating the eyelid myoclonia, absences, and other co-existent seizures. Pharmacologically, clonazepam acts to facilitate recurrent inhibition in nucleus reticularis thalami (nRt) and decrease its inhibitory output onto relay neurons. Intra-nRt $GABA_{A}$-mediated inhibition may thus has an important role in controlling thalamic excitability and the anti-absence actions of clonazepam.[7] It may also play a role in the eyelid myoclonia seen in our patients.

Table 4. Response to clonazepam of eyelid myoclonia precipitated by eye closure in Yogyakarta (N=72)

Duration of medication	Responses to drug treatment				Dosage of clonazepam
	No response n (%)	Fair n (%)	Good n (%)	Excellent n (%)	
Two weeks	7(10)	65 (90)	0	0	0.5 mg/day: 72 patients
One month	0	37 (51)	19 (26)	16 (23)	0.5 mg/day: 0 patients 1.0 mg/day: 72 patients
Three months	0	22 (31)	21 (29)	29 (40)	1.0 mg/day: 23 patients 1.5 mg/day: 49 patients
Six months	0	12 (17)	19 (26)	41 (57)	1.0 mg/day: 12 patients 1.5 mg/day: 60 patients
One year	0	0	30 (42)	42 (58)	1.5 mg/day: 53 patients 2.0 mg/day: 19 patients
Two years	0	0	14 (19)	58 (81)	1.5 mg/day: 46 patients 2.0 mg/day: 26 patients
Three years	0	0	7 (10)	65 (90)	1.5 mg/day: 44 patients 2.0 mg/day: 28 patients

The definition of fair, good and excellent responses is described in "methods".

Table 5. Comparison between cases of eyelid myoclonia with absence from Giannakodimos & Panayiotopoulos[1] and the present series

	Eyelid myoclonia with absence, Giannakodimos (N=11)[1]	**Childhood eyelid myoclonia, Yogyarkarta (N=72)**
Prevalence	2.7% of epilepsies >16 years	Unknown
Sex distribution	All were female	Male predominance (82%)
Family history	Family history of epileptic seizure common	3% has similar seizure among siblings
Age of onset	Childhood, mean 6 years	Childhood, mean 7 years
Eyelid myoclonia	Predominant symptom	Predominant symptom
Absence	Present but mild, automatism absent	Present with automatism in some cases, particularly those with photoconvulsive response.
Other seizure manifestations	Deviation of eyes and head, jerks of hand may be present	Deviation of eyes and head, head nod, and arm jerks seen in some cases, particularly those with photoconvulsive response.
Generalized tonic clonic seizure	Probably universal but infrequent	Absent
Other neurological abnormalities	Nil	Hyperactivity behavior or inattentiveness common
Ictal EEG	Polyspikes, polyspike and slow wave 3-6 Hz	Generalized 3-6 Hz polyspike and slow wave among those with photoconvulsive response, other generalized discharges among those without photoconvulsive response.
Photoconvulsive response	Present in all.	17%
Precipitation of eyelid myoclonia by eye closure	Present in all.	Present in all
Response to drug treatment	Response to sodium valproate, but may need combination therapy	Good response to clonazepam
Long term prognosis	May be life long	Unknown

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