Diagnostic and Therapeutic Role of Long Term Video-EEG Monitoring in Patients With Psychogenic Non-Epileptic Attacks

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1. Background

Most of the neurologists, psychiatrists and general practitioners working in emergency departments face commonly with patients suffering from Psychogenic Non-epileptic Attacks (PNEA). Sometimes it is difficult to diagnose PNEA and some years may take away from the initial manifestation of the disease to correct diagnosis (1, 2). PNEA is a neuropsychiatric disorder that has a lot of direct and indirect economical and psychosocial burden not only on patients and their families, but also on society and health systems. Sometimes disabilities due to PNEA are more serious than epilepsy. Misdiagnosis of PNEA as epilepsy usually leads to prescription of unnecessary anti-epileptic drugs (AEDs) and causes potentially dangerous side effects and also unnecessary costs for the patient. Contrary to the initial impression, PNEA is not a rare disease. Its prevalence in the society is estimated to be as common as MS (two to 33 per 100,000 patients) (3).

According to published studies by the great epilepsy centers across the world, 10 to 40% of the patients with refractory seizures referred to epileptologists are PNEA (3-7). None of the clinical features, psychological tests, interview or questionnaire can be relied as a confident diagnostic way for confirming of PNEA (8-11). Clinically, PNEA can mimic all the signs and symptoms of epileptic seizures. The main difference between them is that the psychogenic events are not the result of abnormal electrical discharge of brain. PNEA places on the border of specialties of neurology and psychiatry and for that reason less attention has been regarded to it. Applying Long-term video-EEG Monitoring (LTM) in differential diagnosis of epilepsy has led to significant development of knowledge on PNEA during the last two decades. Diagnosis of PNEA includes two stages: 1) clinical suspicion, 2) confirmation of diagnosis.

Several clinical and unusual features of attacks suggest some index of suspicion by treating physician that the patient not to have epilepsy. Unusual features may include: no response to AEDs, repeated normal or nonspecific EEG, and other neurological examinations.

Implication for health policy/practice/research/medical education: Definite diagnosis of PNEA not only significantly reduces unnecessary use of anti-epileptic and psychotropic drugs, but also increases patient's productivity and emotional wellbeing. In addition, it leads them to accept diagnosis and follow appropriate treatment.

Keywords: Epilepsy; Antiepileptics; Psychogenic; Electroencephalography

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cific findings on routine EEG, seizures triggered by emotions, prolonged and unusual semiology of events and occurrence of attacks in presence of audiences. In case of ignoring the suspicion in diagnosis, the correct diagnosis may be delayed even for many years. Unfortunately, in case of repeated paroxysmal episodes, diagnosis of epilepsy is much easier applied and accepted than other differential diagnosis (particularly psychogenic). LTM with high certainty can help the treating physician to diagnose the nature of attacks definitively. LTM has been known gold standard way in definite diagnosis of PNEA. Correct and early diagnosis of PNEA has been regarded as the first step in treatment. According to the studies, following the clear diagnosis of PNEA by video-EEG monitoring and making an appropriate description and explanation about the nature of disease by neurologist for the patients and their family; it has been revealed that occurrence of attacks ceases or decreases significantly in more than half of the patients (7, 12-15).

2. Objectives
The aim of this study is to investigate occurrence of PNEA in patients admitted to the Razavi epilepsy department and role of LTM in definite diagnosis of PNEA.

3. Materials and Methods
This study was retrospectively performed and required information was gathered from the database of patients admitted in epilepsy department of Razavi Hospital during a period of one year (from March 2011 to April 2012). All patients with the final diagnosis of PNEA were included in the study. The following patients were excluded from the study:

1) Patients who did not have any attacks during LTM
2) Patients whose interictal scalp’s EEG showed specific epileptiform discharges
3) Patients with coincidental real seizures
4) Patients with sensory or subjective attacks

Diagnosis of PNEA was confirmed when:
1) The patient had at least one habitual attack,
2) The corresponding EEG did not show any abnormal electrical activities before, during and after attack and
3) The clinical signs were not consistent with a seizure that may lack characteristic EEG changes (such as frontal partial seizures).

One of the patient’s close relatives was always present in the monitoring room and after any attacks, s/he was confirming whether the patient’s event was similar to the previous ones or not. Electrodes had been applied according to 10/20 international system with additional electrodes in temporal and frontal lobes (F9, F10, TP9, TP10, T9, T10). In addition to EEG; sound, video and ECG was also recorded simultaneously.

All the video and EEG files of patients were reviewed by two neurologists working in epilepsy monitoring department and the required data were gathered. Patients were contacted with telephone thereafter to assess their clinical status. 29 out of 33 patients replied to several following questions about frequency of their attacks, sort and dose of their prescribed drugs during the recent last month of interview. In addition, they were asked to compare their emotional wellbeing state before and after performing LTM. Based on self-report they answered to the options (better, no change and worse). The collected data were analyzed by SPSS. Independent-sample T-test and Chi-square tests were applied after approving the normality of data distribution. Paired T-test was used to compare number of drugs before and after the diagnosis.

4. Results
From 182 patients who had been referred to the epilepsy department due to refractory attacks, final diagnosis of 33 (18%) patients was PNEA. Mean age of the patients was 27.61 years old (SD: 9.37 and Range: 11-47) and two-third of them were female. Mean duration of disease in patients was 28.15 months (Table 1). On admission, 29 patients (87%) were treated with AEDs and 26 patients (78%) with psychotropic drugs. The mean number of drug for each patient was 1.6 (Range: 0 - 5, SD: 1.12) and 1.88 (Range: 0 - 4, SD: 1.27) for AEDs and psychotropic drugs respectively.

| Table 1. Descriptive Data | No. | Min | Max | Mean (SD) |
|---------------------------|-----|-----|-----|-----------|
| Age, y                    | 33  | 11  | 47  | 27.61 (9.74) |
| Duration of disease, mo   | 33  | 3   | 120 | 28.15 (33.51) |
| Duration of admission, h  | 33  | 12  | 72  | 31.27 (19.43) |
| Number of attacks         | 33  | 1   | 15  | 4 (3.49) |
| First spontaneous attack  | 20  | 20  | 420 | 130 (109.88) |
| Number of AEDs before LTM | 33  | 0   | 5   | 1.61 (1.16) |
| Number of AEDs after LTM  | 29  | 0   | 2   | 0.31 (0.541) |
| Number psychotropic drugs before LTM | 33  | 0  | 4  | 1.88 (1.269) |
| Number psychotropic drugs after LTM | 29  | 0 | 3  | 1.17 (1.002) |

Duration of video EEG monitoring for each patient varied between 12 to 72 hours. The patients on average had four attacks during LTM. The mean latency of the first spontaneous attack was 130 (20 - 420) minutes. Since the time of providing suggestive tests in different patients was not similar, onset latency of suggestive attacks were not calculated. The first attack in 60.6 % cases was spontaneous and without suggestion. In general, 70% of patients had spontaneous attacks and 9% had attacks as the result of verbal suggestion which accompanied by photic stimulation or hyperventilation. Because of ethical con-
sideration invasive suggestive tests such as placebo injection, were not used in any patients.

Four patients (12.1%) had attacks during sleep. In these cases, EEG was showing awaked alpha waves shortly before onset of the attack. 72.2% of patients described a kind of aura before their attacks. 13 patients (39.4%) had at least one epilepsy risk factor in their history (Table 2). More than half of the patients reported that they lost their consciousness during the attacks. Some of them had history of injury during attacks. (Table 3)

### Table 2. Prevalence of Epilepsy Risk Factors in Patients With PNEA

| Risk factors                        | Frequency | Valid Percent | Cumulative, % |
|-------------------------------------|-----------|---------------|---------------|
| Family history of epilepsy          | 3         | 9.1           | 9.1           |
| Head trauma+                        | 7         | 21.2          | 30.3          |
| Family history+, head trauma+       | 1         | 3.0           | 33.3          |
| Meningitis in childhood             | 1         | 3.0           | 36.4          |
| Febrile convulsion+, family history+| 1         | 3.0           | 39.4          |
| No clear risk factors               | 20        | 60.6          | 100.0         |
| Total                               | 33        |               |               |

### Table 3. Occurrence of Red Flags in Patients With PNEA

| Red Flags                          | Frequency | Percent |
|------------------------------------|-----------|---------|
| Aura before attacks                | 24        | 72.7    |
| Injury during attacks              | 3         | 9.1     |
| LOC during attacks                 | 17        | 51.5    |
| History of epilepsy risk factors   | 13        | 39.4    |
| Attacks during sleep               | 4         | 12.1    |

The patients were clinically divided into four groups (16, 17):

- **Group I:** The patients whose seizures accompanied with severe motor symptoms (Hypermotor).
- **Group II:** The patients who had some motor symptoms during the attack, but its intensity was not so severe (Minor Motor).
- **Group III:** The patients whose attacks were not associated with obvious motor symptoms (Dialeptic).
- **Group IV:** The patients whose symptoms clinically were variable or associated with combination of mentioned attacks (Mix)

Base on this classification:

- 30.3% of patients had Dialeptic attacks
- 27.3% of patients had Hypermotor attacks
- 15.2% of patients had Minor Motor attacks
- 27.3% of patients had Mix attacks

### 5. Discussion

This study showed that the proportion of diagnosis of PNEA in patients with refractory attacks in our center is similar to other worldwide epilepsy centers. In terms of age range and sex ratio, our patients have nearly the characteristics to those of other studies (4-7, 18, 19). According to above findings, it can be concluded that the biological factors play more important role than racial, socioeconomic and cultural factors in pathogenesis of non-epileptic attacks with psychological origin. Before the clear diagnosis of PNEA with LTM, many of patients (78%) were treated with psychotropic drugs. This finding implies that the treating physicians had had some suspicions about psychogenic factors in triggering of the attacks; however, because of uncertainty of diagnosis, they had prescribed AEDs in the same time. In the present study, first spontaneous attack occurred within the average delay of 130 minutes which was lower in comparison with other studies (16, 20). Seventy percent of the patients had attack without applying suggestive and provocative techniques that is lower than other similar studies (21, 22).

Our impression is that the restriction in length of monitoring (due to cost of hospitalization) and early use of provocative and suggestive techniques in the first day of monitoring can be considered as the reasons (23). In addition, due to lack of pervious familiarity of our patients with verbal suggestive maneuvers and video-EEG monitoring, these tests were more successful to induce attacks in compare to other studies (7, 18, 19, 21). In general, all of the included patients experienced attacks (spontaneous or suggestive) in the first 24 hours. We concluded that a session of 24-hour LTM can be sufficient in suspected patients to confirm diagnosis of PNEA. As in our country cost of LTM is not covered by insurance companies, above mentioned results are important to convince cost-benefits of this diagnostic tool (24-26).

In our country, most of neurologists traditionally differentiate epileptic seizures from non-epileptic attacks by using following red flags: unusual semiology of attacks, occurring of attacks during sleep, history of epilepsy risk factors, presence of aura before attacks, loss of consciousness or injury during attacks. Our study showed that these red flags cannot be reliable criteria for distinction between epileptic seizures and non-epileptic attacks (9-11, 13, 27).

Mean duration of suffering from recurrent attacks in this study was 28 months, which was lower in comparison with other studies [five years and six months in Jones' study (2), and seven years and two months in Reuber's study (1)]. Since video-EEG monitoring in Iran is quiet new and many professional healthcare providers are not familiar with it, thus many patients with long history of disease had not been referred to our center for further evaluations, this issue may somehow interpret statistical differences between the present study and others.
Twenty nine out of 33 patients participated in follow up assessment. Mean follow up duration was 8.33 (±3.13) months. Among 29 patients who followed, more than half of them (51.7%) were seizure free. According to self-report, 82.8% percent of patients were satisfied and got better following the clear diagnosis by LTM. 86.2% of patients have been following their treatment under the care of a specialist and the treating physician of most of them (65%) was psychiatrist. There was no significant statistical difference in age, sex, duration of disease and semiology of attacks between seizure free group and who were not improved.

Number of AEDs which patients were taking in the follow-up interview was significantly decreased (P < 0.001). Furthermore, in follow up the average number of psychotropic drugs interestingly decreased in PNES patients (P = 0.029). These findings indicate that the diagnosis of PNEs by LTM method can reduce unnecessary use of medications (both AEDs & psychotropic drugs). Similar results concluded in other studies (7, 12, 28).

Applying of LTM as a diagnostic method for differential diagnosis of recurrent paroxysmal attacks when associated with provocative suggestive techniques (even for 24 hours) can lead to definite diagnosis of psychogenic non-epileptic attacks. After definite diagnosis and describing the nature of disease for patients and their family and guiding them toward the appropriate treatment, more than half of patients will improve. In addition, use of unnecessary drugs in these patients (at least in the short term follow-up) significantly will decrease. The improvement rate in patients with PNEA does not have any significant relation between age, sex, duration of disease and clinical type of attacks.

There are some limitations in this study which necessitate further studies. The following limitations should be considered in next studies:
1) Retrospective study
2) Short duration of follow-up
3) Self-reported evaluation of emotional wellbeing
4) No applying of psychological tests to all patients
5) Limited number of study population
6) Exclusion of patients with unclear diagnosis and subjective attacks

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Authors’ Contribution
Study concept and design: Mohsen Aghaee Hakak, Ali Gorji, Hossein Amiri. Interpretation of data: Mohsen Aghae Hakak, Ali Gorji, Hami Ashraf. Drafting of the manuscript: Mohsen Aghaee Hakak, Hossein Amiri, Hami Ashraf and Malihe Mohammadpour. Doing Critical revision of the manuscript for important intellectual content: Mohsen Aghaee Hakak, Ali Gorji.

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