Peri-Ictal Urinary Dysfunction in Patients With Epilepsy A Cross-Sectional Study

Mahmoud Motamedi,¹ Mohammad Reza Nikoobakht,² Mehdi Aloosh,^{1,3} Sara Ebrahimi Nasrabady,⁴ Azadeh Afshin,³ Amirhossein Orandi,³ Fatemeh Talei Khatibi³

Purpose: To evaluate the prevalence of peri-ictal urinary symptoms and their association with seizure type in patients with epilepsy.

Materials and Methods: A total of 115 patients with epilepsy were recruited consecutively from neurology clinic between January 2006 and January 2008. Peri-ictal period was defined as the period ranging from 2 minutes prior to seizure attack up to 48 hours after it, and post-ictal period was the time up to 48 hours after regaining consciousness. Peri-ictal urinary complaints were gathered with interview and data were analyzed using Pearson's Chi-square, Fisher's Exact test, and independent sample *t* test.

Results: The study population consisted of 57 (49.5%) men and 58 (50.4%) women, with the mean age of 26.83 ± 10.01 years. The frequency of at least one urinary symptom in studied patients was 39.1%. Incontinence, frequency, urgency, retention, and hesitancy were reported by 28 (24.3%), 14 (12.2%), 19 (16.5%), 10 (8.7%), and 8 (7%) patients, respectively. Women expressed more symptoms than men and a higher frequency of peri-ictal retention. Although overall urinary complaints were more frequent in patients with partial seizures, there was a higher frequency of urgency in patients with partial seizure (P = .037). Furthermore, apart from retention, there was no significant correlation between peri-ictal urinary symptoms and the patients' age.

Conclusion: Our findings suggest that peri-ictal urologic dysfunction is a common problem among patients with epilepsy and post-ictal urinary retention might also be considered as a post-ictal deficit (Todd's deficit).

Urol J. 2011;8:222-6. www.uj.unrc.ir

Keywords: epilepsy, complications, urination disorders, cross-sectional studies

¹Iranian Center of Neurological Research, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran ²Urology Research Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran ³Research Development Center of Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran ⁴Neurobiology Sector, International School for Advanced Studies, Trieste, Italy

Corresponding Author: Mohammad Reza Nikoobakht, MD Sina Hospital, Emam Khomeini St., Tehran, Iran Tel/Fax: 98 21 6671 6546 E-mail: nikoobakht_r@live.com

> Received July 2010 Accepted January 2011

INTRODUCTION

Seizures that arise from or spread to areas in the central autonomic network can mimic the stimulation of autonomic afferents or modify autonomic expressions. As a result, different types of seizures, especially tonic-clonic and complex partial ones originating from the temporal or extratemporal areas often lead to sympathetic activation at different ages.^(1,2) Activation or inhibition of areas in the central autonomic network can lead to cardiovascular, gastrointestinal, cutaneous, and genitourinary manifestations.⁽²⁻⁵⁾

Genitourinary complications, including urgency, frequency, hesitancy, dribbling, and overt incontinence, reflect alterations in the bladder function, mediated by the parasympathetic nervous system.^(2,6) While these urinary symptoms influence the life style greatly, few studies have evaluated the frequency of these peri-ictal complaints in patients with epilepsy.^(1,2,4) Even the number of studies that have been carried out examining the brain control of the bladder function is relatively limited.

The purpose of this study was to evaluate the frequency of peri-ictal urinary symptoms in patients with epilepsy in order to achieve a better health care for this public health problem.

MATERIALS AND METHODS

A cross-sectional study design was used to determine the peri-ictal urinary dysfunction among all the patients with epilepsy referred to the neurology clinic of Sina Hospital in Tehran, Iran from January 2006 to January 2008. This study was approved by the ethics committee of Tehran University of Medical Sciences.

Epilepsy was diagnosed and classified based on the International League Against Epilepsy criteria⁽⁷⁾ and the neurologist's perspective. Patients in the age range of 12 to 50 years were recruited. Those with a positive history of urogenital diseases, such as urinary tract infection, urolithiasis, malignancies, benign prostatic hyperplasia, and anatomic disorders (prolapsed of the uterus or bladder) were excluded from the study. Furthermore, patients in whom the urinary disorder was secondary to other neurologic diseases, such as dementia or multiple sclerosis, were also excluded.

Of 206 patients with epilepsy, 115 eligible subjects with urologic complaints enrolled in the study, consecutively. All of the subjects gave written informed consent. Thereafter, they were interviewed and a data sheet was completed. Eligible subjects that were able to answer questions were questioned directly and in case of mental retardation or any inability to answer questions, patient's family was approached.

Peri-ictal period was defined as the period ranging from 2 minutes before occurrence of seizure until 48 hours following the attack. Post-ictal period was the time up to 48 hours after regaining consciousness.⁽⁸⁻¹¹⁾

The data were analyzed by SPSS software (the Statistical Package for the Social Sciences, version

13, SPSS Inc., Chicago, Illinois, USA), using Pearson's Chi-square, Fisher's Exact test, and t test, when appropriate. A *P* value < .05 was considered statistically significant.

RESULTS

Participants consisted of 57 (49.5%) men and 58 (50.4%) women, with the mean age of 26.83 + 10.01 years. There was no significant difference between the mean age of the men and women. Forty-five (39.1%) patients reported at least one urinary symptom during the periictal phase. Urinary incontinence was the main complaint of participants (24.3%). Frequency, urgency, urinary retention, and hesitancy were reported by 14 (12.2%), 19 (16.5%), 10 (8.7%), and 8 (7%) patients, respectively. All the subjects with urinary retention reported it as a post-ictal problem. Table 1 demonstrates the peri-ictal urinary symptoms reported by patients with respect to the subjects' gender. Women expressed more symptoms than men (49 versus 30) and a higher frequency of retention (P = .049).

Generalized, partial, and unclassified seizures were noted in 76 (66.1%), 37 (32.2%), and 2 (1.7%) patients, respectively. All of the patients were taking antiepileptic drugs; 76 (66.1%) patients were using single drug, 31 (26.9%) two drugs, and 8 (6.9%) more than two drugs. Table 2

Table 1. Peri-ictal urinary symptoms considering the subjects
gender

Variables	Male	Female	Total	Р
Incontinence	15	13	28 (24.3%)	.63
Urgency	6	13	19 (16.5%)	.09
Frequency	5	9	14 (12.2%)	.27
Hesitancy	2	6	8 (7%)	.14
Retention	2	8	10 (8.7%)	.049

Table 2. Peri-ictal urinary symptoms acc	cording to type of seizure
--	----------------------------

	3 3 1		8 <u>,</u> 1	
Variables	PS ± SG (%)	GS (%)	Unclassified	Р
Incontinence	11 (29.7)	17 (21.8)	0	.24
Frequency	5 (13.5)	8 (10.2)	1	.42
Urgency	10 (27)	9 (11.5)	0	.03
Hesitancy	4 (10.8)	4 (5.1)	0	.43
Retention	6 (16.2)	4 (5.1)	0	.07
Overall urinary symptoms	18 (48.6)	26 (33.3)	1	.10

 $\mathsf{PS} \pm \mathsf{SG}$ indicates partial onset seizures with or without secondary generalization; and GS, generalized seizures.

demonstrates the frequency of different urinary symptoms regarding the type of seizure. Periictal urinary complaints were more frequent in patients with partial seizures; however, the difference was not statistically significant (P = .109). Peri-ictal urinary urgency was more frequent in patients with partial seizure than those with generalized seizure (P = .037) and in subjects aged ≥ 40 years old (P = .014). Apart from urgency, there was no significant correlation between the peri-ictal urinary symptoms and the patients' seizure type.

DISCUSSION

Different aspects of autonomic function, including the parasympathetic, sympathetic, and adrenal medullary systems, may be affected during ictal, post-ictal, and inter-ictal stages of partial or generalized epilepsies.⁽⁶⁾ Seizures typically activate the sympathetic nervous system and increase the heart rate and blood pressure as a result. On the other hand, parasympathetic activation or sympathetic inhibition may predominate during partial seizures.⁽²⁾ While postictal focal neurologic deficits, such as hemiparesis, aphasia, and visual field disturbances, are wellknown, post-ictal urinary disorders are not clearly reported. Furthermore, there are large varieties in defining peri-ictal period.^(4,12-14) Todd described the regional loss of function of the brain after seizure attack (Todd's paralysis) as a condition usually lasting for a few minutes; however, it may persist for 48 hours in certain cases.⁽¹¹⁾ Therefore, urinary symptoms may appear before (seconds to minutes) or after (few minutes to 48 hours) a lucid inter-ictal period of seizure.

Among urinary dysfunctions, incontinence is a frequent symptom in generalized tonic-clonic seizure. Urinary incontinence is not secondary to increased bladder pressure, but it occurs due to the bladder sphincter relaxation during the muscular recovery phase of the seizure.^(2,15) While urinary incontinence occasionally complicates the partial seizure, it possibly results from a combination of increased bladder pressure and loss of cortical inhibition of the micturation reflex.⁽⁶⁾

Oliva and colleagues reported 84 consecutive patients with at least one convulsive event during

video electroencephalography monitoring. Incontinence occurred in 23% (15/66) of patients. They could not find any relationship between type of epilepsy, lateralization, and the prevalence of incontinence.⁽¹⁶⁾ In another study on 28 subjects with epilepsy, 78.6% reported incontinence.⁽¹⁷⁾ In our study, in line with other studies, incontinence was the main urologic complaint (24.3%). Discrepancy in reported rates could have various reasons, such as interaction between central and peripheral effects, ictal autonomic discharges, and side effects of antiepileptic drugs. Therefore, more studies are necessary to elucidate the mechanisms of autonomic changes in epilepsy.

Ictal "desire to void" is an autonomic manifestation of temporal lobe epilepsy (TLE) reported in 0.3% to 8% of the cases. Aura of a "desire to void" and increased bladder pressure are infrequent manifestations of focal seizures.⁽¹⁸⁾ Janszky and associates reported peri-ictal vegetative symptoms (PIVS) in 141 patients with TLE, and assessed frequency, gender effect, and lateralizing value of peri-ictal autonomic signs. Peri-ictal vegetative symptoms were present in 93% of women and 77% of men.⁽⁴⁾ They found urge to void in 3 patients, which was contradictory to previous studies.^(3,19,20) The presence of PIVS had no lateralizing value, which may be linked to a low frequency of occurrence of PIVS.⁽⁴⁾ Ictal urinary urgency appears to occur in patients with non-dominant hemispheric focal epilepsy, most notably, TLE.⁽¹⁹⁾ Urge to void and incontinence have been described in patients with right hemispheric strokes.⁽¹⁸⁾ In the current study, 19 (16.5%) patients had urinary urgency. Furthermore, compared with generalized seizure, partial seizures were accompanied by a higher frequency of peri-ictal urgency. However, as this study was only based on clinical presentations, it was impossible to distinguish frontal and TLE in these subjects.

Acute urinary retention is well-documented in patients with acute destructive lesions in various parts of the brain, including the frontal lobe, paraventricular white matter, internal capsule, basal ganglia, and pontine tegmentum.⁽²¹⁾ Metaanalysis of positron emission tomography and functional magnetic resonance imaging studies have shown that the thalamus, insula, prefrontal cortex, anterior cingulate, periaqueductal gray matter, pons, medulla, and supplementary motor area are activated during urinary storage⁽²²⁾ and connections between the forebrain and brainstem structures are involved in the control of the bladder and sphincter in the human. Pontine micturation center is the final common pathway from the brain to the spinal cord.⁽²³⁾ Periaqueductal gray matter has multiple connections that enable it to coordinate and control voiding, and appear to perform much of the required signal processing. However, pontine micturation center acts as a switch between the storage and voiding phases. For voiding, the pontine micturation center requires both an excitatory signal from the periaqueductal gray matter and a safe signal from the hypothalamus.⁽²⁴⁾ Following focal seizure, there may be a localized paralysis, Todd's paralysis, which may last from minutes to hours, in the previously involved region.^(8,11) This category refers to transient paralysis that may occur following some partial epileptic seizures with focal motor components or somatosensory symptoms.

Wieser and colleagues showed that aura can be long-lasting, continuous, or recurrent⁽²⁵⁾ and Engel defined post-ictal symptoms as "manifestations of seizure induced by reversible alterations in neuronal function, but not structure".⁽¹⁰⁾ Vander and Ifergane reported 3 cases of transient postictal urinary retention, which were all men with different types of seizure.⁽²⁶⁾ On the contrary, of the 10 subjects presented with post-ictal urinary retention in our study, 8 were women. Janszky and associates also found that PIVS were more common in women,⁽⁴⁾ which is compatible with our study.

CONCLUSION

Post-ictal urinary retention should be kept in mind and asked during history taking; and if present, the patient should be referred to urologists for further treatment. Further studies are necessary to better elucidate the mechanisms of peri-ictal autonomic changes in epilepsy and prevent their undesirable effects.

ACKNOWLEDGEMENTS

We are indebted to the Iranian Center of Neurological Research as well as Research Development Center of Sina Hospital for their support.

CONFLICT OF INTEREST

None declared.

REFERENCES

- 1. Devinsky O. Effects of Seizures on Autonomic and Cardiovascular Function. Epilepsy Curr. 2004;4:43-6.
- Baumgartner C, Lurger S, Leutmezer F. Autonomic symptoms during epileptic seizures. Epileptic Disord. 2001;3:103-16.
- Horvath R, Kalmar Z, Feher N, Fogarasi A, Gyimesi C, Janszky J. [Brain lateralization and seizure semiology: ictal clinical lateralizing signs]. Ideggyogy Sz. 2008;61:231-7.
- Janszky J, Fogarasi A, Toth V, et al. Peri-ictal vegetative symptoms in temporal lobe epilepsy. Epilepsy Behav. 2007;11:125-9.
- Nikoobakht M, Motamedi M, Orandi A, Meysamie A, Emamzadeh A. Sexual dysfunction in epileptic men. Urol J. 2007;4:111-7.
- 6. Blok BF. Central pathways controlling micturition and urinary continence. Urology. 2002;59:13-7.
- Mazzoni P, Pearson T, Rowland LP, Merritt HH. Merritt's neurology handbook. 2 ed. Philadelphia: Lippincott Williams & Wilkins; 2006:585-90.
- So N. Epileptic Auras. In: Wyllie E, ed. *The treatment* of epilepsy: principles and practice. 3 ed. Philadelphia: Williams & Wilkins; 2001:297-340.
- Dreifuss FE, Penry JK, Bancaud J, Henriksen O, Rubio-Donnadieu F, Seino M. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. Epilepsia. 1998;22:489-501.
- Engel J. Seizures and epilepsy: FA Davis Co.; 1989:346.
- Todd RB. Clinical lectures on paralysis, certain diseases of the brain, and other affections of the nervous system. 2 ed. London: Churchill; 1856:291-302.
- 12. Badawy R, Macdonell R, Jackson G, Berkovic S. The peri-ictal state: cortical excitability changes within 24 h of a seizure. Brain. 2009;132:1013-21.
- 13. Boylan LS. Peri-Ictal Behavioral and Cognitive Changes. Epilepsy Behav. 2002;3:16-26.
- Surges R, Scott CA, Walker MC. Enhanced QT shortening and persistent tachycardia after generalized seizures. Neurology. 2010;74:421-6.
- Gastaut H, Orfanos A, Lob H. Polygraphic study of enuresis during grand mal attacks. Electroencephalogr Clin Neurophysiol. 1964;16:626-7.
- 16. Oliva M, Pattison C, Carino J, Roten A, Matkovic Z,

O'Brien TJ. The diagnostic value of oral lacerations and incontinence during convulsive "seizures". Epilepsia. 2008;49:962-7.

- Imam I, Talabi OA, Sanya EO, Ogunniyi A. The determinants of seizure severity in Nigerian epileptics. Niger J Clin Pract. 2005;8:94-6.
- Kuroiwa Y, Tohgi H, Ono S, Itoh M. Frequency and urgency of micturition in hemiplegic patients: relationship to hemisphere laterality of lesions. J Neurol. 1987;234:100-2.
- Loddenkemper T, Foldvary N, Raja S, Neme S, Luders HO. Ictal urinary urge: further evidence for lateralization to the nondominant hemisphere. Epilepsia. 2003;44:124-6.
- Baumgartner C, Groppel G, Leutmezer F, et al. Ictal urinary urge indicates seizure onset in the nondominant temporal lobe. Neurology. 2000;55: 432-4.
- 21. Sakakibara R, Hattori T, Yasuda K, Yamanishi T. Micturitional disturbance after acute hemispheric

stroke: analysis of the lesion site by CT and MRI. J Neurol Sci. 1996;137:47-56.

- 22. DasGupta R, Kavia RB, Fowler CJ. Cerebral mechanisms and voiding function. BJU Int. 2007;99:731-4.
- Tadic SD, Griffiths D, Schaefer W, Resnick NM. Abnormal connections in the supraspinal bladder control network in women with urge urinary incontinence. Neuroimage. 2008;39:1647-53.
- Blok BF, Sturms LM, Holstege G. A PET study on cortical and subcortical control of pelvic floor musculature in women. J Comp Neurol. 1997;389: 535-44.
- Wieser HG, Hailemariam S, Regard M, Landis T. Unilateral limbic epileptic status activity: stereo EEG, behavioral, and cognitive data. Epilepsia. 1985;26: 19-29.
- Vander T, Ifergane G. Transient postictal urinary retention: presentation of three cases. Eur J Neurol. 2004;11:207-8.