Current Journal of Neurology

Original Paper

Curr J Neurol 2020; 19(4): 167-72

Assessment of cognitive functions and related risk factors in Iranian patients with generalized epilepsy as compared to patients with non-epileptic neurological disorders

Received: 25 May 2020
Accepted: 27 Aug. 2020

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Keywords
Generalized Epilepsy; Cognitive Dysfunction; Risk Factors; Drug Resistant Epilepsy; Seizures

Abstract

Background: The cognitive impairment in patients with generalized epilepsy may affect their social efficiency and quality of life (QOL). The aim of this study is to determine the cognitive dysfunction and related risk factors in patients with generalized epilepsy as compared to patients with non-epileptic neurological disorders.

Methods: In the present descriptive cross-sectional study, the cognitive function was assessed by Montreal Cognitive Assessment (MoCA) test in 62 patients with generalized epilepsy and also 62 patients with non-epileptic neurological diseases who referred to the Neurology Clinic, Semnan University of Medical Sciences, Semnan, Iran. The relationship between cognitive impairment and related risk factors was also investigated. The data were analyzed by SPSS software.

Results: The mean score of MoCA in the patients with generalized epilepsy and the control group was 22.80 ± 4.14 and 26.48 ± 2.85, respectively ($P < 0.050$). The results indicated significantly lower MoCA scores in the epileptic group rather than the non-epileptic one ($P < 0.001$). Moreover, there was a significant relationship between MoCA score and age, education level, living place, the dose and rate of medicines, and the number of seizures in patients with epilepsy ($P < 0.001$). Gender and the duration of disease had

How to cite this article: Masoudian N, Moradpour M, Samaei A, Ehsani F, Ziari A. Assessment of cognitive functions and related risk factors in Iranian patients with generalized epilepsy as compared to patients with non-epileptic neurological disorders. Curr J Neurol 2020; 19(4): 167-72.

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no significant effects on the cognitive impairment of patients with epilepsy (P > 0.05).

Conclusion: Patients with epilepsy had a significant cognitive impairment as compared to the patients with non-epileptic neurological disorders. Age, education level, living place, the dose and rate of medicines, and the number of seizures were the risk factors of cognitive impairment in the patients with epilepsy, while duration of disease and gender had no effects on the intensity of cognitive deficits.

Introduction

Epilepsy is the second most burdensome neurologic disorder in societies that severely affect the quality of life (QOL) of patients.[1] The epilepsy refers to recurrent attacks occurring due to sudden, intermittent, and excessive electrical discharge of brain neurons for at least twice (unprovoked).[2] The incidence of epilepsy is 48 per 100 thousand and 139 per 100 thousand persons years in countries with high income and low or middle income, respectively.[3] Studies have also shown that 1.5 to 5.0% of the population may experience epileptic seizure.[4]

Epilepsy is associated with 11.6% of mental problems, 56.6% of feelings of shame, fear, anxiety ,and low self-confidence, and also 26.6% of social problems.[5] Epilepsy can cause reducing self-confidence, life satisfaction, and also increasing psychological distress, anxiety, and interpersonal problems such as isolation and poor social performance.[6,7] In addition, high rate of suicide in patients with epilepsy was reported in some studies that declared the necessity of effective interventions for these patients.[8] Some studies also indicated that epilepsy can change cognitive and behavioral functions and then lead to extreme poor social performance in patients with epilepsy.[8-10] Repeating the epileptic discharges affect functional and structural changes of brain during both focal and generalized epilepsy, which can induce cognitive, behavioral, and emotional dysfunctions.[10] In this regard, some studies reported that all cognitive domains such as attention, language, executive functions, memory, problem solving, and insight are impaired following seizures in patients with epilepsy, which reduced the patients' QOL.[11,12] On the other hand, other studies have not shown any cognitive deficits in patients with epilepsy and even some studies reported positive effects of some drugs on cognition of patients with epilepsy during intervention.[13-15] However, various studies indicated that patients with generalized epilepsy show poorer performance in semantic mastery compared to normal individuals.[16] Besides, there is evidence suggesting that some factors such as gender, education level, living place, etc. may affect the intensity of cognitive dysfunction in patients with generalized epilepsy.[3,17] So that, identifying the intensive factors of cognitive impairment may strongly help to achieve an effective intervention planning. Therefore, the detection of risk factors seems necessary for minimizing cognitive function deficits, having proper social efficiency, and high QOL in patients with epilepsy. However, according to the available acknowledgment, there is a controversy in the results of studies available in this issue. The purpose of this study is to determine the cognitive function status and also related risk factors in Iranian patients with generalized epilepsy as compared to other patients with non-epileptic neurological disorders.

Materials and Methods

This study was approved by the Human Ethics Committee, Semnan University of Medical Sciences (IR.SEMUMS.REC.1397.081) and performed according to the ethical standards laid down by the Declaration of Helsinki (DoH). The present analytic cross-sectional study was conducted in the Neurology Clinic, Semnan University of Medical Sciences during 2018. In this study, following convenient sampling, 62 patients with generalized epilepsy were assigned to the epileptic group and 62 patients with non-epileptic neurological diseases without any cognitive impairment were included in the control group. The study sample size was determined based on a similar previous study.[18] The inclusion criteria for the patients with epilepsy group were definitive diagnosis of generalized epilepsy, which was approved by the neurologist, and also having the age more than 18 years old. The exclusion criteria included having structural abnormality in magnetic resonance imaging (MRI) or computed tomography (CT)-scan, severe psychiatric disorders such as schizophrenia bipolar disorder, hearing and visual disorders, severe comorbidities such as kidney, heart, and liver failures, thyroid dysfunctions, and progressive central nerve system (CNS) disorders such as dementia and Parkinson's disease.

First, the patients in both groups were explained about the purpose and method of the project and assured that their information would be used only for research purpose. Then, the informed consent forms were obtained from all

participants. Demographic characteristics and some of risk factors such as age, gender, educational level, the number of anticonvulsants the patients took, the duration and number of seizures, and the experience of patients were also recorded in a researcher made checklist. The Montreal Cognitive Assessment (MoCA) test as a valid and reliable scale was used to measure the cognitive function of patients. The MoCA cognitive assessment test consists of 7 parts to assess different skills of cognition. It is scored out of 30 points and a score of 26 or above is considered to be normal. One score is added to the total score of the patients with less than 12 years of education.[19]

After collecting the data, all the data were entered the SPSS software (version 18, SPSS Inc., Chicago, IL, USA) for analysis. The Kolmogorov-Smirnov test was applied to investigate the normality of data distribution for the variables tested. The independent t-test was utilized to evaluate the baseline values between the groups. In addition, the statistical correlation of cognitive functions and gender, education, living place, the medicine the patient took, and the number of seizure factors were assessed by Pearson or Spearman correlation test, linear regression, independent t-test or Mann-Whitney U test.

Results

The mean ± standard deviation (SD) of age of the epileptic and non-epileptic patients was 31.47 ± 13.40 and 30.96 ± 12.16 (with age range of 18-63 and 19-65 years), respectively. There was no significant difference between the groups in age ($P > 0.050$). 29 (46.8%) and 33 (53.2%) patients were respectively males and females in the epileptic group. In the control group, 26 (41.9%) and 36 (58.1%) patients were respectively males and females. 29 (46.8%), 19 (30.6%), and 14 (22.6%) participants of the epileptic group and 31 (50.0%), 16 (26.0%), and 15 (24.0%) of the participants of non-epileptic group had under diploma, diploma, and academic degrees, respectively. The frequency of sex composition and education level in the two groups was not significantly different ($P > 0.050$). The durations of epilepsy was shorter than one year for 8 patients and longer than one year for 54 patients in the epileptic patients group. Moreover, 33 (53.2%), 14 (22.6%), and 8 (12.9%) patients received respectively one medicine, two medicines, and more than two medicines in the epileptic patients group. Additionally, 26 (41.9%) patients experienced no seizure, 18 (29.0%) patients once, and 18 (29.0%) patients experienced seizure twice or more.

The results indicated significantly lower MoCA scores in the epileptic group rather than the non-epileptic group ($P < 0.001$). The mean score of MoCA in the patients with generalized epilepsy and the control group was 22.80 ± 4.14 and 26.48 ± 2.85, respectively ($P < 0.050$). There was also a significant correlation between the MoCA scores in the group of patients with epilepsy and age ($r = -0.55$, $P < 0.001$), while there was not significant correlation between gender and MoCA scores in the patients with epilepsy group ($P > 0.050$) (Table 1). As shown in table 1, there was a significant difference in the MoCA score in the group of patients with epilepsy based on the educational levels ($P < 0.001$). Participants with a high level of education had less cognitive dysfunction. Moreover, there was a significant difference in the MoCA scores of the patients based on living place ($P < 0.001$). Participants who lived in the city had higher MoCA scores. Furthermore, there were significant differences in the MoCA scores in the patients with conventional epilepsy who received no medicine (24.14 ± 1.57) or who received one medicine (25.21 ± 2.82) as compared to those who obtained two medicines (19.21 ± 2.45) or several medicines (18.01 ± 4.34) ($P < 0.001$).

Table 1. Montreal Cognitive Assessment (MoCA) scores based on gender, education level, and location between the epileptic and non-epileptic groups

Variable		Group		P
		With epilepsy	Other disease	
		Mean ± SD	Mean ± SD	
Gender	Male	22.41 ± 4.31	26.26 ± 2.64	> 0.050
	Female	23.15 ± 4.03	26.63 ± 3.01	
Education level	Illiterate	15.10 ± 2.01	18.02 ± 2.15	< 0.001
	Under diploma	20.55 ± 4.04	23.33 ± 3.24	
	Diploma	23.36 ± 3.16	26.05 ± 1.29	
	Academic degree	26.71 ± 1.85	28.01 ± 1.47	
Location	City	23.69 ± 3.96	26.87 ± 2.44	< 0.001
	Village	20.95 ± 3.99	20.75 ± 2.21	

MoCA: Montreal Cognitive Assessment; SD: Standard deviation

Comparing the severity of cognitive impairment based on the different parts of the MoCA test (visual/spatial, executive, language, attention, concentration and memory, verbal, abstraction, delayed recall, and time and place awareness), the MoCA scores in the patients with conventional epilepsy were significantly more than the patients with drug-resistant epilepsy ($P < 0.001$, Table 2). However, there was no significant difference in the scores obtained from the verbal part of the test between the patients with conventional epilepsy and those with drug-resistant epilepsy (Table 2). Whereas, the scores obtained from the visual, spatial-executive, attention, concentration and memory, abstraction, delayed recall, and time and place awareness parts by the patients with drug-resistant epilepsy were lower than those of the patients with conventional epilepsy ($P < 0.001$).

The results also indicated that there was no significant relation between the cognitive impairment score and the duration of disease in the patients with epilepsy ($P > 0.050$). However, there was a significant relation between the cognitive impairment score and the number of seizures in the patients with epilepsy ($P < 0.001$). The MoCA scores in the patients with epilepsy who had not seizure (25.61 ± 2.38) were significantly more than the scores in the patients who experienced once seizure (20.05 ± 3.22) and more than once seizure (21.50 ± 4.59) ($P < 0.001$).

Discussion

The results of the present study indicated that the cognitive impairment is significantly higher in the patients with epilepsy in comparison with patients without epilepsy, which are similar to the results of previous studies.[18,20-22] However, some studies demonstrated that patients with epilepsy have not cognitive deficits.[13-15,23] It seems that one of the main causes of this discrepancy in the findings of the current study and the study by You[23] is the difference in the type of the disease of the patients with epilepsy. Our study and most previous studies, which indicated cognitive impairment in the patients with epilepsy, included the older patients with epilepsy,[10-12,16] while in the aforementioned study, child patients with epilepsy were assessed.[23] In addition, the finding of the current study showed that age is a significant risk factor in the inducing cognitive impairment of these patients. Therefore, the older patients with epilepsy are expected to suffer more cognitive deficits as compared to child patients with less than 9 years.[3]

The findings of the current study also showed that the obtained scores in the patients with epilepsy who used more than two medicines with maximum dose, were lower than the scores of other patients with epilepsy who used less than two medicines. These results were consistent with the results of some studies in this field.[20,21,24-26] There is evidence that antiepileptic medicine can have inverse effects on cognitive functioning by prohibiting nervous irritability or increasing prohibition of neuron transfers.[24] The present study also indicated that there was a significant correlation between the dose and rate of medicines and the intensity of cognitive impairment in patients with epilepsy.[25,27]

Table 2. Montreal Cognitive Assessment (MoCA) scores between the patients with conventional epilepsy and patient with drug-resistant epilepsy

Station	Patients	MoCA (mean ± SD)	P
Visual, spatial/executive	Conventional epilepsy	4.47 ± 1.03	< 0.001
	Drug-resistant epilepsy	3.22 ± 0.92	
Memory	Conventional epilepsy	2.87 ± 0.51	< 0.001
	Drug-resistant epilepsy	2.22 ± 0.68	
Attention, concentration	Conventional epilepsy	3.70 ± 1.09	< 0.001
	Drug-resistant epilepsy	2.09 ± 0.68	
Verbal	Conventional epilepsy	2.52 ± 0.40	> 0.050
	Drug-resistant epilepsy	1.72 ± 0.70	
Abstraction	Conventional epilepsy	1.40 ± 0.74	< 0.001
	Drug-resistant epilepsy	0.90 ± 0.52	
Delayed recall	Conventional epilepsy	4.20 ± 0.96	< 0.001
	Drug-resistant epilepsy	2.86 ± 0.71	
Time and place awareness	Conventional epilepsy	5.75 ± 0.98	< 0.001
	Drug-resistant epilepsy	5.04 ± 0.65	

MoCA: Montreal Cognitive Assessment; SD: Standard deviation

The present study also indicated that there was a significant correlation between the number of seizures and cognitive impairment. In this regard, the findings of some studies confirm the result of the current study.[25,27] Vingerhoets,[25] Thompson and Duncan,[26] and Merkena[27] found that there is a significant correlation between the number of seizures and cognitive impairments. They showed that patients who experienced more seizures had higher cognitive impairment.

The results of this study also showed that duration of disease has no association with the severity of cognitive impairment in the patients with epilepsy, which is consistent with the findings by Thompson and Duncan[26] and Merkena.[27] However, the current study indicated that there was no significant relationship between male and female patients in the intensity of cognitive impairment. This finding was not consistent with that of the latter study,[27] which found a higher cognitive impairment in women than men. It seems that one of the causes of this controversy is lower sample size of the present study as compared to that of the latter one. Natham et al.[18] also reported higher cognitive impairment in women than men. However, this study assessed cognitive function by Mini-Mental State Exam (MMSE), while it was assessed by MoCA in the present study. Therefore, the difference in the results was due to high sensitivity of the MoCA test as compared to the MMSE in the assessment of cognitive impairment.

Assessment of the cognitive impairment showed that the verbal part of MoCA test was not different between patients with epilepsy and drug-resistant epilepsy group. Whereas, other parts of MoCA indicated higher changes for the patients with drug-resistant epilepsy, which was in line with the results of the studies by Miller et al.[20] and Phabphal and Kanjanasatien.[22]

In this study, we included only the patients with epilepsy with the age of more than 18 years. Therefore, conducting further studies to investigate the cognitive function and its risk factors in younger patients with epilepsy (less than 18 years) is suggested. The other limitation of this study was disregarding the type of the antiepileptic medicine used by patients. It is suggested to assess the effects of type of the antiepileptic drugs on cognitive function in patients with epilepsy in the future studies.

Conclusion

The results of the present study showed that patients with generalized epilepsy have higher cognitive impairment as compared to patients with non-epileptic neurological disorders. Age, education level, living place, dose and rate of medicines, and number of seizures were considered as the risk factors of cognitive impairment in the patients with epilepsy. Whereas, gender and the duration of disease had no significant effects on the cognitive impairment of patients with generalized epilepsy.

Conflict of Interests

The authors declare no conflict of interest in this study.

Acknowledgments

The authors would like to appreciate the Clinical Research Development Unit, Kowsar Hospital, Semnan University of Medical Sciences for cooperation and providing facilities to this work.

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