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Short communication

Metabolic syndrome in young adults with epilepsy

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ABSTRACT

Purpose: Persons with epilepsy have higher cardiovascular mortality and morbidity compared to general population and alteration of their biochemical milieu is one of the proposed mechanisms. We aimed to study the prevalence of metabolic syndrome and cardiovascular risk factors in young adults with epilepsy and the association with antiepileptic drug use.
Method: An observational study was conducted in persons with epilepsy aged 20–49 years using antiepileptic drugs regularly for the previous three years. The subjects were examined and their blood samples were collected for fasting blood glucose and lipid profile.
Results: Over 18 months, 183 patients (120 males; 63 females) were recruited (mean age 32.5 ± 8.9 years). Metabolic syndrome (MetS) by ATP III criteria was present in 54 (29.5%) subjects. People with MetS in our group had higher frequency of abdominal obesity (50.0%) and hypertriglyceridemia (55.5%) than diabetes/impaired fasting glucose (27.8%). Older age ($p = 0.005$) and use of valproate ($p = 0.012$) were associated with significant risk of MetS.
Conclusion: Clinicians need to be vigilant regarding the risk of MetS while initiating treatment and following up persons with epilepsy.

1. Introduction

Epidemiological studies have shown a higher incidence of cardiovascular morbidity and mortality in persons with epilepsy compared to the general population [1,2]. This association was noted to be more profound in individuals aged below 65 years [2].

Alterations of the metabolic components of the body can lead to adverse cardiovascular and cerebrovascular events. Metabolic syndrome (MetS) was defined by Reaven in 1988 as clustering of multiple interrelated risk factors with attendant two fold increased risk of cardiovascular disease [3]. Drugs used to treat epilepsy are known to alter the metabolic milieu of the body, especially the lipid levels, acute phase reactants and coagulation profile [4,5]. However, very few studies have explored the relationship of epilepsy and its treatment with MetS. The objective of this study was to examine the prevalence of MetS and cardiovascular risk factors in young adults with epilepsy from a tertiary care neurology centre and study their association with antiepileptic drug use.

2. Methods

This observational cross-sectional study was carried out between January 2012 and June 2013 in the weekly Epilepsy outpatient clinic in Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India. On each day of the clinic, we recruited the first five patients who fulfilled the selection criteria and consented to participate in this study.

Persons aged 20–49 years with active epilepsy and using antiepileptic drugs for the past three years or more were eligible for inclusion. Patients with diabetes mellitus, systemic hypertension or dyslipidemia pre-dating the onset of epilepsy, patients on drugs (such as steroids, beta blockers and hormonal contraceptives) known to alter the lipid profile, pregnant women and women in the first 6 months postpartum period were excluded.

The demographic data, characteristics of the epilepsy, presence of metabolic risk factors and cardiovascular disease were recorded on a standard proforma. Fasting blood glucose and lipid profile were evaluated from venous blood drawn after 8 h of fasting.

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A cardiologist carried out the cardiac evaluation and electrocardiography for all subjects.

We used the National Cholesterol Education Program's Adult Treatment Panel III (ATP III) [6] criteria for MetS modified for Asian population [7] which defines MetS as presence of at least three of five features: central (abdominal) obesity (waist circumference >90 cm in males and >80 cm in females), raised triglycerides (≥150 mg/dl or specific treatment for this), reduced HDL cholesterol (<40 mg/dl in males, <50 mg/dl in females or specific treatment for this), raised blood pressure (systolic BP ≥ 130 mm Hg or diastolic BP ≥ 85 mm Hg or treatment of previously diagnosed hypertension) and raised fasting plasma glucose (FPG ≥ 110 mg/dl or treatment of previously diagnosed type 2 diabetes).

Study had the approval of the Institutional Ethics committee and informed consent was obtained from all participants.

Statistical analysis was done with SPSS software for Windows version 21. Means of numeric variables were compared between groups by Student's *t*-test. Proportions were compared by Chi-square test or Fisher's exact test. *p* values of less than 0.05 were taken for statistical significance. We compared the results from our subjects with the general population characteristics from a previous study in one of the Indian states [8] using Student's *t*-test (to compare the means) and Chi-square test (to compare the proportions).

3. Results

We recruited 183 patients fulfilling the inclusion and exclusion criteria from 4312 patients who attended the Epilepsy Clinic during the period of the recruitment. There were 120 (65.9%) males and 63 (34.1%) females with mean age of 32.5 (±8.9) years (range 20–49 years). The demographic and clinical profiles of the subjects are given in Table 1.

All the patients were on antiepileptic drugs at the time of recruitment. More than half of the subjects (51.9%) were on monotherapy and the rest were on two antiepileptic drugs (37.16%) or more than two antiepileptic drugs (10.9%). Carbamazepine, sodium valproate, phenytoin, clobazam and phenobarbitone were used as monotherapy or in combination in 178 (97.27%) of the 183 patients (Table 1). The newer antiepileptic medications (levitiracetam, oxcarbazepine, topiramate, lamotrigine, clonazepam, lacosamide and zonisamide) were used only in 15 (8.19%) patients. Among the monotherapy group, 33 (34.73%) were on valproate, 19 (20.0%) on carbamazepine, 17 (17.89%) on phenytoin, 4 (4.21%) on phenobarbitone, 3 (3.15%) on levitiracetam and 2 (2.11%) on oxcarbazepine.

MetS (by ATP III criteria) was present in 54 (29.5%) patients. In the total cohort, abdominal obesity was detected in 81 patients (44.3%). Eight (4.37%) of the enrolled patients were diagnosed to have diabetes mellitus after the onset of epilepsy and another 10 had impaired fasting blood glucose. 105 (55.56%) patients had high systolic and/or diastolic blood pressure at examination or were on treatment for systemic hypertension. 93 (50.8%) patients had abnormal fasting lipid levels or were on treatment for the same. The distribution of the components of MetS is shown in Table 1.

Five of the patients were smokers and none of them had MetS. Only one patient exercised regularly. Family history of coronary artery disease or stroke was present for 4 patients. These factors were not significantly different between the patients with and without MetS. Two patients in the study cohort had coronary heart disease proven by coronary angiography.

Table 1
Demographic and clinical characteristics of persons with epilepsy with and without metabolic syndrome.

	Total subjects (*N* = 183)	Subjects with metabolic syndrome (*N* = 54)	Subjects without metabolic syndrome (*N* = 129)	*p* value
Males, *N* (%)	120 (65.9)	39 (32.5)	81 (67.5)	0.221
Age group, *N* (%)				
20–29 years	81 (44.26)	14 (25.9)	67 (51.9)	
30–39 years	50 (27.32)	19 (35.2)	31 (24.03)	**0.005**
40–49 years	52 (28.42)	21 (38.8)	31 (24.03)	
Age in years, mean (SD)	32.46 (8.9)	31.94 (9.19)	32.68 (8.86)	0.691
Duration of epilepsy in years, mean (SD)	15.43 (9.84)	14.81 (9.76)	15.68 (9.91)	0.225
Duration of treatment in years, mean (SD)	13.60 (8.97)	12.13 (7.89)	14.20 (9.35)	0.936
Type of epilepsy, *N* (%)				
Primary	45 (24.70)	16 (29.63)	29 (22.48)	
Localization related	127 (69.23)	36 (66.67)	91 (70.54)	0.469
Unclassified	11 (6.04)	2 (3.70)	9 (6.98)	
Antiepileptic drugs, *N* (%)[a]				
Carbamazepine	64 (34.97)	16 (29.63)	48 (37.21)	0.327
Phenytoin	39 (21.31)	14 (25.92)	25 (19.38)	0.324
Valproate	48 (31.69)	21 (38.89)	27 (20.93)	**0.012**
Clobazam	54 (29.51)	15 (27.78)	39 (30.23)	0.110
Phenobarbitone	23 (12.57)	3 (5.56)	20 (15.50)	0.064
Metabolic parameters, mean (SD)				
FBG (mg/dl)	92.78 (16.37)	100.44 (24.32)	89.57 (10.05)	**<0.0001**
Total cholesterol	213.57 (49.91)	224.30 (54.60)	209.09 (47.31)	0.060
LDLc	142.79 (42.68)	148.57 (43.90)	141.78 (42.18)	0.328
HDLc	45.67 (12.81)	39.67 (11.01)	48.18 (12.71)	**<0.0001**
Triglycerides	119.30 (74.43)	179.0 (99.30)	94.30 (40.76)	**<0.0001**
Components of metabolic syndrome, *N* (%)				
Abdominal obesity	81 (44.26)	27 (50.0)	54 (41.9)	
High BP or treatment	105 (57.37)	50 (92.6)	55 (42.63)	
Diabetes mellitus or IFG	18 (9.84)	15 (27.8)	3 (2.3)	
Low HDLc	24 (13.11)	12 (22.2)	12 (9.3)	
High triglycerides	38 (20.77)	30 (55.5)	8 (6.2)	

Abbreviations: %, percentage; FBG, fasting blood glucose; HDLc, high density lipoprotein cholesterol; IFG, impaired fasting glucose; LDLc, low density lipoprotein cholesterol; *N*, number; SD, standard deviation. Bold values indicate the ones which have attained statistical significance.

[a] The comparison is between the proportions of subjects with metabolic syndrome exposed to a given drug against metabolic syndrome with all other drugs.