Early Seizures during Stroke

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Abstract

BACKGROUND: The connections between seizures and stroke, their characteristics, and features are barely developed and also very important for the outcome. The diagnostic problem leads to ineffective treatment due to difficult selection of patients who are subject to prevention with antiepileptic drugs (AEDs) on one hand. On the other hand, it is impossible to examine every stroke patient by EEG. We need an algorithm for screening indicated patients and conducting the EEG. After that, we can include properly AED as a prevention. Their low frequency makes them time consuming to study.

AIM: The aim of the study was to conduct an epidemiological study of early epileptic seizures at the acute stroke phase and to derive principles for screening, diagnosis, and behavior for prevention.

METHODS: To achieve the goal, we have researched retrospective patients, totally amounting to 656.

RESULTS: The factors identified so far in the genesis of seizures such as age, type, and location of cerebrovascular disease; Stroke; Prevention; Screening

CONCLUSIONS: There are no clear criteria to outline the rules for the AED prophylactic in patients with cerebrovascular disease (CVD). The most important indicator is the systematic assessment of the risk of seizures in the course of the disease. Patients at high risk of triggering seizures and developing epilepsy in CVDs are suitable for EEG examinations with a view to timely diagnosis and treatment.

Introduction

The subject of the study was early seizures during stroke as a complication. It means that the main diagnose (stroke) is already present and the possible complication is in the asymptomatic phase which allows us to do secondary prevention at this stage. The relative share of these patients is extremely small, which makes the problem unattractive to scientists and is poorly defined. The risk is below 10%. However, assuming that about 15 million people/year worldwide suffer from stroke, according to the World Stroke Organization, this means that about 1.5 million patients have seizures during or after a stroke [1]. This is a significant number of patients, which makes it a very important topic for study despite the little published data. The diagnostic problem leads to ineffective treatment due to difficult selecting of patients who are subject to prevention with AEDs. On one hand – prevention of seizures among patients who never show such and exposing them to the risk of side effects, and on the other hand – lack of prevention of seizures among patients who are at risk and show this complication in the future with disability and necessary of tertiary prevention.

The “seizure” symptom is considered a harbinger of a stroke, such as in the course of a vascular accident and seizures as residual symptoms after experiencing an acute phase of stroke (early and late) [2]. The connections between seizures and stroke their characteristics and features are also considered. The focus of the scientific literature so far is the seizures in cerebral hemorrhage. The larger number of cerebral hemorrhages makes the research more reliable. Seizures are significantly less affected in cases of cerebral infarction, which necessitates in-depth research on them. Their low frequency makes them time consuming to study. The severity of clinical stroke, regardless of the scale used, is a major factor in the development of post-stroke epilepsy [3], [4], [5], [6], [7]. Particularly, high risk for genesis of seizure is infarction in the anterior cerebral
artery blood supply [4], [8], [9], [10]. The extent of cortical involvement is the next most important risk factor [3], [9], [11], as the involvement of the parietal-temporal cortex increases it [3], [9], [12], [13]. Small vessels disease also has an effect. Lacunar infarcts form about 11% of post-ischemic epilepsy [14]. Epileptic seizures can be caused by ischemic stroke or can be biomarkers for it [15], [16], [17]. A large study [18] in the United Kingdom reported that late-onset epilepsy was associated with a risk of later stroke. Vascular risk factors, including a history of myocardial infarction, peripheral vascular disease, hypertension, elevated total serum cholesterol, and left ventricular hypertrophy, have been associated with late onset of “silent infarction” epilepsy [17], [19]. The younger the patient, the more reactive his nervous system is and the more likely he is to have a seizure in the course of an ongoing stroke [20], [21], [22], [23], [24]. Early prevention of symptomatic epilepsy reduces its incidence in the long run [25], [26], [24]. Studies continue to reveal effective prevention [27] to reduce disability and improve the quality of life of patients with cerebrovascular disease as a socially significant disease [24].

**Contingent and variable**

**Design**

The population at risk are all of the included retrospective patients with acute stroke passed through our clinic from March 2017 to February 2018, amounting to 656. Each patient was evaluated by biological, clinical, and laboratory indicators, which was systematized in a database and has subjected to statistical processing by the method of classification and regression tree with the main dependent variable – “seizures”. The data were obtained through the general hospital electronic archive – retrospectively. Their processing and storage are in accordance with the requirements set out in the Code of Ethics [28].

**Methods**

Classification and regression tree (CART) have been developed and proposed various variants [29], [30], [31], [32], as well as hybrid methods [33]. CART is a hybrid model based on logistic regression [33]. A new regression methodology is the proposed hybrid CART-MARS method [34]. This method is able to classify and predict values for a given dependent variable by identifying the main influencing and most strongly independent variables [35]. The data processing is non-parametric and does not suggest the distribution of the dependent variable. The created tree can be considered as a kind of multidimensional distribution of data [37]. It is successful in cases of missing data on important predictors. Another advantage is that it works well with both small and large data sets, and the results are easy for everyone to interpret. The CART method is defined as a recursive-dividing regression in which data are divided into relatively homogeneous end nodes to obtain a predicted value that is the average observed value for each end node [37]. Homogeneity is expressed as a low standard deviation by the least squares method.

**Results and Discussion**

**Correlation analysis**

From the correlation analyzes, it is clear that there is no relationship between the compared variables, as demonstrated in studies of symptomatic epilepsy in men and women [38]. The ratio of the individual types and locations of cerebrovascular diseases is preserved and the connection with the manifested seizures is weak, which is an applicable conclusion for all 26 variables. Each variable individually does not have the power to influence the manifestation or not of fainting, but this does not exclude the possibility of a combination of individual factors to have a strong impact. The purpose of the correlation analysis is to emphasize that the factors identified so far in the genesis of seizures such as age, type, and location of cerebrovascular accident and proximity to the cortex do not act alone, but in combination with undiscovered internal and external ones.

**Classification and regression tree**

The data processing program simulates multiple variants of a classification and regression tree with different numbers of end nodes and automatically finds the number of end nodes with the lowest statistical error. The tree tracks the patients who have seizures and divides them based on the strongest factor in the daughter nodes, followed by a new division or not at the end nodes. All patients grouped in one end node have similar combination of characteristics and risk factors and it can be concluded that they have the same degree of risk for seizures. Through the model developed in this way, based on laboratory standard tests of all future patients with cerebrovascular diseases, they can be classified and recognized to any of the end nodes, which can be used for screening by EEG. In other words, the indications for electroencephalography can be expanded and the indications for the inclusion of antiepileptic prophylaxis with the future reduction of disability and improvement of quality of life can be determined.

Patients at high risk of seizures and indicated for EEG examination have the following combination of characteristics: The severity of the clinical stroke, regardless of the scale used, is a major factor in
the development of post-stroke epilepsy [1], [28], [29], [30], [31]. Particularly, high risk for epileptogenesis is infarction in the anterior cerebral artery basin [28], [32], [33]. Young age; cerebral hemorrhage or embolic infarction in the dominant cerebral hemisphere and near the cortex; INR ≤1.11; Cholesterol ≥4 mmol/l.

Conclusions

It is recommended to cover as many cases of cerebrovascular diseases with EEG as possible to give them a chance for complex treatment, but also because more information of science is needed; creating a publicly available database of neurological research environments, sharing archives, and engaging more researchers on the topic of the problem. It is also necessary to study the phenotypic variables as a manifestation of the genotypic influence.

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Statement of Ethics

This study protocol was reviewed and approved by Local Ethics Committee of Trakia University – Stara Zagora city, Bulgaria, approval number 14/02 OCT 2020. All patients voluntarily signed an informed consent form before inclusion in the study.

Author Contributions

C. Naydenov – constructing the aim and the design, processing the research, writing the overview, and introduction. V. Mancheva – scientific supervisor, writing the discussion, and conclusions. L. Manchev – coordinating the process and creating local environment and writing the abstract. A. Yordanova – creating the database and statistical processing of the results.

Data Availability Statement

The datasets generated and analyzed in the present study are available from the corresponding author on reasonable request.

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