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Opinion

Cerebrovascular Disease and Epilepsy as a Health Problem

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Received: February 13, 2023; **Published:** February 24, 2023

Cerebrovascular disease and epilepsy are two global health problems that deserve an adequate response [1,2]. They have a very close relationship, since the latter can present as a complication or sequelae of cerebrovascular disease and, in turn, this can be part of its etiology [3]. Therefore, the association between epilepsy and cerebrovascular disease appears to be bidirectional [4].

Cerebrovascular diseases (CVD) are one of the most studied conditions among chronic non-communicable diseases. They are closely related to population aging, a phenomenon that is particularly evident in developed countries, with a similar trend in low- and middle-income countries, where the number of people aged 80 and over is expected to double by 2010 and 2050 [1,5].

Stroke and epileptic seizures are one of the most prevalent neurological problems in the Western world. Cerebrovascular disease is the most common cause of epilepsy in adults, representing around one third of epilepsies of structural etiology with onset in people over 60 years of age. The coexistence of both pathologies worsens the medical and social prognosis, and multiplies the disability associated with each pathology separately [6].

Stroke is associated with a 23 - 35 times increase in the incidence of seizures. The risk of developing epilepsy after a stroke is 17 times higher than in people of the same age without this pathology [7].

Most authors consider that ischemic and hemorrhagic CVD are causes of epilepsy, with onset in adulthood, in one out of ten cases [8].

All of the above coincides with several recent investigations that have shown that the main cause of epilepsy in the elderly is cerebrovascular disease [9].

Post-stroke epilepsy is more likely to occur if the lesion involves the cortex, is extensive or multiple, and is accompanied by acute symptomatic seizures at onset [10,11].

In this regard, some authors have considered that the most frequent cause of acute symptomatic crisis was cerebrovascular disease [12].

With the exception of myocardial infarction caused by cerebral venous occlusion, epileptic seizures after cerebrovascular disease are not a major problem from an epidemiological point of view. Seizures are rare as the initial manifestation of ischemic stroke, and if they do present, the causative mechanism is usually an embolus. More often, they do not arise for months or years after the infarction or hemorrhage [13].

It can be asserted that, since the description of Hippocrates (400 years BC), considering stroke "as the sudden onset of paralysis", cerebrovascular diseases represent a significant social and health problem, since they directly, acutely and disablingly affect to people of any age. It should be considered that the determining factors of the results, both in mortality and in function, are the severity and evolution of neurological damage [14].

Cerebrovascular accidents are the cause of adult-onset epilepsy in 25% of those over 65 years of age in most published series [15].

In addition, patients older than 50 years with newly diagnosed epilepsy have a two to three times higher risk of suffering a stroke compared to the general population, according to studies carried out especially in Europe and North America. In these cases, epilepsy could be secondary to microangiopathic damage with a predisposition to future cerebrovascular events [16].

CVD is considered the third leading cause of death in the world; [4,6,7] after cardiovascular diseases and neoplasias, and most of it occurs in low- and middle-income countries, corresponding to approximately 10% of deaths [17].

Its incidence increases above 55 years (75% in people over 65 years) and it is the main cause of disability in people of productive age (1/3 of the patients permanently) [18].

Most significantly, the following are considered disabling sequelae after stroke: variable degrees of focal motor and sensory neurological deficit, cognitive disorders, visual compromise, spasticity and epilepsy. The latter is the most common neurological sequelae in CVD (10%), known by some authors as post-stroke epilepsy [16].

This sequel arises in relation to the morphological changes at the molecular level in the brain, after the insult received by CVD and whose incidence, according to Alajbegovic, is 0.65 - 3.14% [19].

With regard to the subject related to the presentation of epilepsy/epileptic seizures, subsequent to the encephalic vascular pathology, various articles have been reported in recent years. They have presented various difficulties in terms of terminology and diversity of casuistry, but all agree on the possibility of the presentation of epileptic seizures in the course of encephalic vascular disease.

Post-stroke crisis are classified according to the temporal criteria as early or late. This criterion is not fully established and we can see that it varies according to the studies; The International League Against Epilepsy defines early seizures as those occurring within the first 7 - 14 days after the stroke [20].

In other studies, early seizures are considered to be those that occur in the first 24 hours, 48 hours, one week, two weeks or one month after the stroke. However, for most authors, late seizures are those that occur after the first two weeks.

Other authors agree that seizures can be divided into acute symptomatic seizures (CSA) and unprovoked seizures (NPC), depending on the time of the event. The International League Against Epilepsy (ILAE) defines CSA as that which occurs within the first week after the stroke, while NPC manifests itself after this time. A patient is diagnosed with epilepsy when he has at least one PNC and is predisposed to subsequent seizures. Therefore, when faced with a first NPC after a stroke, the case meets the criteria for post-stroke epilepsy [21].

We consider it necessary to summarize some significant aspects.

Gallmetzer in a study carried out in Vienna, reports the first epileptic seizure after a cerebrovascular accident, with the patient being admitted in 3.19% and the first seizure upon discharge in 2.6%, using the term vascular epilepsy in 2.5% of patients, who chronically maintain such crises in their casuistry. The time of onset of the seizures is not specified in this study [22].

In Tunisia, Triki considers the presentation of early epileptic seizures in hemorrhages in 75% and in ischemic seizures in 38%, as well as recurrent seizures (epilepsy) in 20% of cases. This study also suffers from the inaccuracy of the time of onset of the seizures [23].

In turn, in Macedonia, Arsovska finds epileptic seizures as the initial symptom in 2.7% of her patients [24].

In the Groppe series, in Moldova vascular epilepsy is reported in 4.99% [25].

Medina, for his part, in a rural area of Honduras, finds vascular epilepsy in 2% of his cases with cerebrovascular pathology [26].

The term post-stroke epilepsy is used by Tidsskr and specifies in his cases, that the crises appear after one year of the cerebrovascular accident, in 2.5% and after 5 years in 4.4% [27].

In the data published by Lamy., *et al*. [28] when the epileptic seizures appeared in the first week of the accident, but not from the beginning, it was observed in an average of 2% to 4% of the cases and half of the patients presented another epileptic seizure in the following years, usually isolated. It might not be surprising that the rate of seizures is higher after hemorrhagic strokes than after ischemic strokes, and in the latter category, larger cortical strokes were less likely to end in a seizure disorder.

Lossius reports that in his patients vascular epilepsy is present in 2.5% of his cases [29].

Post-CVD crisis are present in 10.5%, according to the Naess series [30].

For his part, Silverman considers epileptic seizures in 10% of CVD [31].

Regarding the prognosis, Arboix points out a high mortality rate in atherothrombotic infarction with epileptic seizures in the first 48 hours (19.5%) [32].

Camilo and Goldstein, regarding all of the above, consider that the interpretation of the studies is complicated by the heterogeneous and inconsistent terminology, scarce samples, different periods, and ambiguities in the identification and classification of crises. The estimated rate of ischemic post-CVD crisis is between 2 and 33%. The rate of late seizures between 3 to 67%. The rate of ischemic post-CVD epilepsy 2 to 4% (higher in late seizures). Both authors think of the need for additional work to understand the epidemiology and social impact of post-CVD crisis, their prevention and optimal management [33].

In our case material, epileptic seizures occurred in vascular pathology in 24.60%, which is consistent with the findings of the latter and higher than several of the previous ones [34].

When analyzing other aspects, it is agreed that one of the potential consequences of perinatal hypoxia-ischemic disease is epilepsy. In 40 - 60% of newborns with this condition, seizures may be refractory. They may also have a variable degree of motor weakness (cerebral palsy) and a cognitive disorder accompanied or not by mental retardation [35].

Tang considers that neonatal cerebral infarction is not a rare condition and should be considered as one of the important causes of neonatal epileptic seizures (20%) [36].

Different epidemiological studies show that the frequency of CSA after a stroke is between 3 and 6%. The number is higher in patients with intracerebral hemorrhage (intraparenchymal hematomas, subarachnoid hemorrhage). Some independent risk factors have been described that establish a greater predisposition to a CSA, such as cortical compromise, the greater severity of the stroke and the hemorrhagic transformation of the ischemic stroke [37].

In Italy, Procaccianti., *et al*. reported 10 to 12% of cases of NPC (or post-stroke epilepsy) after a stroke, at 5 to 10-year follow-up. The risk is similar in ischemic or hemorrhagic events. Some factors such as cortical involvement, the size of the stroke, and advanced age are associated with a higher risk of first crisis or recurrence [38].

Another risk group are those patients with subarachnoid hemorrhage (SAH) and associated intraparenchymal hemorrhage (IPH) (33% at 5 years) [39].

In relation to subarachnoid hemorrhage, Lin specifies in his casuistry that 1/5 pctes present crises after the bleeding and that half present in the perioperative period. Late epilepsy in these cases is shown in 7.8% [40].

Arteriovenous malformations are also a section to be analyzed. They present in the Stapf casuistry with hemorrhage in 46%, with epileptic seizures in 29%, with headache in 13% and with neurological effect in 7% [41].

Cavernomas, arteriovenous malformations (AVMs), and venous angiomas cause focal epilepsy. The former are the most frequent cause of vascular malformation in epilepsy and are associated with an excellent prognosis after epilepsy surgery in children and adults with single lesions [42].

Extensive infarcts, with deviation from the midline and the need for craniectomy also have a higher risk (45% in the first year). According to studies carried out in Israel, the incidence of crises in lacunar infarcts is very low, less than 1%. No difference has been reported in the frequency of seizures secondary to infarcts due to large-vessel involvement compared to embolic infarcts [43].

The risk of epilepsy is greater in cortical infarcts and lobar hemorrhages and the greater frequency of epileptic seizures in the first 7 days, according to Midil. This author also considers that acute CVD is a common cause of Status Epilepticus (and a direct cause of death), with most crises being simple (focal or generalized). He, in turn, considers that the incidence of status epilepticus in the elderly is almost twice that of the general population and CVD is the common cause. In his case material, he found the presentation of status in ischemic CVD in 80.3% and in hemorrhagic CVD in 19.7% [44].

For his part, in this regard, Velioglu found 9% of his patients with status epilepticus and considers that this early condition is associated with a high risk of status recurrence and a higher mortality rate [45].

Afsar also thinks that CVD is the most common cause of status epilepticus, finding it in 28% of his patients, more frequent in non-convulsive patients [46].

Status epilepticus is particularly frequent in the elderly, and marks the onset of epilepsy, or it can be established in the context of acute symptomatic seizures [47].

The clinical picture of focal nonconvulsive status epilepticus is similar to delirium in its various manifestations. The most frequent anatomical location in electroencephalograms of non-convulsive status epilepticus follows the following order: temporal lobe 44%, frontal lobe 28%, central 14%, occipital lobe 8-14% and parietal lobe 3% [48].

However, other authors have published that epilepsy of the temporal lobe is not frequent in the elderly, but that of the frontal lobe, which is the most affected during cerebrovascular accidents [49].

In our opinion, epilepsy/epileptic seizures in the course of cerebrovascular disease should be taken into consideration as a health problem, especially in adult life, and can cause recurrent seizure symptoms and even status epilepticus, which in turn can be a direct cause of death.

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Volume 15 Issue 3 March 2023