CORRELATION BETWEEN EARLY AND LATE EPILEPTIC SEIZURES AND DIABETES MELLITUS DURING AND AFTER STROKE

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SUMMARY

Diabetes mellitus is a well-known risk factor for cerebrovascular diseases, but not so well-known for determining early and late epileptic seizures during and after stroke. Early and late epileptic fits recorded at the University Department of Neurology in Sarajevo during a 10-year period (from January 1, 1989 until December 31, 1998) in 7001 stroke patients were retrospectively evaluated so as to determine the impact of diabetes on the onset of stroke and of the early and late epileptic seizures. Out of 114 patients with epileptic seizures, 34 (29.8%) had diabetes mellitus (7.9% type 1 and 20.2% type 2). The mean age of patients was 60.0 years, with standard deviation of 12.52 years. The mean duration of diabetes was 10 years in patients with late seizures, and 14.7 years in patients with early fits. In the group of patients with early seizures, there were 19 patients with diabetes mellitus (3 patients with type 1 and 12 patients with type 2). In the group with late fits, there were 15 diabetics (3 patients with type 1 and 11 patients with type 2). Hyperglycemia was significantly more common in the group of patients with early fits than in the group with late fits (60.9%). The most frequent type of epileptic manifestations were partial seizures with secondary generalization. Diabetes mellitus was found to be a significant risk factor for the onset of stroke as well as for the occurrence of early epileptic seizures during stroke ($p<0.1; \chi^2=3.472$). There was no statistically significant effect of diabetes on the onset of late epileptic seizures. The study showed no statistically significant difference between the patients with normal and elevated blood glucose according to the type of epileptic manifestations.

INTRODUCTION

Diabetes is the most common metabolic and endocrine disease. According to the World Health Organization (WHO), it is defined as a syndrome consisting of a group of metabolic entities characterized by chronic hyperglycemia as the result of inadequate insulin resistance and/or resistance to its biological effect (1). For many reasons (longer life span, inheritance, reduced physical activity, unhealthy nutrition, etc.) diabetes has reached epidemic proportions (2,3). Between 2% and 5% of the adult population of Europe suffer from diabetes (1,2,4). A very frequent complication in diabetes is stroke. According to Kannel, diabetes is four times more common in stroke patients than in the general population (5). Stroke is a focal neurologic dysfunction of the central nervous system with acute onset as a consequence of a pathologic disorder of vascular origin (6,7). In diabetics, stroke is the result of diabetic macroangiopathy (1,4).

According to the Framingham and Rochester studies, diabetes has shown itself as an independent risk factor for the occurrence of stroke; however, when combined with congestive heart disease it is the least potential
risk factor (8). According to Kuusisto et al. (9) and Sadikario (10), it is the most potential risk factor for the occurrence of stroke. Stroke is the leading cause of death and the main cause of disablement in the adult population of Europe (11,12). Helsinki declaration from 1959 (13) identifies optimal care for patients and evaluation of care for survivors (13-15), based on the high mortality (8,9,17-20) and a variable degree of disablement and need of 24-hour care in 60% of stroke survivors.

From the pathophysiologic point of view, stroke can be ischemic (infarct) or hemorrhagic (intracerebral hematoma or subarachnoid hemorrhage). The symptomatology depends on the system involved by the vascular incident. The symptoms of stroke in the carotid system include hemiplegia, hemiparesis, hemihypersthesia, various consciousness impairments, amaurosis, and speech disorders such as dysarthria or aphasia. Involvement of the vertebrobasilar system shows the symptoms of bilateral weakness, consciousness impairments, hemianopia, diplopia, dysphasia, vertigo, ataxia, and nystagmus.

Epilepsy is a clinical phenomenon, a syndrome of primary cerebral origin, which is characterized by recurrent episodes during which continuous movement or behavioral disturbances occur (21).

Epilepsy can occur as the first symptom of stroke (associated seizure) during the acute stroke phase (early epileptic seizure) within two weeks of the stroke onset or as a consequence of stroke after 14 days or later (late epileptic seizures). Acute phase of stroke lasts for two weeks, so seizures in this acute phase are called early seizures. Epileptic seizures arising after an acute phase are called late seizures.

Cerebrovascular insult is a permanent damage of the brain (22). The pathophysiologic basis of early epileptic seizures are molecular changes that occur primarily in ischemia and secondarily in hemorrhage. The basis of late epileptic seizures are morphologic changes following various types and subtypes of stroke. The risk of epileptic seizures is associated with cortex involvement, whereas deeper hemispheric or infratentorial lesions less frequently lead to late epilepsy.

The aim of the study was to determine the impact of diabetes on the occurrence of early and late epileptic seizures during and after stroke among patients suffering from various types and subtypes of diabetes.

PATIENTS AND METHODS

The study included 167 patients with various epileptic manifestations during and after stroke. Out of 7001 patients treated for stroke at the University Department of Neurology, Sarajevo University Clinical Center, during the 10-year study period, 111 had late epileptic seizures and 56 early epileptic seizures. Data on the presence of diabetes were available for 114 patients, whereas in 53 patients no such reliable data were available and these patients were excluded from statistical analysis. The diagnosis of stroke was confirmed clinically and by computed tomography, clearly specifying the type and subtype of stroke. The study was retrospective in design, covering a 10-year period (January 1, 1989 – December 31, 1998).

All patients with diabetes were tested for the type and duration of diabetes. Glycemia was determined and the effect of glycemia level on the occurrence of early and late epileptic seizures was assessed on admission, during clinical treatment, and at discharge from the hospital.

RESULTS

Out of 7001 patients with stroke treated during the 10-year period at the University Department of Neurology, Sarajevo University Clinical Center, there were 167 patients with epileptic seizures (111 with late seizures and 56 with early seizures). Diabetes data were evaluated in 114 patients, whereas in 53 patients no reliable data on their diabetes were available and they were excluded from statistical analysis. On statistical analysis, arithmetic mean, standard deviation, t-test and χ²-test were used. Results are presented in tables.

There were 34 diabetics (15 with late seizures and 19 with early seizures). There were significantly more patients with type 2 than with type 1 diabetes. There were significantly more patients with type 1 diabetes in the group with early seizures as compared to the group with late seizures. The group with early seizures included significantly more diabetics than the group
with late seizures ($\chi^2=28.77; df=1, p<0.01$). There were statistically significantly more patients without than with diabetes ($\chi^2=18.561; df=1, p<0.01$). Exact data on diabetes duration were available in 21 patients. According to Student’s t-test, difference in the mean duration of diabetes between the groups with early and late seizures was not statistically significant ($t=1.062$). The mean patient age was 60.0 years, with standard deviation of 12.52 years. The mean duration of diabetes after stroke was 10.8±7.62 and 14.7±7.1 years in the groups with late and early seizures, respectively (Tables 1-3).

Based on the statistical analysis illustrated in Table 3, it is evident that there was no statistically significant difference in the number of patients with elevated blood glucose at the time of admission ($\chi^2=0.008; n=1$). Difference in the number of patients according to the level of blood glucose and time of epileptic seizure onset was not statistically significant at the level of $p<0.05$ but was significant at a lower level ($p<0.1; \chi^2=3.472$).

**DISCUSSION**

The population of diabetics have an increased sensitivity to arteriosclerosis and stroke (3-5,24). Increased values of blood glucose lead to an increased risk of vascular disorders (24). In our study, the population of diabetics accounted for 29.8% of the total sample, which was significantly higher than the results reported by Giroud *et al.* (25) and Arboix *et al.* (26). The higher rate of diabetics in our group of patients with stroke and epileptic seizures could be explained by the higher quality care for diabetics, higher educational level and better health education for the general population regarding nutrition and lifestyle in general in the respective countries.

An increase in the level of blood glucose worsens ischemic brain damage and makes the recovery from stroke more difficult. Because of the increased lactate level in ischemic tissue with local acidosis due to anaerobic glycolysis, it is an imperative to prevent hyperglycemia in stroke, irrespective of whether diabetes or hyperglycemia induced by the liver (glucose uptake) is present. In these hyperglycemias, besides the already disturbed quantity, the quality of the blood that distorts the synergy between constant cerebral flow and brain cell metabolism is impaired. It primarily leads to functional and later to morphologic cell impairment due to hypoxia and later anoxia. The Na-K pump is distorted and the concentration of anaerobic glycolysis products is the pathophysiologic basis for these seizures (27). Hyperglycemia as well as hypoglycemia lead to an increased risk of brain edema, which is within the first 24 hours cytoidal and later vasoactive. Unregulated diabetes leads to the possibility of diabetic coma (ketoacidotic or hypersomolar), which is the basis for the occurrence of new microinfarcts or microhemorrhage (5,24).

The prevalence of hyperglycemia was significantly higher in the group of patients with early seizures (60.9%) because this group included significantly more diabetics, which was statistically significant at a lower

**Table 1. Patient distribution according to the presence of diabetes mellitus and stroke induced early/late epileptic seizures**

<table>
<thead>
<tr>
<th>Patient category</th>
<th>Total</th>
<th>Late seizures</th>
<th>Early seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>n %</td>
</tr>
<tr>
<td>Study sample</td>
<td>114</td>
<td>100</td>
<td>68 100</td>
</tr>
<tr>
<td>Without diabetes</td>
<td>80</td>
<td>70.2</td>
<td>53 77.9</td>
</tr>
<tr>
<td>With diabetes:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>34</td>
<td>29.8</td>
<td>15 22.1</td>
</tr>
<tr>
<td>type I</td>
<td>9</td>
<td>7.9</td>
<td>3 4.4</td>
</tr>
<tr>
<td>type II</td>
<td>23</td>
<td>20.2</td>
<td>11 16.2</td>
</tr>
<tr>
<td>type unknown</td>
<td>2</td>
<td>1.7</td>
<td>1 1.5</td>
</tr>
</tbody>
</table>

**Table 2. Stroke induced early/late epileptic seizures according to diabetes duration**

<table>
<thead>
<tr>
<th></th>
<th>Late seizures</th>
<th>Early seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Mean diabetes</td>
<td>10.8</td>
<td>14.7</td>
</tr>
<tr>
<td>duration (yrs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard deviation</td>
<td>7.62</td>
<td>7.11</td>
</tr>
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</table>

**Table 3. Glycemia on admission to hospital**

<table>
<thead>
<tr>
<th>Glycemia on admission (mMol/l)</th>
<th>Total</th>
<th>Late seizures</th>
<th>Early seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>n %</td>
</tr>
<tr>
<td>Study sample</td>
<td>123</td>
<td>100</td>
<td>77 100</td>
</tr>
<tr>
<td>2.8</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2.9 – 5.9</td>
<td>62</td>
<td>50.4</td>
<td>44 57.1</td>
</tr>
<tr>
<td>6.0</td>
<td>61</td>
<td>49.6</td>
<td>33 42.9</td>
</tr>
</tbody>
</table>
level of confidence. Glycemia higher than 6 mMol/l was recorded in 60.9% of patients, which is in accordance with the results of Neufeld et al. (28).

In the group of patients with late seizures, 57.1% had normal glycemia at the time of admission, confirming that the morphologic changes in the brain in this group of patients followed the pattern of epileptogenic focus, and that glycemia did not significantly influence the discharge of nervous cells which produces various epileptic seizures (29,30).

CONCLUSION

In our sample, diabetes mellitus was shown to be a significant risk factor for the occurrence of stroke. In diabetics with stroke, hyperglycemia is a significant factor that can lead to the occurrence of early epileptic seizures. It is an imperative to prevent hyperglycemia in the acute phase of stroke, as a prevention of early epileptic seizures. Considering late epileptic seizures, it appears that diabetes has no major effect on their occurrence, although changes in the blood glucose level (hypo- and hyperglycemia) can be a preceding factor for epileptic discharge of morphologic brain changes after stroke, in terms of their awakening and behavior according to the type of epileptogenic focus.

REFERENCES


