RISK FACTORS AND ETIOLOGY OF TRANSIENT ISCHEMIC ATTACKS IN PATIENTS WITH BRAIN INFARCTION

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Abstract

INTRODUCTION: Transient ischemic attacks (TIA) are warnings of future stroke. There is no difference in risk factors, pathophysiology and prevention between TIA and brain infarction.

METHODS: Consecutive patients with brain infarction admitted to Ghaem Hospital, Mashhad, Northeastern Iran, were enrolled in a prospective study during 2006. Diagnosis of ischemic stroke was established by a neurologist who also obtained history of TIA and vascular risk factors. All of the stroke patients underwent a standard battery of diagnostic investigations and etiology of ischemic stroke was determined by the Practical Iranian Criteria classification. Fisher's exact test was used for statistical analysis.

RESULTS: 348 stroke patients (186 women, 162 men) were studied. History of TIA was present in 42 patients (29 women, 13 men), i.e. 12% of the stroke patients. TIA was more common in women (df=1, P=0.02). The frequency of hypertension, diabetes and ipsilateral carotid stenosis was not significantly different between patients with history of TIA and other stroke patients (P=0.87, P=0.64 and P=0.61, respectively). Hypercholesterolemia and smoking were significantly more frequent in stroke patients with history of TIA (P=0.011 and P=0.014, respectively). The frequency of TIA was not significantly different among patients with lacunar, versus large vessel territory infarcts (df=1, P=0.84). There was no significant difference in the frequency of various stroke etiologies in patients with and without history of TIA (df=4, P=0.61).

CONCLUSIONS: Stroke patients with history of TIA have vascular risk factors similar to other stroke patients. A positive history of TIA does not affirm any specific etiology of ischemic stroke.

Keywords: Risk factors, etiology, transient ischemic attacks.

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Introduction

Transient ischemic attack (TIA) is defined as a brief episode of focal loss of brain function attributable to ischemia, involving one of the vascular systems and lasting less than 24 hours.[1]

The usual 24-hour criteria has been recognized to be excessive. The typical carotid territory TIA lasts up to 10 minutes.[1] The brief spells have a better correlation with angiographic evidence of carotid stenosis.[1]

TIA may occur with a short-lived embolic mechanism. Embolic TIA tends to last far longer than the usual 5-7 minutes that characterizes most cases of TIA associated with severe stenosis of ICA.[1] However, the prognosis for subsequent stroke appears to be the same whether the spell is brief or long in duration. Severe stenosis or occlusion of the carotid tends to result in TIA with the same characteristics from attack to attack[2].

This stereotypic TIA is repetitive in severity and in clinical details.[2] A drop in systemic blood pressure causes TIA in these patients. TIA could occur in atherosclerosis of the intracranial arteries, as well as the extracranial carotid artery.[2]

TIA is an impressive warning of stroke and its recognition provides the opportunity for therapeutic intervention.

TIA may be related to a small artery disease that causes lacunar infarction. Prior TIA episodes occur in 20% of lacunar cases.[2]

TIA in lacunar infarcts has more episodes and a shorter latency between the first TIA and infarction.[2,3] Capsular warning syndrome consists of clusters of stereotypic hemiparesis without any cognitive or language deficits, which follows within hours or days by a lacunar infarct in the internal capsule.[3]

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Minor ischemic stroke and TIA are not significantly different in terms of risk factors and prognosis. They share the same pathophysiology and mechanisms.[3] High-risk TIA patients include those with multiple recent episodes, with ipsilateral carotid stenosis or ulcerated plaque and cardiac source of emboli.[2] This clinical study was designed to compare the risk factors and etiology of ischemic stroke in patients with and without TIA.

Materials and methods

Consecutive patients with brain infarction admitted to Ghaem Hospital, Mashhad in 2006, were enrolled in a prospective study.

Stroke was defined as an ischemic focal neurological deficit that persisted for at least 24 hours.[4] TIA was determined by taking past history from the patient or guardians. TIA was defined as an acute loss of ocular or focal cerebral deficit related to ischemia lasting less than 24 hours.[4]

The diagnosis and etiologic investigations of stroke were conducted by a stroke neurologist. All of the patients underwent a standard battery of diagnostic investigations,[5] which included brain CT scan, electrocardiography (ECG), measurement of blood electrolytes, blood count and differential, assessment of the coagulation profile, fasting blood sugar (FBS) and lipid profile, duplex sonography of supra-aortic trunks, and transcranial Doppler and transthoracic echocardiography.

24-hour holter monitoring was performed for patients with history of syncope and/or palpitation with non-diagnostic ECG.[5]

Transesophageal echocardiography was performed for patients with non-diagnostic transthoracic echocardiography despite high suspicion of cardioembolism.[5]

Brain MRI, MRA was performed in suspected cases of arterial dissection, arteriovenous malformation, or aneurysm.[5]

Hypertension was defined as using antihypertensive medications or two blood pressure readings (at least 1 week apart) of >140/90 mmHg.[6] Administration of antidiabetic medications or FBS >6.4 mmol/l or >126 mg/dl were definitions of diabetes mellitus.[6]

Hypercholesterolemia was defined as using lipid-lowering medications or a fasting cholesterol concentration >5.2 mmol/l or >200 mg/dl.[6]

Measurement of FBS and lipid profile assessment were part of the routine investigations performed within the first 48 hours of stroke. Patients who smoked more than 5 cigarettes per day in the recent year were defined as smokers.[6]

Etiologic and topographic diagnosis was made using the Practical Iranian Criteria for classification of brain infarction.[7,8] Risk factors and etiology of stroke in patients with history of TIA were compared with other stroke patients. Patients with head trauma, primary intracerebral hemorrhage and subarachnoid hemorrhage were excluded. Data on the patients' demographics, clinical presentation and the results of investigations were entered in SPSS9 software package and registered in Khorasan Stroke Registry Data Bank.[8] Chi-square and Fisher's exact tests were used for statistical analysis and $P>0.05$ was considered as significant.

Results

348 patients with brain infarction (186 women, 162 men) were investigated. History of TIA was present in 42 patients (29 women, 13 men, i.e. 12% of all patients). TIA was significantly more frequent in female stroke patients (df=1, P=0.022).

The mean ± standard deviation of age in patients with and without TIA was 66.78±13.91 and 66.53±15.02 years, respectively, with no significant difference (t=0.15, df=339, P=0.88).

Figure 1 represents the frequency of stroke risk factors in patients with and without TIA.

The frequency of hypertension, diabetes and ipsilateral ≥50% internal carotid artery stenosis was not significantly different between stroke patients with and without TIA (df=1, P=0.87; df=1, P=0.60; and df=1, P=0.61, respectively).

Hypercholesterolemia and smoking were significantly more frequent in stroke patients with TIA (df=1, P=0.011 and df=1, P=0.014, respectively). Ipsilateral middle cerebral artery stenosis was found by transcranial Doppler in 2 stroke patients with TIA and 6 patients without TIA.

TIA was present in 16.5% of lacunar and 17.2% of large vessel territory infarcts (df=1, P=0.084). Table 1 illustrates the frequency of various etiologic mechanisms in our stroke patients with and without TIA. The frequency of these mechanisms was not significantly different between the two groups (df=4, P=0.61).

TABLE 1. The frequency of various etiologic mechanisms in our stroke patients with and without TIA.

Etiology/TIA	Ath	Card	Ath+Card	Uncertain	Misc
TIA+ n=42	21	6	7	8	0
TIA-n=306	163	37	33	63	10

Ath=Atherosclerosis, Card=Cardioembolism, Misc=Miscellaneous

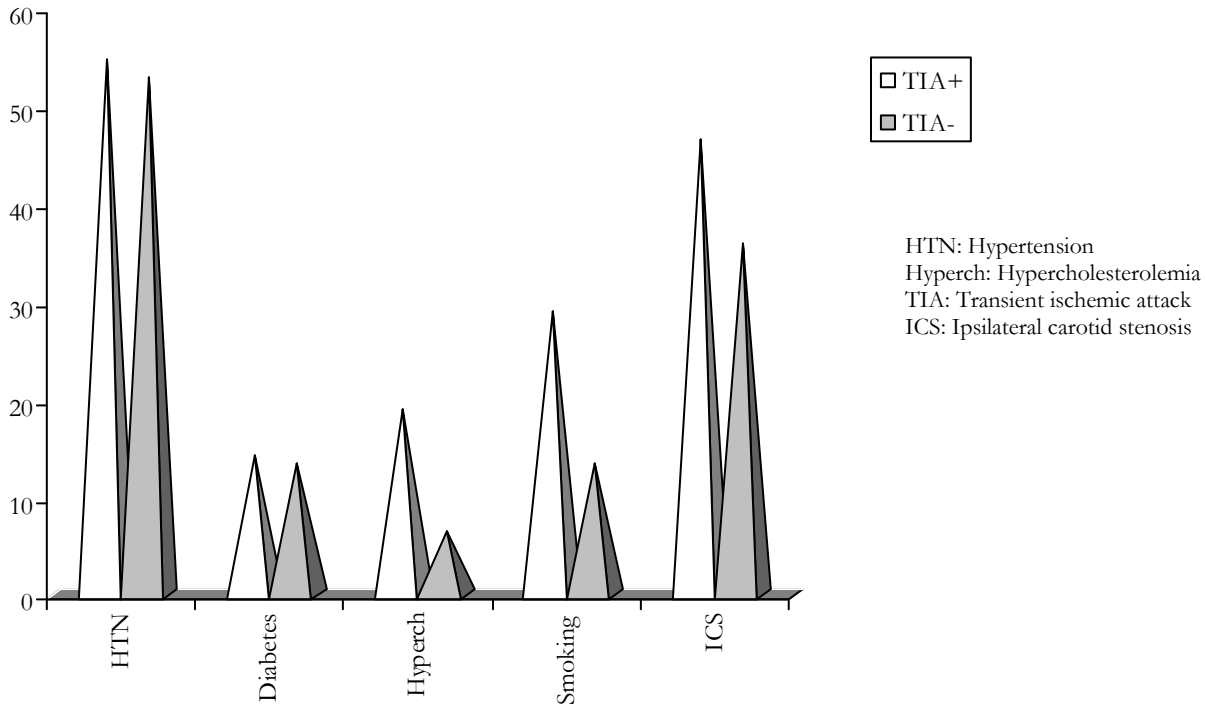

FIGURE 1. The frequency of risk factors in stroke patients with and without TIA. Data are represented in percentages.

Atherosclerosis constituted 50% of etiologic mechanisms, followed by uncertain etiologies (19%) in stroke patients with TIA.

Cardioembolism in isolation or associated with atherosclerosis comprised 14.3% and 16.6% of etiologic mechanisms in stroke patients with TIA, respectively.

Discussion

TIA and brain infarction are caused by the same pathophysiologic mechanisms and require the same prevention strategies. All of the stroke registries include TIA as a risk factor of ischemic stroke. TIA has been reported in 12% of Iranian stroke patients.[8]

This study compared the risk factors and etiologies of stroke in Iranian patients with and without TIA. In our study, TIA was not categorized into carotid territory TIA and vertebrobasilar territory TIA. The frequency of hypertension, diabetes and ipsilateral carotid stenosis was not significantly different between stroke patients with and without TIA; however, hypercholesterolemia and smoking were more frequent in our TIA-positive stroke patients.

The prevalence of vascular risk factors was not significantly different between patients with TIA and ischemic stroke in a community-based study in Spain;[9] however, mean cholesterol levels were not significantly higher in TIA patients[9].

Hypertension (54.7%), smoking (28.6%), hypercholesterolemia (19%) and diabetes (14.3%) were the most frequent vascular risk factors in our TIA-positive stroke patients.

Diabetes, hypercholesterolemia and smoking were the most common risk factors of TIA in a Swiss study and hypercholesterolemia was a marginal risk factor.[10]

Another Spanish case-control study confirmed that all of the modifiable cardiovascular risk factors were associated with a higher risk of TIA, although only hypertension had a significant relationship to TIA.[11]

Accumulation of vascular risk factors increased thromboembolic event rates and had a synergistic effect[12]. Geographic variations should be considered; for example, South Asians with diabetes mellitus have poorer glycemic, blood pressure and lipid control than white Europeans.[13]

An American study found no significant difference in the frequency of vascular risk factors between patients with lacunar, versus large vessel territory TIA.[14]

Our study was not designed to make such a comparison; however, the frequency of TIA was not significantly different between our lacunar and large vessel territory infarcts. The distribution of etiologic mechanisms was similar in patients with TIA and those with brain infarction in the Spanish study conducted by Sempere.[9]

These studies are supported by our results. Indeed, the presence of TIA does not suggest a special etiology such as atherosclerosis in the stroke patients. Early risk of stroke after a first TIA is 2% at 7 days and 4.4% at 30 days.[15] Our study sheds more light on risk factors and etiology of TIA in Iran. Much work needs to be done on the epidemiology of TIA in Iran and other developing countries.

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