Anticoagulant treatment for progressing ischaemic strokes in the elderly

ORIGINAL ARTICLE

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ABSTRACT

Background. Treatment of progressing stroke with anticoagulation remains controversial. This study aimed to evaluate the effect of anticoagulant treatment in selected elderly patients with progressing stroke.

Methods. Records of 41 patients (mean age, 80.1 years) with good functional state (Karnofsky scale of ≥60) treated with anticoagulation (enoxaparin or heparin) for progressing stroke were reviewed. Outcome measures included changes in neurological status such as limb weakness, ataxia, and sensory loss. Those who improved neurologically were compared with those who deteriorated.

Results. 25 (61%) patients showed neurological improvement. Patients with neurological improvement differed from those without improvement in terms of long-standing hypertension only (80% vs. 12.5%, p=0.002). The only predictor for a positive response was the extent of the neurological deficit. Stroke territory did not affect outcome. Three patients had haemorrhagic complications.

Conclusion. In selected elderly patients with progressing stroke, anticoagulation has a positive outcome.

Key words: Aged; Anticoagulants; Strokea

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INTRODUCTION

Progressing stroke or stroke in evolution has been recognised for more than 50 years.[1,2] There is no consensus on its treatment. Anticoagulants were once used for the treatment of acute ischaemic stroke[3] and achieved positive outcomes for progressing stroke.[4-8] However, new studies showed poor effectiveness and increased risk of bleeding from such treatments.[3,9-12] Nonetheless, all previous studies did not consider the influence of comorbidity and included a mixed population of younger and older patients. This study aimed to evaluate the effect of anticoagulants on elderly patients with progressing stroke and to assess the effect of various variables.

MATERIALS AND METHODS

Between 1997 and 2007, 41 patients aged 65 to 94 (mean, 80.1) years with progressing stroke were treated with intravenous heparin (adjusted according to activated partial thromboplastin time) or with subcutaneous enoxaparin. Progressing stroke was defined as an ischaemic neurological deficit that worsened after hospitalisation. It included any worsening of motor function, speech ability, changes in conscious level or the appearance of new neurological findings.

Patients with a relatively good functional state (Karnofsky scale of ≥60), at low risk for bleeding and with no contraindication to anticoagulants

were included. All patients were in sinus rhythm, and did not receive any anticoagulation before hospitalisation. Computed tomographic scanning of the brain was performed to rule out haemorrhage. Patients with severe hypertension, history of bleeding or peptic ulcer disease, or currently using anticoagulants were excluded, as were those with acute comorbidity (acute heart failure or infection), underlying conditions, or marked progression of stroke signs (full paralysis).

Motor neurological deficits were graded as 5 for full strength, 4 for raising limb with slight drift, 3 for raising limb partially, 2 for minimal limb movement, 1 for complete paralysis. Ataxia was scored as 1 for mild, 2 for moderate, 3 for severe ataxia.

Chi squared and Mann-Whitney *U* tests were used to compare neurological changes in those who improved and those who deteriorated. A p value of <0.05 was considered statistically significant. This study was approved by the Shaare Zedek Medical Center Helsinki Committee.

RESULTS

All patients showed some neurological deterioration after hospitalisation after a mean period of 32.4 (range, 1-36) hours. 25 (61%) of them showed neurological improvement after treatment; improvement in 12 were major and in 13 were minor.

Patients with carotid territory stroke (n=19) were subdivided into those who attained 1-to-2-point improvement (n=11) and those who attained 3-to-4-point improvement (n=8) in motor weakness. Patients with vertebrobasilar territory stroke (n=6) were subdivided into those who attained 1-point improvement (n=2) and those who attained 2-point improvement (n=4) in ataxia.

Patients with neurological improvement did not differ significantly from those without improvement (4 of them continued to deteriorate) in terms of age, gender, previous stroke, and comorbidity, except for long-standing hypertension (80% vs. 12.5%, p=0.002, **Table**). The only predictor for a positive response was the extent of the neurological deficit. Stroke territory did not affect outcome.

The mean duration of hospitalisation was 8.8 (range, 4-53) days. Three (7%) of the patients had haemorrhage and their anticoagulant treatment was discontinued. The site of haemorrhage involved the brain in 2 and the urinary tract in one. Five (12%)

Table
Characteristics of 41 patients with progressing stroke*

Parameter	Improved (n=25)	Stable or deteriorated (n=16)	p Value
Age (years)	78±9	80±7	0.48
Male	17 (68)	9 (56.3)	0.446
Admission systolic blood pressure	146±21	154±30	0.362
Admission diastolic blood pressure	78±10	80±16	0.914
Previous stroke	11 (44)	7 (43.8)	0.987
Diabetes mellitus	8 (32)	5 (31.3)	0.96
Hypertension	20 (80)	2 (12.5)	0.002
Smoking	4 (16)	1 (6.3)	0.352
Hours before admission	25.8±39	37.9±85	0.914
Aspirin/clopidogrel use	16 (64)	9 (56.3)	0.923
Carotid territory stroke	19 (76)	12 (75)	0.94
Vertebrobasilar territory stroke	6 (24)	4 (25)	0.94
Glucose (mg/dL)	126±49	123±21	0.83
Creatinine (mg/dL)	1.21±0.2	1.12±0.1	0.95
Heparin treatment	11	9	0.98
Enoxaparin treatment	10	11	0.94

* Data are presented as mean±SD or No. (%) of patients

of the patients died during hospitalisation, 3 from hospital-acquired sepsis, one from cerebral bleeding and another from ischaemic stroke expansion.

DISCUSSION

The pathophysiological mechanism responsible for progressing stroke is not completely clear. Extension of a thrombus resulting in reduction of the effective arterial lumen is considered the main cause for the neurological deterioration.[13-15] Other possibilities include extensive oedema[16] and haemorrhagic transformation.[17]

Anticoagulants did not improve outcomes in most patients with progressing stroke, and some even developed bleeding complications.[18-20] The positive response to anticoagulation is likely due to the selection of patients. Patients with uncompleted stroke, with relatively good functional state, without immediately dangerous comorbidity, with strict control of anticoagulant use, and without any risk of bleeding were likely to have improved outcomes.

The positive effect of anticoagulants was noted in patients with vertebrobasilar or carotid territory stroke. Recent use of anti-platelet aggregating agents (aspirin or clopidogrel) did not improve outcomes. Nor did comorbidities (smoking history, diabetes, hypercholesterolemia) affect outcomes. The only positive predictor was long-standing hypertension, which may play a protective role owing to the development of collaterals in the brain circulation. Only 3 of our patients had bleeding. This finding is important, as the mean age of our patients was 80 years and approximately 60% were concurrently on treatment with anti-platelet aggregation medications. The frequency of haemorrhagic complications has been 3 to 14% in stroke patients treated with anticoagulants.[3,19,21] The only identifiable risk factor for systemic haemorrhage was age >60 years.[21]

This study was non-randomised and retrospective. Its statistical power was limited by the small sample size, being a one medical centre experience, and using selected patients. Nevertheless, anticoagulation may be effective and appropriate for treating progressing stroke in selected elderly patients. Further studies are recommended.

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