LOWER STROKE DEATH RATES IN PATIENTS RECEIVING BLOOD PRESSURE LOWERING THERAPY BEFORE THE ONSET OF A STROKE

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SUMMARY

The objective of this study was to compare stroke death rates among patients with and without blood pressure lowering treatment before the onset of the stroke. During two consecutive years all patients with acute stroke were recorded by 178 Belgian general practitioners of the sentinel network. In total 511 patients with acute stroke were recorded. The death rate after one month was found significantly higher among the untreated patients (33%; n = 84) compared to those receiving blood pressure lowering treatment (23%; n = 61) (p = 0.007). Blood pressure lowering treatment before the onset of stroke had a beneficial effect on survival in a backward stepwise logistic regression (OR 0.38; 95% CI 0.20-0.72). In conclusion, stroke mortality is significantly lower among patients receiving blood pressure lowering treatment before the onset of stroke compared to those without blood pressure lowering treatment.

Key words: stroke, mortality, incidence, sentinel surveillance, Belgium, cerebrovascular disease

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INTRODUCTION

A decline in stroke incidence and mortality in industrialised countries was noticeable in the decades between 1950 and 1980, and continued during the nineties (1). The reason for the declining stroke incidence was, at least partly, found in the more aggressive management of modifiable risk factors for stroke including hypertension, diabetes, increased cholesterol and obesity. It has been proven that drug treatment including blood pressure lowering drugs, aspirin and statins have been effective in stroke prevention (2–4). The increased survival results, at least partly, from the improved acute stroke care.

Lowering high blood pressure is one of the most effective features in the prevention of stroke. This has been confirmed by many studies (5–7). Thereupon, it has been proven that lowering blood pressure in normotensive patients prevents secondary recurrence of a stroke (8).

Less evidence is available about the effect of blood pressure lowering treatment on stroke mortality. Some might expect that mortality is higher among patients without hypertension. On the other hand lowering blood pressure is more important than the way blood pressure is lowered. It seems interesting to compare stroke mortality among patients using blood pressure lowering treatment compared to those who don't use or don't need blood pressure lowering treatment.

The aim of this study was to compare stroke mortality among patients treated with blood pressure lowering drugs before the onset of stroke with mortality among patients without blood pressure lowering treatment. Additionally, the impact of other risk factors on stroke mortality was analysed.

MATERIAL AND METHODS

The data for this nation-wide prospective registration were collected during two consecutive years by the Belgian network of sentinel general practitioners. This network has been a reliable source of the surveillance of morbidity and mortality in Belgium since 1979 (9, 10). Such a surveillance system is currently being applied in a number of countries (11) and it has been tested and found effective (12, 13). The Belgian network of sentinel general practices consists of physicians who, with respect to age and sex, are representative of the general practitioners in Belgium. The sentinel practices are evenly distributed over the territory as proven by means of a cluster analysis based on epidemiological criteria (9).

The sentinel population was estimated to consist of 138 342 patients corresponding to 1.4% of the Belgian population. All results are adjusted for age and gender according to the Belgian population.

The data for this study were collected from the 178 sentinel general practitioners who regularly participated in the registrations. The registration concerned every patient who encountered a persistent or transient stroke. No limitations concerning age

or co-morbidity were applied. Ischemic as well as hemorrhagic cerebrovascular attacks were recorded. For the analysis in this manuscript only patients with symptoms persisting for 24 hours or more or leading to death were selected.

Patients for whom the general practitioner (GP) was the first medical aid, as well as patients who were hospitalised without a preceding contact with the GP were recorded.

On the initial form gender, age, medical history, disability, outcome, mortality and blood pressure lowering therapy before the onset of the stroke were recorded. One, six and twelve months after the stroke, the physician was sent a follow-up questionnaire with additional questions on the outcome of the stroke, including persistent disability and mortality.

SPSS-PC 12® (SPSS Inc., Chicago, IL, USA) was used for analysis and statistical processing. Significant differences between continuous variables were detected with the independent-samples t-test. The cross-tables were used to detect differences between groups by means of χ^2 tests. Multivariate analyses were performed with backward stepwise logistic regression.

Hypertension was not defined or measured on itself but it was recorded whether or not the patients received a blood pressure lowering therapy before the occurrence of the stroke.

Because of an unexpected character of the results we have excluded the possibility of methodological errors by double-checking the report forms, the code tables and the data entries.

RESULTS

Over the two years 511 patients (52% women; n = 266) with acute stroke were recorded. The cause for the strokes was in 16% (n = 82) hemorrhage, in 66% (n = 337) ischemia and in 18% (n = 92) unknown. Treated hypertension was recorded in 51% (n = 261) of the patients and diabetes in 22% (n = 112). Thirty percent (n = 153) had a stroke history. The baseline characteristics for patients with and without blood pressure lowering treatment are displayed in Table 1. No significant differences between both groups were observed.

Death rates were 5,7% (n = 29) within the first 24 hours and 28% (n = 145) within the first month. In total, 47% (n = 238) died within the twelve months following the stroke. Mortality within the first 24 hours was significantly higher among women (8,3%; n = 21) than among men (3,3%; n = 8) ($p < 0.018$). However, total mortality within the first twelve months was not significantly higher among women (50%; n = 133) than among men (43%; n = 105).

Among the patients with blood pressure lowering treatment, 3.5% (n = 9) died within the first 24 hours compared to 8.0% (n = 20) of patients without blood pressure lowering treatment before the onset of stroke ($p = 0.049$). The death rate within the first month was significantly higher among the untreated (33%; n = 84) compared to the patients receiving blood pressure lowering treatment (23%; n = 61) ($p = 0.007$). This trend between treated and untreated patients continued during the first 12 months after the stroke resulting in a significantly higher death rate among the untreated (56%; n = 139) compared to the patients receiving blood pressure lowering treatment (38%; n = 99) ($p = 0.0001$) (Fig. 1).

To confirm these findings we built a mortality model on the basis of patients' characteristics using backward stepwise logistic regression, with survival of stroke after one year as a dependent variable (Fig. 2). Diabetes ($p = 0.04$), stroke history ($p = 0.03$), hemorrhagic character of stroke ($p = 0.001$), coma ($p = 0.005$), swallow deficit ($p = 0.03$) and urinary incontinence ($p = 0.004$) had negative influence on the survival. Survival was significantly better when the patient had been treated for hypertension before the onset of the stroke ($p = 0.006$). Age, gender, speech deficit and motor deficit were not retained in the equation.

Table 1. *Baseline characteristics of patients with and without blood pressure lowering treatment.*

	Blood pressure lowering treatment n = 261 (51%)	No blood pressure lowering treatment n = 250 (49%)	P
Men (n = 245)	48% (n = 125)	48% (n = 120)	0.981
Age	73 years	74 years	0.333
Stroke history (n = 153)	29% (n = 76)	31% (n = 77)	0.678
Hemorrhagic stroke (n = 82)	17% (n = 44)	15% (n = 38)	0.610

DISCUSSION

Limitations of the Study

This study was limited because we didn't record the class of blood pressure lowering drugs. For that reason we can't provide any information about the influence of the different classes of blood pressure lowering drugs on stroke mortality.

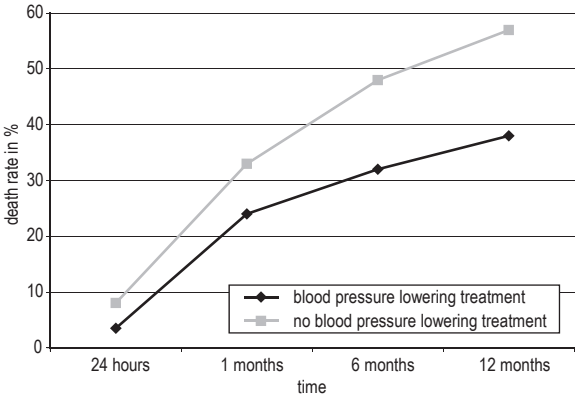

Fig. 1. *Evolution of stroke mortality in patients with and without blood pressure lowering treatment before the onset of the stroke.*

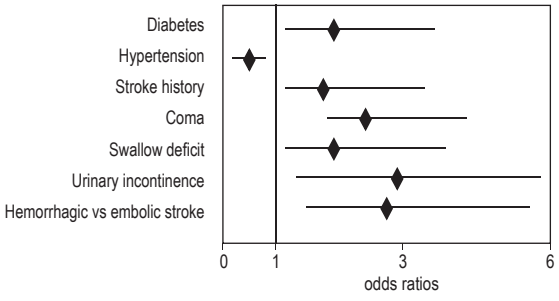

Fig. 2. *Independent predictors of one-year stroke mortality (odds ratios result from backward stepwise logistic regression).*

The main disadvantage of the study is that we did not record the blood pressure levels in the two groups which are compared. This leaves a state of uncertainty regarding the effect of the blood pressure or the drugs themselves.

The differences observed could also be confounded by the use of other drugs such as statins and aspirine. Unfortunately, the use of these drugs was not recorded.

This observational study was not randomised and therefore subject to bias and confounding. The age of the treated hypertensive patients is lower by one year and this in itself could be reason of possible systematic error, as there is considerable epidemiological evidence that the risk of stroke is related to age. However, the difference in age was not significant and in our logistic regression model, age seemed to have no influence on mortality. On the other hand, the results of the two groups have been adjusted for age and gender which corrected this systematic error.

Unfortunately the total mortality after 12 months was recorded but not the specific cause of death. In such a long period death can be caused by a lot of pathological processes. However, we assume that in the majority of cases death was caused by stroke itself or its complications or its causes such as atherosclerosis.

Representativeness of our Data and Comparison with other Studies

Our death rates are similar to those obtained with the Belgian death certificates registration. In Europe, the highest stroke age-adjusted death rate is found in Bulgaria (228 per 100 000 inhabitants) and the lowest in Switzerland (33 per 100 000 inhabitants) (14). The Belgian stroke death rate (88 per 100 000 inhabitants) is in between these values. It is similar to the Danish death rates (28% mortality within the first month, 42% within the first twelve months) (15).

Factors Influencing Stroke Mortality

Our previous registrations in 1984 and 1989 already found a correlation between stroke mortality and the occurrence of diabetes, coma and urinary incontinence (16). The positive correlation between stroke mortality and urinary incontinence is confirmed in the present study. Urinary incontinence could be related to the age of the patients but also to previous stroke. The positive correlation between mortality and swallow deficits is probably to a large extent related to the previous stroke.

There is no doubt about the positive correlation between mortality and hypertension (17) or hemorrhagic strokes (18). Hypertension is considered to be one of the most important risk factors for mortality from stroke and coronary heart disease (19, 20). We might expect that mortality would be high among the hypertensive patients. However, in contrast to most epidemiological registrations (17), our study showed that treated hypertension had a beneficial effect on stroke survival. Treated hypertension was not found to be a predictor of stroke mortality. Mortality was even lower among the patients treated for hypertension before the onset of stroke compared to those without blood pressure lowering treatment.

Hypothesis about the Mortality

The lower mortality among the patients treated with blood pressure lowering drugs before the onset of stroke could simply indicate that elderly persons are the survivors in a population in which significant mortality already eliminated those with the worst risk pattern (21). The same is however true for untreated survivors.

In some clinical studies the highest prevalence of hypertension was found in small-vessel disease, which was associated with the lowest stroke severity and mortality (22). In some recent studies the beneficial effect of antihypertensive treatment beyond blood pressure lowering was highlighted (5–8).

On the other hand it may be possible that blood pressure lowering in the acute stage of a stroke may have a negative influence on stroke survival. Decreasing high blood pressure in the acute stage may hamper the blood flow in the ischemic areas. Therefore it may be beneficial for the survival to have a high blood pressure in the acute stage of the stroke because the blood flow in the damaged cerebral part will improve (21). However, these data are not supported by our findings and no large trials have assessed whether blood pressure should be altered actively during the acute phase of a stroke (23). In some trials the outcome was worse when blood pressure was lowered in the acute phase with calcium channel blockers (24, 25). In the pooled Cochrane results (28 trials) no effect of calcium antagonists on poor outcome (OR 1.07, 95% CI 0.97–1.18), or on death (OR 1.10, 95% CI 0.98–1.24) was found (26).

CONCLUSION

Diabetes, stroke history, hemorrhagic stroke, coma, swallow deficits and urinary incontinence seem to be important determinants in stroke mortality. Mortality was significantly lower among patients treated for hypertension before the onset of stroke compared to those without blood pressure lowering treatment. The latter ones were probably an inhomogeneous group without hypertension or with untreated hypertension. The findings of this study are in accordance with recent randomised clinical trials which showed a beneficial effect of blood pressure lowering treatment on the recurrence of fatal and non-fatal stroke among hypertensive and normotensive patients.

The clinical message in this study (i.e. blood pressure treatment before the onset of a stroke decreases mortality) should be supported by further research evaluating the benefit of blood pressure lowering therapy among patients at risk for stroke but without hypertension.

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