Original Article

Prevention of ischemic Stroke

Badrul Haque¹, Quazi Deen Mohammad², Shah Md. Keramot Ali³.

Abstract

Carotid atherosclerosis is associated with ischemic stroke. It is common in the elderly and the condition can be controlled or improved by drugs. In order to find out the role of antioxidant vitamins (β carotene [USP 6 mg], Vitamin C [BP 200 mg] and Vitamin E [BP 50 mg]) and aspirin, aspirin and ACE- inhibitor (Ramipril) or aspirin alone in prevention of ischaemic stroke due to plaque in or near carotid artery bifurcation diagnosed by carotid color duplex ultrasonography and patients attended in Dhaka Medical College Hospital were studied to justify that these are effective.

Methodology

A total 150 patients from the Stroke Clinic, inpatient and outpatient of Dhaka Medical College Hospital, run by the Department of Neurology fulfilling the inclusion and exclusion criteria were recruited for the study. These patients have clinically evident first attach of stroke where ischeamic nature of was confirmed by CT scan of the head. They did not have any life threatening conditions. Patients with lipid lowering drugs, having previous history of stroke, having Intra Cranial Space Occupying Lesion (ICSOL) and abnormal cardiac conditions were excluded.

Among the selected patients 50 were placed in Group A (aspirin only), 50 patients in Group B (aspirin and antioxidant like Beta carotene USP 6 mg, vitamin C BP 200mg, and vitamin E BP 50 mg) and the rest 50 patients in Group C (Aspirin plus ACE inhibitor). Total blood count, blood glucose, serum lipid profile, X-ray chest, electro cardiograph, CT scan of brain, carotid Doppler, serum urea, serum creatinine in three groups were done at 3 months intervals up to 12 months. In every visit dietary and exercise education were imparted.

Results

The overall mean age of the subjects was 56.73 ±10.76 years. More than seventy percent subjects were male and 27.3% were female. One group was given Aspirin alone, another group was given Aspirin plus Antioxidant (Beta carotene, vitamin C, and vitamin E) and third group was given Aspirin plus ACE- inhibitor (Ramipril). At the end of the study significant reductions of intima medial thickness (IMT) were observed in RCCA, LCCA, RICA and LICA in group who were treated with ACE inhibitor (ramipril) and Aspirin in comparison with other two groups. At final follow up 24.04%, 26.23%, 22.79% and 24.05% reductions of intima media were observed in group C whereas in group A and group B 3.05% and 2.42%, 2.89% and 3.14%, 5.09% and 2.79%, 7.19% and 7.40% in RCCA, LCCA, RICA and LICA respectively.

Conclusion

Patients treated with ACE- inhibitor plus Aspirin showed 24.04% improvement relatively good percentage in reducing the plaque size and thickness than those patients who were treated with Aspirin alone and Aspirin plus Antioxidant.

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Introduction
Stroke has been defined as a focal neurological deficit of sudden onset vascular in origin lasting longer than 24 hours. Stroke is the third most common cause of death in industrialized countries. It is estimated to be between 100 and 200 new strokes per 100,000 inhabitants per year\(^1\). The best UK data from the Oxfordshire Community Stroke Project shows incidence rate for first stroke is 1.6 per 1000 person years at risk. Risk increased rapidly with age\(^2,3\). Death from stroke ranks higher in East Asian countries including Japan, China and Taiwan (more than 100 per 100,000) then New Zealand and Australia (50-80 per 100,000). The mortality rate associated with stroke remains low in South-east Asian countries including Thailand, Malaysia, Indonesia and the Philippines (below 20 per 100,000)\(^4\).

The disturbance of cerebral function is caused by three morphological abnormalities, i.e., stenosis, occlusion, or rupture of the arteries. There are substantial differences in frequency from place to place and cerebral thrombosis is usually the most frequent form of stroke encountered in clinical studies, followed by hemorrhage. Subarachnoid hemorrhage and cerebral embolism come next as regard both mortality and morbidity.

Ischemic strokes and TIAs are frequently caused by cerebral embolism from an atherothrombotic plaque or thrombosis at the site of plaque rupture\(^5\). Although the degree of lumen obstruction is a relevant marker of the risk of stroke\(^6,7,8\), the recognition of the role of the vulnerable plaque has opened new avenues in the field of atherothrombotic stroke. The vulnerability is dictated in part by plaque morphology, which, in turn, is influenced by pathophysiologic mechanisms at the cellular and molecular level \(^9\). Stroke risk with more than 80 percent stenosis was nearly ten times higher then the risk with less than 40 percent stenosis. \(^.\)

The Heart Outcomes Prevention Evaluation study (HOPE), has shown beneficial effects of the angiotensin converting enzyme inhibitor ramipril on cardiovascular events and disease progression\(^10\). The findings have clearly shown that ramipril substantially decreased the risk of stroke and transient ischaemic attacks in 9297 patients with high cardiovascular risk. A 32.0% relative risk reduction was found, while the reduction in blood pressure was only 3.8 mm of Hg (systolic) and 2.8 mm of Hg (diastolic)\(^11\). The results have important implications for the primary and secondary prevention of stroke. The angiotensin converting enzyme inhibitor ramipril decreased the risk for stroke independent of reduction in blood pressure. There is a beneficial effect even in patients with blood pressure less than 129/79 mm of Hg. The beneficial effects of the treatment were seen in all subgroups examined. This shows that high risk patients should be treated with ramipril in addition to other preventive measures irrespective of their initial blood pressure. The underlying mechanisms by which angiotensin converting enzyme inhibitors prevent vascular events have been discussed widely. The protective effects of these drugs on the vascular wall are possibly explained by decreased oxidative stress and decreased proliferative and inflammatory responses resulting in a beneficial effect on the progression of atherosclerotic plaques. The antiinflammatory response of angiotensin converting enzyme inhibition may lead to more plaque stabilization.

Stroke is not uncommon in Bangladesh but clinical experienced of experts says that stroke is increasing day by day. The literature supports that the effectiveness of ACE- inhibitor, antioxidant or antiplatelete in combination or alone can reduce the size and shape of atherosclerotic plaque, which will reduce the occurrence of repeated stroke, and for that matter the study is designed and conducted.

Methodology
This clinical trial was carried out on 150 randomly selected patients ranging from 27 years to 70 years of age referred for better treatment with clinical features of stroke. Among the 150 patients 50 were enrolled in Group A, 50 in Group B and the rest 50 patients in Group C. Patients of group A were given aspirin, group B were given aspirin plus antioxidant and group C were given aspirin plus ACE inhibitor (Ramipril). Investigations were done, complete blood count, blood sugar, serum lipid profile, X-ray Chest, electrocardiography, Computed Tomography of brain, Carotid Doppler, serum urea and serum creatinine at 3 months intervals up to 12 months. The laboratory examinations were done by established methods. In every visit dietary and exercise education were imparted.

The dietary advice included a total daily intake of only 10.0% calorie from fat. Weight in Kgs and
Height in meter was determined for the measurement of BMI. Moderate exercise of 30 min, at least 5 times a week was advised.

**Inclusion criteria:**
Patients giving consent and willing to comply with the study procedure, the patients with age below 70 years, patient with clinical features of stroke proven by computed tomography scan of head as ischaemic stroke, patient with first attack of ischemic stroke, hospitalized stroke patients having no major life threatening condition.

**Exclusion criteria:**
Stroke patient refusing to be included in the study: Prior history of stroke, presentation to the hospital more than 6 months after stroke, patients already on lipid lowering drugs, patients with intracranial space occupying lesion (ICSOL) presenting with stroke like features, patients with abnormal cardiac condition giving rise to stroke e.g. valvular heart disease, atrial fibrillation etc, patients having systemic disease like vasculitis, e.g. systemic lupus erythematosus (SLE), polyarteritis nodosa (PAN), infective disease of brain and meninges, very sick patients with too many complication beside stroke, patient with intracerebral or subarachnoid haemorrhage

**Patients screening**
We selected ischemic stroke patients for over a period of 36 months during 2004-2007 by predetermined criteria. By CT scan of brain and Carotid Doppler confirmation the patient were selected. When carotid artery becomes blocked partially, the condition may be diagnosed by hearing a bruit. The other diagnosis is made by: Doppler ultrasound- Carotid duplex ultrasonography (CUS) highly reliable, and the risks associated with CUS are less than those associated with angiography.

Follow up studies on patients undergoing surgery or conservative treatment, Characterization of atherosclerotic plaque and its relationship with symptoms and histology. The Carotid Doppler ultrasound has been developed primarily as a screening technique and for measuring percentage changes with plaque for carotid vascular disease. Treatment is a part of prevention. Aspirin is a known antithrombotic, antioxidants have lipid lowering and prevention of oxidative damage property. People who eat foods high in antioxidants such as, vitamin A, vitamin C and vitamin E have less carotid stenosis. We will advise the stroke patient to eat only 10.0% energy from dietary fat (restricting saturated fat). So it is expected that cerebral infract may yield to these therapy.

**Statistical analysis of data**
Statistical analyses of the results were obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-13) (SPSS Inc, Chicago, IL, USA). The results were presented in tables, figures and diagrams. During analysis frequency distribution for all the variables were worked out and produced in tabular form. 2 tests were used to compare proportions. One way ANOVA with post hoc Bonferroni test was applied for testing differences among continuous variables. A two-sided p value 0.05 was considered significant at 95% level.

**Results**
A total of 150 patients were included in the present study. The subjects were divided into three groups according to simple random sampling method. Among them 50 patients were allocated in Group A who were treated with aspirin, 50 patients were treated with aspirin and antioxidant (Vitamine A, Vitamin E and Vitamin C) enrolled in Group B and the rest 50 patients who were treated with Aspirin plus ACE inhibitor (Ramipril) enrolled in Group C. Out of 150 patients 14.67% (22 subjects) could not completed four times follow up. So, these subjects were not included in this analysis.

The mean age was 54.23 + 10.34, 59.5 + 11.7, and 56.29 + 9.65 for A, B and C groups respectively. The overall mean age of the subjects was 56.73 + 10.76. 72.7% were male and 27.3% were female. For socio economic and cultural reasons hospital attendance of female patients is always less than male patients in our country.
Table I: Age distribution of the patients

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>1 (2.5) §</td>
<td>1 (2.3)</td>
<td>1 (2.2)</td>
<td>3 (2.3)</td>
</tr>
<tr>
<td>36-45</td>
<td>9 (22.5)</td>
<td>6 (14.0)</td>
<td>7 (15.6)</td>
<td>22 (17.2)</td>
</tr>
<tr>
<td>46-55</td>
<td>13 (32.5)</td>
<td>9 (20.9)</td>
<td>13 (28.9)</td>
<td>35 (27.2)</td>
</tr>
<tr>
<td>56-65</td>
<td>12 (30.0)</td>
<td>17 (39.5)</td>
<td>17 (37.8)</td>
<td>46 (35.9)</td>
</tr>
<tr>
<td>66 and above</td>
<td>5 (12.5)</td>
<td>10 (23.3)</td>
<td>7 (15.6)</td>
<td>22 (17.2)</td>
</tr>
<tr>
<td>Total</td>
<td>40 (100.0)</td>
<td>43 (100.0)</td>
<td>45 (100.0)</td>
<td>128 (100.0)</td>
</tr>
</tbody>
</table>

Mean ± SD

54.23±10.34 | 59.51±11.79 | 56.29±9.65 | 56.73±10.76*

§ Figure within parenthesis denoted corresponding percentage

* ANOVA test was done to measure the level of significance.
F value=2.624; df= 2, 125; p value= 0.076

Out of all patients of the study groups maximum, 46 (35.9%) were within 56 to 65 years age group followed by 27.2% within 46 to 55 years age range, 17.2% within 36 to 45 years, similar number within 66 and above age group and 2.3% within 25 to 35 years age range. Maximum patients (32.5%) of group A were within 46 to 55 years, 39.5% patients of group B and 37.8% of group C were within 56 to 65 years age range.

ANOVA test revealed that no statistical significance difference in term of mean ages of the study groups (p>0.05).

Table II: Sex distribution of the subjects

<table>
<thead>
<tr>
<th>Groups</th>
<th>Sex</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male (%)</td>
<td>Female (%)</td>
</tr>
<tr>
<td></td>
<td>(n=40)</td>
<td>(n=43)</td>
</tr>
<tr>
<td>Group A</td>
<td>32 (80.0) §</td>
<td>8 (20.0)</td>
</tr>
<tr>
<td>Group B</td>
<td>34 (79.1)</td>
<td>9 (20.9)</td>
</tr>
<tr>
<td>Group C</td>
<td>27 (60.0)</td>
<td>18 (40.0)</td>
</tr>
<tr>
<td>Total</td>
<td>93 (72.7)</td>
<td>35 (27.3)</td>
</tr>
</tbody>
</table>

§ Figure within parenthesis denoted corresponding percentage

* Chi square test was done to measure the level of significance; Chi square value=5.604, df=2, p value= 0.061
Of all the patients males were dominant. Male to female ratio of all patients was 2.7:1. Male to female ratio of group A, Group B and Group C was 4:1, 3.8:1 and 1.5:1 respectively. No significant difference was observed in term of sex among groups statistically (p>0.05).

Table III: Education of the subjects by groups

<table>
<thead>
<tr>
<th>Educational status</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illiterate</td>
<td>9 (22.5)§</td>
<td>5 (11.6)</td>
<td>7 (15.6)</td>
<td>21 (16.4)</td>
</tr>
<tr>
<td>Primary</td>
<td>20 (50.0)</td>
<td>21 (48.8)</td>
<td>19 (42.2)</td>
<td>60 (46.9)</td>
</tr>
<tr>
<td>SSC &amp; HSC</td>
<td>8 (20.0)</td>
<td>7 (16.3)</td>
<td>9 (20.0)</td>
<td>15 (11.7)</td>
</tr>
<tr>
<td>Graduate and above</td>
<td>3 (7.5)</td>
<td>10 (23.3)</td>
<td>10 (22.2)</td>
<td>23 (18.0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>40 (100.0)</strong></td>
<td><strong>43 (100.0)</strong></td>
<td><strong>45 (100.0)</strong></td>
<td><strong>128 (100.0)</strong></td>
</tr>
</tbody>
</table>

§ Figure within parenthesis denoted corresponding percentage
* Chi square test was done to measure the level of significance; Chi square value=5.6, df=6, p value= 0.467

From Table III it is clear that illiterate patients 16.4% have fewer strokes. But increased stroke patients 46.99% was found in the groups who had primary education. From secondary, higher secondary and graduate level, the stroke rate decreases, which may be due to proper understanding of the disease, proper regular treatment and to follow strict diet control.

Table IV: Income distribution by groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low class</td>
<td>16 (40.0)</td>
<td>17 (39.5)</td>
<td>7 (15.6)</td>
<td>40 (31.3)</td>
</tr>
<tr>
<td>Middle class</td>
<td>14 (35.0)</td>
<td>16 (37.2)</td>
<td>16 (35.6)</td>
<td>46 (35.9)</td>
</tr>
<tr>
<td>Higher class</td>
<td>10 (25.0)</td>
<td>10 (23.3)</td>
<td>22 (48.9)</td>
<td>42 (32.8)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>40 (100.0)</strong></td>
<td><strong>46 (100.0)</strong></td>
<td><strong>42 (100.0)</strong></td>
<td><strong>128 (100.0)</strong></td>
</tr>
</tbody>
</table>

Table IV shows that 31.3% patients were from low income groups, 35.9% patients were form middle income groups and 32.8% patients were from high income groups. Middle and higher income groups are more prone to ischemic stroke with carotid atherosclerosis than low income group patients.
Figure 1 shows that the mean intima medial thickness of RCCA at different follow ups of all study groups. The unit of the graph is measured in mm. The mean intima medial thickness of group A increased from about 0.92 mm at baseline until it reached a peak of 0.95 mm at 1st follow up. From this point onwards it is continued decline until it remained constant at 0.87 mm from 2nd follow up to final.

In group B mean intima medial thickness at baseline was 0.91 mm. From this point onward mean thickness climbed from 0.92 mm at 1st follow up and reached 0.94 mm at 2nd follow up. From this point onward declining trend was observed. At final follow up mean thickness of intima media of group B was 0.87 mm.

In contrast, the thickness of intima media of RCCA of group C dropped steadily from baseline to onward. Thickness of intima media in group C at baseline was 0.96 mm, 0.9 mm at 1st follow up, 0.82 mm at 2nd follow up and 0.73 mm at final follow up.

Figure 2: Intima media thickness (mm) of LCCA
Figure 2 shows that the mean intima medial thickness of LCCA at different follow ups of all the study groups. The unit of the graph is measured in mm. The mean intima medial thickness of group A increased from about 0.98 mm at baseline until it reached a peak of 1.02 mm at 1st follow up. From this point onwards began to decline until it remains constant at 0.92 mm from 2nd follow up to the final.

In group B mean intima medial thickness at baseline was 0.97 mm. From this point onward mean thickness climbed to 0.99 mm at 1st follow up and declined to 0.96 mm at 2nd follow up. At final follow up mean thickness of intima media of group B was at 0.92 mm.

In contrast, the thickness of intima media of LCCA of group C dropped steadily from baseline to onward. Thickness of intima media in group C at baseline was 0.98 mm, 0.94 mm at 1st follow up, 0.86 mm at 2nd follow up and 0.72 mm at final follow up.

Figure 3 shows that the mean intima medial thickness of RICA at different follow up of all study groups. The unit of the graph is measured in mm. The mean intima medial thickness of group A increased from about 0.85 mm at baseline until it reached a peak of 0.88 mm at 1st follow up. From this point onwards it is started to decline and was at 0.87 mm at 2nd follow up and 0.82 mm at final follow up.

In group B mean intima medial thickness at baseline was 0.85 mm. From this point onward mean thickness climbed at 0.88 mm at 1st follow up and then declined to reach 0.87 mm at 2nd follow up and 0.82 mm at final follow up.

In contrast, the thickness of intima media of RICA of group C dropped steadily from baseline to onward. Thickness of intima media in group C at baseline was 0.91 mm, 0.86 mm at 1st follow up, 0.79 mm at 2nd follow up and 0.69 mm at final follow up.
Figure 4 shows that the mean intima medial thickness of LICA at different follow up of all study groups. The unit of the graph is measured in mm. The mean intima medial thickness of group A increased from about 0.88 mm in baseline until it reached a peak of 0.94 mm at 1st follow up. From this point onwards it declined to 0.85 mm in 2nd follow up and 0.79 mm at final follow up.

In group B mean intima media thickness at baseline was 0.85 mm. From this point onward mean thickness climbed to 0.89 mm at 1st follow up and then declined to reach 0.85 mm at 2nd follow up and 0.79 mm at final follow up.

In contrast, the thickness of intima media of LICA of group C dropped steadily from baseline to onward. Thickness of intima media in group C at baseline was 0.94 mm, 0.88 mm at 1st follow up, 0.83 mm at 2nd follow up and 0.72 mm at final follow up.

Figure 5: Reduction of plaque of RCCA after final follow up measured by cross sectional area reduction method (C method) and by North American symptomatic carotid endarterectomy trial method (N-method)
In figure 5 RCCA shows 3.74% reduction of stenosis in group A in (C) method and 8.36% in (N) method, in group B 1.29% reduction in (C) method and 5.33% in (N) method and in group C 14.42% in (C) method and 16.59% in (N) method respectively after final follow up.

Figure 6: Reduction of plaque of LICA after final follow up measured by cross sectional area reduction method (C method) and by North American symptomatic carotid endartectomy trial method (N-method)

Figure 6 shows that LICA plaque reduction in both (C) and (N) method in group A is 3.12% and 7.92%, in group B is 4.28% and 4.39% and in group C is 16.36% and 17.97% respectively.

Figure 7: Reduction of plaque of RICA after final follow up measured by cross sectional area reduction method (C method) and by North American symptomatic carotid endartectomy trial method
Figure 7 shows that RICA plaque reduction in both (C) and (N) method in group A is 2.02% and 2.98%, in group B is 2.76% and 2.42% and in group C is 13.19% and 16.85% respectively.

Discussion

Patients were treated with aspirin enrolled in Group A, patients treated with aspirin and antioxidant (? Carotene, Vitamin E and Vitamin C) enrolled in Group B and patients who were treated with ACE inhibitor (Ramipril) plus aspirin enrolled in Group C. Out of 150 patients, 22 (14.67%) patients could not complete three times follow up. Out of 150 patients 128 patients were completed the all three follow up. Among them 40 patients were in Group A, 43 patients were in Group B and 45 patients were in Group C and these patients were not included in analysis.

Age is the single most important risk factor for stroke. The older the person is, the greater the risk for stroke\textsuperscript{12}. For each successive 10 years after age 55, the stroke rate more than doubles in both men and women\textsuperscript{13}. In the present series, it was revealed that middle and old age people are more prone to stroke than the younger age group. Maximum patients of this study were above 46 years. American Heart Association (AHA) revealed the same fact on 2006 that the older are at the greater risk for stroke\textsuperscript{12}. Hayee et al.\textsuperscript{14} also support this finding. A study conducted in Pakistan in 2002 showed that the mean age was 53.0 years for all cases of stroke while mean age in males and females was 56.2 and 48.9 years respectively\textsuperscript{15}.

The mean age of the patients of our series was 54.23 + 10.34, 59.5 + 11.7, and 56.29 + 9.65 years for A, B and C groups respectively. The overall mean age of the subjects was 56.73 + 10.76 years.

American Heart Association\textsuperscript{12} revealed that stroke is more common in men than in women. In the present study 93 (72.7%) were male and 35 (27.3%) were female. For socio economic and cultural reasons hospital attendance of female is always less than male. In the present study, it was also found that stroke is common in male than female. In the present study the over all male and female ratio was 2.7:1 and in group A, Group B and Group C this ratio was 4:1, 3.8:1 and 1.5:1 respectively (p>0.05). This result is supported by some other studies. Feigin et a\textsuperscript{16} Basharat et a\textsuperscript{15} found that male were attacked by stroke more than female. In Bangladesh, some previous study also revealed the male dominant picture\textsuperscript{14,17,18}. All of these studies were hospital based; not community based. In underdeveloped countries, females are given less priority in all respect including treatment for illness. So, this figure may not reflect the real picture of the country like Bangladesh.

From our series it is clear that illiterate patients (16.4%) had fewer strokes. But increased stroke patients (46.9%) were found in the groups who had primary education. From secondary, higher secondary and graduate level, the stroke rate decreases, which may be due to proper understanding of the disease and regular treatment and also due to follow strict the diet control.

In the present study 40 (31.3%) patients were from low income groups, 46 (35.9%) patients were form middle income groups and 42 (32.8%) patients were from high income groups. Middle and high income groups are more prone to ischemic stroke with carotid atherosclerosis than low income group patients.

The SECURE (the study to evaluate carotid ultrasound changes in patients treated with ramipril and vitamin E) trail\textsuperscript{19} findings on atherosclerosis are concordant with the result of the HOPE (Heart Outcome Prevention Evaluation Study) trail on clinical events. Together, these studies show that ramipril reduces atherosclerosis progression and prevents major vascular events. In our series it is also found that increase atherosclerotic plaque in the carotid artery or its bifurcation increases stroke incidence. The atherosclerotic plaques occurs due to increased levels of cholesterol and low levels HDL cholesterol and are strong and important risk factors for coronary atherosclerosis and causing stroke. There is evidence indicating that increased levels of total cholesterol and low levels of HDL cholesterol are strong and important risk factors for coronary atherosclerosis and symptomatic coronary heart disease. At the end of the study significant reductions of intima medial thickness (IMT) were observed in RCCA, LCCA, RICA and LICA in Group C who were treated with ACE inhibitor (Ramipril) and aspirin in comparison with other two groups. At final follow up 24.04%, 26.23%, 22.79% and 24.05% reductions of intima media thickness were observed in group C whereas in group A and group B 3.05% and 2.42%, 2.89% and 3.14%,
Patients treated with ramipril had significantly lower atherosclerosis (from 0.9 to 0.7 mm) progression rates as observed by different trials. The progression rate of the mean maximum IMT was 0.0217 mm/year in the placebo group, 0.0180 mm/year in the ramipril 2.5-mg/day group, and 0.0137 mm/year in the ramipril 10-mg/day group (p = 0.033 for the overall effect of ramipril). Although the absolute difference in atherosclerosis progression rates between ramipril and placebo-treated patients is small, the relative reduction in mean maximum IMT was 37% for ramipril 10 mg/day versus placebo in Lonn et al series\textsuperscript{19}, which was quite considerable and similar to the 32% reduction in the risk for stroke observed in the HOPE trial\textsuperscript{11}. In Hosomi et al\textsuperscript{20} series after two years follow up with ACE inhibitor (Enalapril, 10 mg) 49.0% reduction in the annualized IMT slope was observed. Our finding was consistent with these studies. ACE inhibitor is a highly cost-effective agent available for preventing and treating ischaemic stroke due to carotid artery stenosis. In our study it was revealed that in combination with aspirin and ACE inhibitor (Ramipril) can significantly reduce carotid plaque than aspirin and antioxidant alone. Furthermore low cost of these agents can make this therapy is an effective armamentarium for the prevention of stroke due to carotid artery stenosis. Angiographical support would have a strong benefit for validity. But due to lack of fund and time it was dropped. However small sample size and drop out was the main limitation of the study. So, before mass use of this result of intervention further multicentre study with a large sample size is recommended.

Summary

Carotid atherosclerosis is associated with ischemic stroke. It is common in elderly and the condition can be controlled or improved by drugs. In order to find out the role of antioxidant vitamins and aspirin, aspirin plus ACE-inhibitor or aspirin alone in prevention of stroke caused by plaque in or near carotid artery bifurcation diagnosed by carotid color duplex ultrasonography and blood lipid profile in stroke patients admitted in Dhaka Medical College Hospital, General Medicine inpatient and from specialized Neurology stroke clinic.

A total 150 patients were collected from the Stroke Clinic of Dhaka Medical College Hospital, run by the Department of Neurology. All CT scan proven clinically manifested first attack of ischaemic stroke patients without having any major life threatening conditions were enrolled. Patients with lipid lowering drugs, previous history of stroke, having ICSOL and abnormal cardiac conditions were excluded.

Among the selected patients 50 were placed in Group A (aspirin only), 50 patients in Group B (aspirin and antioxidant) and the rest 50 patients in Group C (Aspirin plus ACE inhibitor). Complete Blood Count, Blood Sugar, Lipid Profile, X-ray Chest, Electrocardiography, Computed Tomography of Brain, Carotid Doppler, Serum Urea and Serum Createnine were done at 3 months intervals up to 12 months. At every visit dietary and exercise education were imparted.

The overall mean age of the subjects was 56.73 ±10.76 years. More than seventy percent subjects were male and 27.3% were female. One group was given Aspirin alone, another group was given Aspirin plus Antioxidant and third group was given Aspirin plus ACE-inhibitor. At the end of the study significant reductions of intima media thickness (IMT) were observed in RCCA, LCCA, RICA and LICA in group who were treated with ACE inhibitor (ramipril) and Aspirin in comparison with other two groups. At final follow up 24.04%, 26.23%, 22.79% and 24.05% reductions of intima media thickness were observed in group C whereas in group A and group B 3.05% and 2.42%, 2.89% and 3.14%, 5.09% and 2.79%, 7.19% and 7.40% in RCCA, LCCA, RICA and LICA respectively. Patients treated with ACE-inhibitor plus Aspirin showed relatively higher percentage in reducing the plaque size and thickness than patients treated with Aspirin alone and Aspirin plus Antioxidant.
**Conclusion**

Aspirin plus Ramipril treated patient shows significant reduction in atherosclerotic plaque size and thickness by one year of intervention but no toxicity was observed in the study subjects, rather than Aspirin alone or Aspirin plus Antioxidant.

A combined dose of aspirin 300 mg and ramipril 10 mg daily in ischemic stroke patient with atherosclerotic plaque in carotid artery found effective in preventing stroke by reducing plaque size within one year.

**Bibliography**


