Comparison of the Efficacy of Aspirin, Aspirin+Dipyridamole and Warfarin in Patients with Amaurosis Fugax Secondary to Mitral Valve Prolapse

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Abstract

Purpose: To determine the efficacy of three therapeutic regimens for the treatment of amaurosis fugax secondary to embolic sources from the heart

Methods: Sixty patients randomly divided into 3 groups (20 patients in each group). Group 1 received 100 mg Aspirin/day, group 2 received the same dose of Aspirin plus dipyridamole 75 mg twice daily and group 3 received 10 mg warfarin for 3 days followed 5 mg thereafter. All patients were followed every 6 months for relapse of amaurosis fugax and cardiac status. Data were collected and analysed.

Results: Forty-nine patients (81.6%) were female and 11 patients (18.4%) were males. The mean ages of patients in group 1, 2, 3 were 44.85±14.56, 45.55±15.49 and 4490±14.87, respectively (P=0.98). The mean duration of amaurosis fugax stroke was 7 minutes (ranged 4-11 minutes). 91.6% of the patients had type A personality by anxiety and neurosis. Stroke was seen in 47 (78.3%) patients in both eyes, in 10 patients (16.6%) in the left eye and in 3 cases (5.1%) in the right eye. After one year of treatment, relapse of amaurosis fugax stroke was developed in 7 (35%) patients in Aspirin group, 5 (25%) in Aspirin plus dipyridamole group and 1 (5%) in warfarin group. Warfarin group had lower relapse than those in other groups (P=0.022).

Conclusion: The results show that warfarin has better efficacy for the treatment of amaurosis fugax than Aspirin or Aspirin plus dipyridamole.

Keywords: Aspirin, Dipyridamole, Warfarin, Amaurosis Fugax, Mitral Valve Prolapse
Introduction
Amaurosis fugax is a transient visual loss (TVL), with several etiologies such as migraine, intermittent angle closure glaucoma, embolism, vasospasm, vascular occlusive disease, hypercoagulability, temporal arteritis, positional retinal detachment, and papilledema.\textsuperscript{1,2} This syndrome usually lasts for 5-10 minutes, and includes three main types: cholesterol emboli arise from carotid artery, calcific emboli from damaged cardiac valves, and platelet-fibrin emboli from abnormalities of heart or great vessels.\textsuperscript{2,3} Common causes of amaurosis fugax are carotid disorders followed by cardiac source, and mitral valve prolapse (MVP) is another source.\textsuperscript{2,3}

Transient ischemic attacks secondary to embol from the mitral valve due to endothelial disruption have been reported. Antiplatelet aggregation agents such as Aspirin should be given to patients with transient ischemic attacks, and if the therapeutic response was poor, anticoagulants (warfarin) should be used.\textsuperscript{4}

Transient ischemia of retina (Amaurosis fugax) is one of the most important symptoms of MVP which causes patient very anxious and unilateral or bilateral retinal artery occlusion is one of the most threatening complications.\textsuperscript{5} So diagnosis and treatment of this condition is very important. The aim of this study was to compare the therapeutic effect of three different regimens for the treatment of stroke of amaurosis fugax secondary to embolic sources from the heart.

Methods
This study was performed in randomized clinical trial and single blinded. Inclusion criteria were the patients with amaurosis fugax secondary to MVP with normal intraocular pressure (IOP), normal retina and no strabismus. The patients had 2-5 attacks of amaurosis fugax before entering into the study. Exclusion criteria were history of other valvular disease, MI, disorder of coagulation, migraine, significant carotid stenosis, carotid surgery, mitral stenosis and ischemic heart disease. Initially the patient with symptoms of source of ophthalmologic, neurologic and cardiological exams were done to rule out the source of TVL from migraine, vasospasm, optic neuropathy, papilledema, temporal arteritis, hypercoagulability and cardiovascular disorders. For all patients carotid Doppler sonography for carotid stenosis evaluation was performed. All the patients examined with transthoracic echocardiography and EKG. In this manner 60 patients with pure amaurosis fugax by source of MVP selected and divided randomly into three groups, by random allocation (the first patient in Aspirin group, the second patient in Aspirin+Dipyridamole group and the third patient in Warfarin group, and every group contained 20 patients) and treated by Aspirin, Aspirin+Dipyridamol, Warfarin, between 1996 to 2007. The duration of treatment was one year for each patient and CBC, PT, transthoracic echocardiography was performed for all of the patients. The method of administration of drug was: in Aspirin group, Aspirin 100 mg once a day (in patient with gastritis administered $\frac{1}{2}$ tablet Aspirin MC). In Aspirin+Dipyridamole group, Aspirin 100 mg and Dipyridamole 75 mg twice a day. In Warfarin group, 10 mg Warfarin for 3 days then checked PT, if it was 17-18, Warfarin was continued by maintenance dose. For evaluation of relapsing of amaurosis fugax, the patient was visited every 3 months by ophthalmologist and for evaluation of new cardiovascular disorders was visited every 6 months by cardiologist and echocardiography was performed in each visit.

Method of data collection was by questionnaire for every patient, data were collected and entered into SPSS and analyzed by $\chi^2$ and T-test and $P<0.05$ was considered as significant. Ethically since all of these drugs are being used for the treatment of amaurosis fugax the complications of the drugs was explained to every patient, so all patients accept that the conditions, and were enrolled. The ethical committee approved the study and all the patients gave their informed consent.

Results
Forty-nine patients (81.6%) were female and 11 patients (18.4%) were male. The mean age of the patients under Aspirin, Aspirin+Dipyridamole and Warfarin were 44.85±14.56, 45.55±15.49, and 44.90±14.87 years, respectively ($P=0.987$). Mean duration of amaurosis fugax stroke was 7 minutes (min: 4 minutes and max: 11 minutes). Involvement of both eyes, left and right eyes
were seen in 47 (78.3%), 10 (16.7%) and 3 (5%). 1.5 years follow-up for three groups showed that: 7 patients (35%) in Aspirin group and 5 patients (25%) in Aspirin+Dipyridamole group and 1 patient (5%) in Warfarin group had relapse. Therefore relapses in Warfarin group were significantly lower than that of the other groups (P=0.022).

### Table 1. Characteristics and outcome of therapy in the treated groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean age±SD</th>
<th>Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>44.85±14.56</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>Aspirin+Dipyridamole</td>
<td>45.55±15.49</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Warfarin</td>
<td>44.90±14.87</td>
<td>1 (5%)</td>
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</tbody>
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**Discussion**

Although MVP is a benign disease, but may be associated with endocarditis, regurgitation, retinal artery occlusion, cardiac arrhythmia, atypical chest pain, dyspnea and sudden death.\(^5\)

In some conditions, MVP is the source of thromboembolic episodes that may obstruct the cerebral or retinal artery and causes TIA or amaurosis fugax (RARELY RETINAL ARTERY OCCLUSION).\(^5\) Patients with amaurosis fugax mostly refer to ophthalmologists, so MVP should be considered as a differential diagnosis of amaurosis fugax. This is an important issue to consider for preventing the complications of MVP.\(^5\)

In this study we found less relapsing in Warfarin group (5%) and more relapsing in Aspirin group (35%) (P=0.022). Watson studied 8 patients with TIA and 3 patients with partial non-progressive strokes associated with MVP and treated them by Aspirin or Warfarin and found that only one episode of ischemia developed on Aspirin treatment, whereas non recurred on sodium Warfarin.\(^6\)

In this study we found that the older persons were resistant to treatment and the disease has a more malignant clinical course. In Aspirin group the mean age of the relapsing cases was 61.34±2.57 years and in Aspirin+Dipyridamole was 62.54±2.45 years, and relapsing in older patients significantly was more than that in younger patients (P<0.05). Our findings were in consistence with the results of Tippin et al, they studied on 83 patients before the age of 45 with cerebral TIA, they concluded that amaurosis fugax and ocular infarction occurring in younger patients are probably associated with more benign clinical course than those seen in the older persons.\(^7\)

Wilhelm reported 3 patients out of 7 patients had monocular amaurosis fugax (42.8%) (8), but in our study 21.7% of the patients were monocular and 78.3% were binocular. We postulate that the reason of high binocular involvement in our patient was embolus arose from mitral valve to go to carotid arteries and to bilateral ophthalmic arteries to involve both eyes.

Hashimoto et al in etiologic study on 16 patients with amaurosis fugax performed on 1998 reported that the mean age of patient was 62 years.\(^9\) But in this study the mean age was 45 years.

Petty et al performed study on frequency of complication of Aspirin, Warfarin and heparin in TIA during 4 years follow-up found that the complication rates for Warfarin were lower than those for Aspirin and heparin.\(^10\)

Chen at 2000 in fundoscopic examination on patients with amaurosis fugax observed multifocal embolization in the vessels.\(^11\)

Conclusion of studies of Mosso et al in 2000 on patients with TIA, they believed that one drug could not be useful.\(^12\) But in our study Warfarin was the best.

**Conclusion**

In conclusion the results of our study showed that the efficacy of Warfarin is better than that of Aspirin or Aspirin plus Dipyridamole in treating amaurosis fugax. Some of the limitations of this study include the fact that the amaurosis fugax is a subjective condition with only symptoms and no clinical signs and it can be appear at other circumstances.

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References