

Warfarin versus Aspirin in The Prevention of Recurrent Stroke in patients of Al-Muthanna province\Iraq

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ABSTRACT

Background and Purpose: Despite chronic used of antiplatelet like aspirin in secondary prevention of ischemic stroke ,there is a lot of cases with recurrence .For this reason , this study investigates use of anticoagulation ,warfarin, instead of Aspirin in secondary prevention and to show if warfarin is superior or equal to Aspirin in prevention of recurrent stroke in noncardioembolic ischemic stroke.

Methods: it is double-blind, randomized , clinical trials study that compare between two groups patients ,each group number(50) with first time noncardioembolic ischemic stroke, one group on warfarin with adjusted dose as INR between (1.8-2.8) and other groups on Aspirin with dose adjusted (100mg) and follow them if there is recurrence or not within one year.

Results: there is significant difference between two groups, that show group on warfarin is associated with less percentage of recurrence than patients with Aspirin with significant P-value(0.001)

Conclusion: this comparative and randomized study over one year show a mark difference between used warfarin and Aspirin in secondary prevention of recurrence as warfarin was superior than Aspirin mainly in noncardioembolic stroke. We need more clinical research to support this result in secondary prevention.

Keywords: Warfarin therapy, Recurrent stroke, Antiplatelet therapy and Noncardioembolic stroke.

INTRODUCTION

For a long time, antiplatelet was used as secondary prevention for ischemic stroke from recurrence, while warfarin was superior to antiplatelet in cardioembolic risk factor recurrence stroke. Many doubts was presented about used anticoagulants in secondary prevention for noncardioembolic stroke¹. This study based on that the rate of first stroke in patients with atrial fibrillation was lower with warfarin about (70%) as compared with other therapies also the efficacy of warfarin in preventing vascular event in patient with peripheral atherosclerotic disease or major vessel atheroma like aortic artery^{2,3}, the side effect of warfarin at lowest rate found at INR between (1.5-2.8)⁴.

METHODS

Study Design: This double-blind ,clinical trial study was done on 100 patients with single noncardioembolic stroke in Al-Muthanna teaching hospital\iraq. Those patients were organized into two groups ,one group on warfarin with INR(1.8-2.8) and other on aspirin(100mg) and follow up them for one year ± one month .INR was calculated Automated analyzed by using HummaClot junior machine.

Patients Selection: Patients who are eligible for study with age between (30-85) years with previous non cardioembolic stroke with mild disability within 30days . Those patients with INR above (1.4), stroke due to carotid artery intervention and patients with atrial fibrillation are ineligible for study. Patients are fully evaluated with brain computed

tomography, Magnetic Resonance imaging, echocardiography and Doppler ultrasound of carotid artery. Then follow up for one year from January 2019 to March 2020.

Medication and Blinding: The medication that used were Aspirin tablet (Bayer Company) 100mg and warfarin tablets (Bristol Company) 1mg,3mg and 5mg with adjusted INR between (1.4-2.8).

Blood samples from patients were sent on the same day for doing INR monthly in AL-Muthanna teaching hospital with regular registration.

Follow Up & Primary End Points: Follow up of patient by telephone with neurological team for informed them if there is any complication like bruising , epistaxis , genitourinary or gastrointestinal bleeding that made stopping warfarin mandatory. And follow INR monthly if it elevated above (4.5) which need adjustment of dose. Also, patients are follow if there is new clinical feature indicate recurrent stroke that lasting more than 24 hours or confirmed it by radiological studies like computed topography(CT) or magnetic resonance imaging(MRI) that read by special radiologist in hospital. Outcome of patients during year of follow up include death or recurrent stroke.

Statistical Analysis: All continuous data follow a normal distribution , so mean and standard deviation was used to represent the data. Warfarin or Aspirin used patients were presented as charts and tables in simple proportion and comparisons of subgroups were done by using Pearson

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Chi-square test. Data of the research was analyzed by using SPSS version 23. The statistical significant difference for P-value less than 0.05 was taken at confidence interval of 95% .

Objective of Study: This study investigates use of anticoagulation ,warfarin, instead of Aspirin in secondary prevention and to show if warfarin is superior or equal to Aspirin in prevention of recurrent stroke in noncardioembolic ischemic stroke.

Ethical Consent: Informed consent was taken from the patient’s relatives or the patient himself when he was still conscious with keeping the patients’ records confidential in all stages of the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

RESULTS

Clinical trials , double blind study was conducted on 100 patients with noncardioembolic stroke divided them into two groups. Male : Female ratio 1.2:1 and mean age 64.7±11.699. 50 patients continue on warfarin and same number on Aspirin for one year and show (40.6%) of total patients had recurrent stroke for one year.

(29.3%) from recurrent stroke patients on warfarin while (70.7%) from recurrent stroke patients on Aspirin and This percentage was statistically significant that mean warfarin is more effective in secondary prevention than Aspirin.

Table 1: Percentage male to female

		Frequency	Percent
Valid	Male	60	59.4
	female	40	39.6
	Total	100	100.0
Total		100	100.0

Table 2: Percentage of warfarin to aspirins taken

		Frequency	Percent
Valid	warfarin	50	50.0
	Antiplatelet	50	50.0
	Total	100	100.0
Total		100	100.0

Table 3: Recurrent stroke with patients taken warfarin

		Frequency	Percent
Valid	Recurrent	41	40.6
	not recurrent	59	58.4
	Total	100	99.0
Total		100	100.0

Table 4: Compare follow up during one year versus secondary prevention

		secondary prevention		P –value, Total Fisher's Exact Test
		warfarin	Antiplatelet	
follow up during one year	Recurrent	12	29	0.001
	not recurrent	38	21	
Total		50	50	100

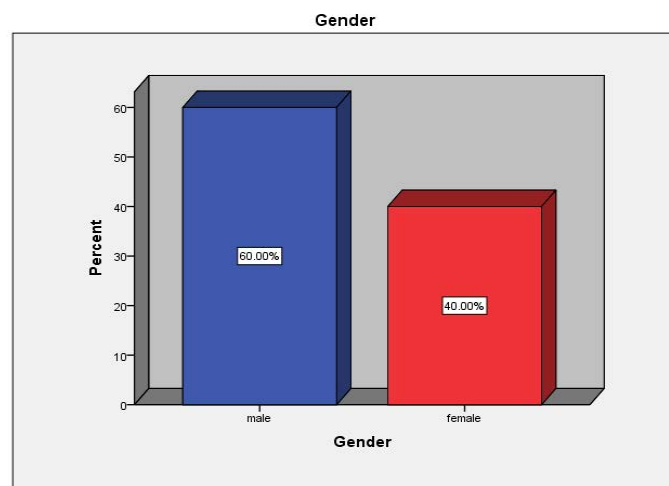


Figure 1: Gender

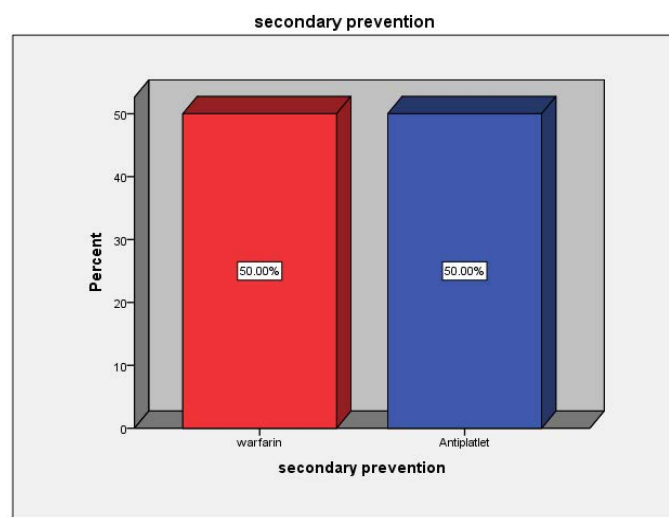


Figure 2: Secondary Prevention

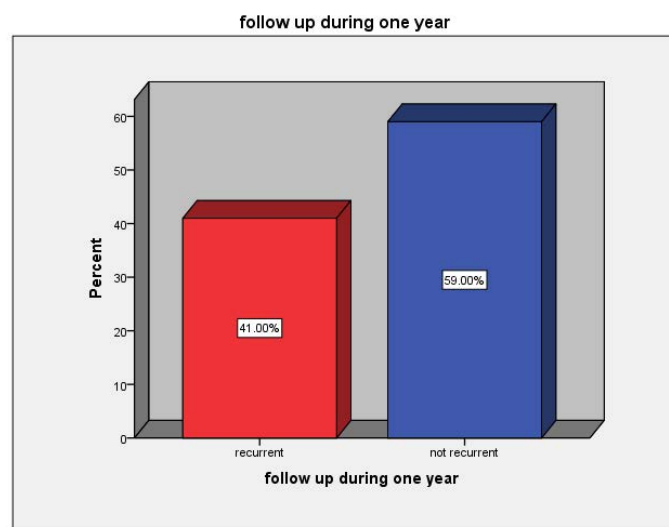


Figure 3: Follow-up During one year

DISCUSSION

The optimal medical treatment for secondary prevention for ischemic stroke was depend on understanding the pathophysiology of each type of stroke and vascular modifiable risk factors⁽⁵⁾. Many study express that a lot of patients with peripheral vascular disease are increased risk of myocardial infarction and stroke because the common pathology for both is atherosclerosis⁶. Study show anticoagulant (warfarin) was more effective in management of atherosclerosis in peripheral vascular disease than Aspirin for secondary prevention from stroke or myocardial infarction^{7,8}.

So, these study can explain that warfarin effective in treating atherosclerosis in peripheral vessels so it's also effective secondary prevention from recurrent stroke by managing atheroma in central vessels like cerebral vessels (Table 1-4). Also, other study which done on patients with atheroma in aortic artery with not receiving anticoagulation show higher incidence of vascular event like stroke and myocardial infarction (45%) in contrast to those with anticoagulation (5%) these result explain that warfarin had major effect on atherosclerosis in major vessels like aortic artery . Middle cerebral artery and internal carotid artery (Figure 1) are branches from aortic artery so that warfarin isis efficacious in preventing stroke in both of them⁹ (Figure 2,3). While The WARSS trial compared warfarin and aspirin in patients with noncardioembolic stroke and concluded they had similar efficacy in the prevention of recurrent ischemic stroke and thus in contrast with our study as these study used large number sample for long time with large percent of patients are dead or missed follow up so there is discrepancy between there and our result¹⁰ (Figure 4). Also, atherosclerosis can be regarded one of the modifiable risk factor for stroke¹¹.

CONCLUSION

Warfarin drug was more effective than Aspirin in secondary prevention from noncardioembolic stroke as warfarin show effect on atherosclerosis as well as clardiac emboli or atrial fibrillation.

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Competing Interest: None

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