Journal of Clinical Cardiology and Cardiology Research
2023 Volume 3, Issue 4
DOI: 10.59657/2837-4673.brs.23.016

BioRes Scientia
Value your Research

Review Article

Open Access

Warfarin or Aspirin: The Better Drug for Myocardial Infarction

Victor O. Adedara*

Department of Medicine, St George's University School of Medicine, True Blue, GND, Unted States.

Abstract

Non-communicable diseases, particularly cardiovascular diseases (CVD), pose a global health threat, with low and middle-income countries experiencing a disproportionate burden. The majority of global deaths, 71%, are attributed to non-communicable diseases, with 78% occurring in these countries. Notably, 44% of these deaths result from cardiovascular diseases, including ischemic heart disease and stroke. Addressing this challenge offers a significant opportunity to mitigate NCD-related morbidity, particularly by prioritizing prompt and efficient responses to ischemic heart disease and stroke.

Ischemic heart diseases and strokes, categorized under coronary artery disease (CAD), are pivotal contributors to CVD-related fatalities. CAD, marked by plaque deposition narrowing circulatory vessels, leads to events like heart attacks when blood clots replace ruptured plaques. Anticoagulant and antiplatelet drugs, such as Warfarin and Aspirin, are crucial for long-term thrombosis and MI management.

This study explores the efficacy of Aspirin and Warfarin, both individually and in combination, in the context of acute ischemic heart diseases. Three randomized studies conducted in the late 1990s and early 2000s form the basis of this investigation, comparing various doses and combinations of the two drugs in post-MI patients.

Results indicate that a combination of Warfarin and Aspirin demonstrates superior efficacy in preventing events after myocardial infarction compared to either drug alone. However, this combined approach is associated with a higher incidence of major bleeding. Despite controversies surrounding its use, aspirin remains widely prescribed for its ease of administration, low cost, and efficacy.

In conclusion, while a combination of Warfarin and Aspirin emerges as the most effective treatment for post-MI events, careful consideration is warranted due to the increased risk of major bleeding. This study contributes valuable insights into the ongoing debate on the merits and demerits of anticoagulant and antiplatelet combination therapy in managing acute ischemic heart diseases.

Keywords: cardiology research; aspirin therapy; warfarin therapy; ischemic heart disease; doses

Introduction

Non-communicable diseases, especially cardiovascular diseases (CVD), are emerging as a global health concern, especially among low and middle-income countries [1]. Around 71% of deaths globally are due to non-communicable diseases, and 78% of global NCD deaths occur in low and middle-income countries [2]. Ischemic heart disease and stroke have been identified as leading causes of CVD-related deaths for more than a decade [2].

As identified earlier, ischemic heart diseases and strokes are two significant causes of CVD-related deaths and can be categorized as coronary artery disease (CAD). CAD is the most common type of CVD, which narrows the circumference of circulatory vessels supplying oxygenated blood to the heart due to the deposition of plaque [1]. When the plaque ruptures, it is replaced by blood clots in arteries, causing blockage of blood supply to the heart muscles. This adversity increases the likeliness of damage to the myocardial cells, which, in turn, increases the risk of myocardial infarction, commonly known as a heart attack [2].

Anticoagulant agents and platelet-inhibiting drugs are the choice for the long-term management of thrombosis and MI [3,4]. Aspirin, also known as Acetylsalicylic acid, acts as an acetylating agent, which irreversibly inactivates platelet-dependent enzyme cyclooxygenase (COX)-1 and suppresses the generation of thromboxane A2, creating the antiplatelet effect [5]. It further reduces inflammatory responses in CAD and inhibits the progression of atherosclerosis. Aspirin is prescribed as a secondary preventive measure in CVD patients [4].

Hypothesis

Although there have been controversies on the short-term and long-term merits and demerits of combination therapy of anticoagulant and

antiplatelet, their intrinsic and extrinsic effects may clinically benefit the treatment of acute ischemic heart diseases. Generally, Aspirin is preferred over Warfarin because of its ease of administration, low cost, compatibility, and efficacy [6,7]. Earlier studies have established that the beneficial effects of Warfarin compared to placebo are known to prevent new events of MI [8,9]. Further, Warfarin is known to have superior benefits over Aspirin, whereas Aspirin is the most widely used drug currently [10].

Methods

Three randomized studies of Aspirin and Warfarin in different doses and combinations aided in the knowledge of the use of two drugs in the case of patients with MI [8,9,11,12].

The first 1997 study is a randomized, double-blind comparative study in the USA on fixed low-dose Warfarin and Aspirin with Aspirin alone after MI. 8803 MI patients, of the age group of 21-85 years, post an event of MI, with elevated myocardial enzyme concentration, along with chest pain or changes in electrocardiograph, were either treated with a daily dose of 160 mg Aspirin or 1mg Warfarin + 80mg Aspirin or 3 mg Warfarin + 80 mg Aspirin based on random allocation. All the drugs were identical in appearance, including the placebo. There was an interim analysis conducted by an independent data and safety monitoring board to ensure safety, efficacy, and futility.

Second, is a comparative study of the 2002 hypothesis that the combination of Aspirin and Warfarin was more effective than Aspirin alone. A randomized open-label controlled study with 2.7-year follow-up across 78 Department of Veterans Affairs medical centers in the United States. 5059 (median age 62 y, 98% men) who had an acute MI were administered daily with Warfarin (target international normalized ratio [INR] 1.5 to 2.5 IU) + Aspirin (81 mg/dl) or Aspirin (162 mg/dl) alone.

A comparative efficacy study of Aspirin (160 mg daily), Warfarin with a combination of doses of Aspirin (75 mg daily), and Warfarin as an open-label, multi-centric, randomized controlled trial post-MI. Patients of both genders, less than 75 years of age, with acute myocardial infarction as per the World Health Organization recommendations: chest pain, change in electrocardiograph, creatine kinase <250 U/litre, aspartate aminotransferase <50 U/litre were included in the study. Treatment continued until a predetermined number of events occurred, and no interim analyses were conducted.

Results

The daily dose of 160 mg Aspirin or 1mg Warfarin + 80mg Aspirin (1mg W+ 80mg A) or 3 mg Warfarin + 80 mg Aspirin (3mg W+ 80mg A) showed similar efficacy with less than 1% change of the difference between the three treatments [11]. The relative risk of the primary event across the three groups was:

Table 1: The relative risk of primary event across the three groups [11].

Treatment Group	Relative Risk of primary event
160mg A compared with (3mg W+ 80mg A)	0·95 (95% CI 0·81–1·12, p=0·57)
160mg A compared with (1mg W+ 80mg A)	1·03 (0·87–1·22, p=0·74)
(1mg W with 80mg A) compared with (3mg W+80 mg A)	0·93 (0·78–1·11, p=0·41)

In the study of Warfarin+ Aspirin against Aspirin alone, a 15% reduction in annual mortality was observed in a combination dose of Warfarin + Aspirin as opposed to Aspirin alone, along with major bleeding (1.28 vs 0.72 events per 100 person-years of follow-up P < 0.001) [9]. However, intracranial hemorrhage rates were identical in both groups (14 patients each) [9]. In the efficacy study of Warfarin, Aspirin, or both, statistically, there was no difference in the overall mortality rate among the three groups (Aspirin (160 mg daily) and Warfarin in combination dose with Aspirin (75 mg daily) and Warfarin) [12].

Discussion

In patients with an episode of Myocardial Infarction, no additional clinical benefits were observed in low, fixed-dose Warfarin (1 mg or 3 mg) combination with low-dose Aspirin (80 mg) and 160 mg aspirin alone [11]. Neither did the combination dose of Warfarin (at a mean international normalized ratio of 1.8) with a low dose of Aspirin have any added clinical benefits [11]. Warfarin was an effective drug when administered alone or in combination with Aspirin, as compared to Aspirin alone [9]. There was a reduction in the incidence of several events after an acute myocardial infarction, but it was associated with

a higher risk of bleeding [9]. A large number of patient withdrawals were observed in patients on Warfarin due to bleeding, percutaneous coronary intervention, or coronary artery bypass grafting, which may have impacted the effect of Warfarin [9].

Conclusion

Thus, a Combination dose of Warfarin and Aspirin was the most effective drug for preventing events after myocardial infarction when compared with Aspirin or Warfarin alone. However, major bleeding occurred more frequently with combination doses.

References

1. Karunathilake SP, Ganegoda GU. (2018). Secondary Prevention of Cardiovascular Diseases and Application of Technology for Early Diagnosis. *Biomed Res Int*.
2. World Health Organization. (2014) The top 10 causes of death. World Health Organisation.
3. Gelbenegger G, Postula M, Pecen L, et al. (2019). Aspirin for primary prevention of cardiovascular disease: A meta-analysis with a particular focus on subgroups. *BMC Med*. 17(1):198.
4. Ittaman S V, Vanwormer JJ, Rezkalla SH. (2013). The Role of Aspirin in the Prevention of Cardiovascular Disease. *Clin Med Res*. 12:3-4.
5. Mekaj YH, Daci FT, Mekaj AY. (2015). Therapeutics and Clinical Risk Management Dovepress New insights into the mechanisms of action of aspirin and its use in the prevention and treatment of arterial and venous thromboembolism. *Ther Clin Risk Manag*.
6. Dai Y, Ge J. (2012). Clinical Use of Aspirin in Treatment and Prevention of Cardiovascular Disease.
7. Paez Espinosa E V, Murad JP, Khasawneh FT. (2012). Aspirin: Pharmacology and Clinical Applications, 15.
8. Krumholz HM, Radford MJ, Ellerbeck EF, et al. (1995). Aspirin in the Treatment of Acute Myocardial Infarction in Elderly Medicare Beneficiaries. *Circulation*. 92(10):2841-2847.
9. Fiore LD, Ezekowitz MD, Brophy MT, Lu D, Sacco J, Peduzzi P. (2002). Department of Veterans Affairs Cooperative Studies Program Clinical Trial Comparing Combined Warfarin and Aspirin With Aspirin Alone in Survivors of Acute Myocardial Infarction. *Circulation*. 105(5):557-563.
10. Oh VM. (2002). Warfarin combined with low-dose aspirin in MI did not provide clinical benefit beyond that of aspirin alone. *ACP J Club*. 137(2):47.
11. Fuster V. (1997). Randomised double-blind trial of fixed low-dose warfarin with aspirin after myocardial infarction. *Lancet*. 350(9075):389-396.
12. Hurlen M, Abdelnoor M, Smith P, Erikssen J, Arnesen H. (2002). Warfarin, Aspirin, or Both after Myocardial Infarction. *N Engl J Med*. 347(13):969-974.

Cite this article: Victor O. Adedara. (2024). Warfarin or Aspirin: The Better Drug for Myocardial Infarction. *Journal of Clinical Cardiology and Cardiology Research*, BioRes Scientia Publishers. 3(4):1-3. DOI: 10.59657/2837-4673.brs.23.016

Article History: **Received:** November 30, 2023 | **Accepted:** November 22, 2024 | **Published:** November 29, 2024