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Comparison between 5 mg and 10 mg warfarin loading doses therapy in cardiac care unit patients at Elobied Hospital, Elobied City- Sudan

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Abstract

Background and objectives: Warfarin sodium therapy is usually initiated with a loading dose to reduce the time needed to reach the target international normalized ratio (INR). The right initial dose of warfarin is controversial. This study aimed to determine the best initial dose of warfarin in terms of safety and efficacy.

Patients and methods: This is a prospective hospital-based study. Fifty-nine patients who were admitted to the coronary care unit with clinical indication for warfarin were assigned to use the initial dose of warfarin 5 mg or 10 mg with the target INR of 2-3. An ethical clearance was obtained from the state ministry of health. A written consent was taken from each patient. An INR was measured at baseline and then after 72 hours. The data were then collected using a data sheet including age, gender, baseline INR, initial dose of warfarin, INR after 72 hours and whether the patient developed bleeding or not. Patients on Aspirin and other non-steroidal anti-inflammatory drugs were excluded. The data were analyzed using SPSS version 18.

Results: A total number of 59 patients were enrolled in the study. In this series, 59% of patients were females. The mean age of patients was 56 years. Five mg loading dose was used in 35 of patients (59%) while 10 mg was used in 24 patients (41%). The mean INR after 72 hours was 2.8 for those with the initial dose of 5 mg. For those with the initial loading dose of 10 mg the mean INR after 72 hours was 3.2. Minor bleeding occurred in three patients, two of them used the initial loading dose of 5mg and only one patient from the group of 10mg.

Conclusion: From this study, it seems that 5 mg loading dose of warfarin is reasonable and cost effective; nevertheless, 10mg initial loading dose is not associated with increased risk of bleeding.

Keywords: Warfarin; INR; Loading dose; Cardiac care; Elobied City

1. Introduction

Cardiovascular disease is a general term for condition affecting the heart or blood vessels, the role of platelets and fibrinogen in atherosclerotic process and subsequently in the pathophysiology of cardiovascular disease is essential as platelets in addition to their contribution to thrombosis and hemostasis modulating inflammatory reactions and immune response, these interactions establish a localized inflammatory response that promotes the atherosclerotic

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process [1]. Cardiovascular disease remains the leading cause of mortality and morbidity despite the identification of major risk factors and risk reduction strategies [2]. The goals of therapy in cardiac disease are the expedient restoration of normal coronary blood flow and the maximum salvage of functional myocardium. These goals can be met by several medical interventions and adjunctive therapies [3]. Anticoagulant therapy is often initiated with a combination of unfractionated heparin or low-molecular-weight heparin therapy together with warfarin [4]. Warfarin sodium therapy is usually started with a loading dose to shorten the time needed to reach the target INR. However, some patients with acute thrombosis may require rapid induction regimens while others, for example certain atrial fibrillation patients, may be suited to a slower commencement [5]. Warfarin loading doses are associated with early over anticoagulation and the development of a potential hypercoagulable state [4]. To monitor therapy, INR between 2.0 and 3.0 is generally accepted for these conditions except for valve replacements where a higher INR between 2.5 and 3.5 is usually recommended. The loading dose of warfarin range from 10 mg up to 1 mg which is sometimes used in the elderly [6]. This study aimed to determine the best initial dose of warfarin in terms of safety and efficacy.

2. Material and methods

The current study is a prospective hospital-based study. Fifty-nine patients who were admitted to the coronary care unit with clinical indication for warfarin were randomly assigned to use initial dose of warfarin 5mg or 10 mg with the target INR of 2-3. An ethical clearance was obtained from state ministry of health. A written consent was taken from each patient. venous blood has been collected, from each subject, in 3.8% trisodium citrate (9:1 vol/vol). The samples were centrifuged at 2000 g for 15 minutes to obtain platelet-poor plasma (PPP). Plasma was separated from cells into plane container. PPP will be stored and refrigerated on (2 - 8 c) and tested within 4 hours [7]. Prothrombin time and INR were measured at baseline and then after 72 hours by Coagulometer semi-automated (Urit 610). The data were then collected using a data sheet including age, gender, baseline INR, initial doe of warfarin, INR after 72 hours and whether the patient developed bleeding or not. Patients on aspirin and other non-steriodal. Data analysis was performed using statistical package for social science (SPSS) software version (18).

3. Results

A total number of 59 patients were enrolled in the study. In this series 59% of the patients were females. The mean age of patient was 56 years. Initial loading dose of 5 mg was used in 35 of patients (59%) while 10 mg was used in 24 patients (41%).In 81% Of the patients, the indication of warfarin use was atrial fibrillation. The other indications were pulmonary embolism (10%) and left n ventricular thrombus (9%). The mean INR After 72 hours was 2.8 for those with the initial dose of 5 mg. For those with the initial loading dose of 10 mg the mean INR after 72 hours was 3.2. Minor bleeding occurred in 3 patients, 2 of them used the initial loading dose of 5mg and only one patient from the group of 10mg.No patient developed thromboembolic complications.

4. Discussion

The goal of anticoagulant therapy is to administer the lowest possible dose of anticoagulant to prevent clot formation or expansion. Warfarin is the oral anticoagulant most frequently used to control and prevent thromboembolic disorders. Prescribing the dose that both avoids hemorrhagic complications and achieves sufficient suppression of thrombosis requires a thorough understanding of the drug's unique pharmacology [8]. In this study, 59 patients were included, 35 of them used 5 mg of warfarin as a loading dose. While 24 participants used 10 mg. The mean INR after 72 was higher in the group of 10 mg loading dose. Mark et.,al came up with the similar result [4]. In our study there was no difference in INR after 72 hours in different age group. Jerry H. et al reported increased anticoagulant response to warfarin with increasing age [9]. No major bleeding was detected but minor bleeding was reported in three patients. One study showed a major bleeding occurred in the group which received 10 mg initial dose. Although it is not detected in our study, some researchers found that the use of 10 mg loading dose can result in achieving the target INR in shorter time compared to 5 mg [10]. Another study conducted by Sidnei et.,al Comparison of initial loading doses of 5 mg and 10 mg for warfarin therapy concluded that, Initial therapeutic warfarin doses of 5 mg or 10 mg are equally effective and safe for in-patient anticoagulant treatment of thromboembolic disease, irrespective of underlying disease [11]. There were several limitations to our study, the major one of this study was undertaken in a small patient's population.

5. Conclusion

Although 5mg loading dose of warfarin is reasonable, 10mg loading dose is no associated with increased risk of bleeding. Age and gender do not seem to affect efficacy and safety of warfarin.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors report no conflicts of interest.

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