OPTIMAL MAINTENANCE DOSE OF WARFARIN IN PATIENTS WITH PROSTHETIC HEART VALVES IN KERMANSHAH, WEST OF IRAN

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Warfarin is a widely-used anticoagulant drug in clinical practice. However, its use is with caution due to serious side effects including gastrointestinal bleeding (up to 5%) and mortality (0.5% – 2.0%). Therefore, the correct dosing of warfarin is of paramount importance. We examined warfarin maintenance dose requirements in 115 outpatients in Kermanshah, North-West of Iran, who had a history of isolated aortic or mitral valve replacement and were on stable maintenance doses of warfarin with international normalized ratios (INR) of 2.0 – 2.5. The mean daily warfarin requirement was 4.6 ± 1.8 mg, with 75% of patients requiring < 5 mg/day. No significant difference was noted between the two sex groups; however, there was a noticeable decline in dose requirement by increasing age.

This study suggests that a relatively small dose (as low as 5 mg) of warfarin is required for maintaining anticoagulation in our patients.

Keywords: Anticoagulant • heart valve replacement • international normalized ratio • prothrombin time (PT) • warfarin

Introduction

Warfarin is the most widely-used drug for prophylactic and therapeutic options of venous and arterial thrombosis and in patients with prosthetic heart valves.1

Despite many efforts to improve anticoagulant treatment based on moves to standardize the prothrombin time (PT), the relatively high incidence of hemorrhagic events (up to 5%), puts these patients in a high-risk group for treatment-induced mortality (0.5% – 2.0%) and morbidity.1 Therefore, the correct dosing of warfarin is of paramount importance in regard to the drug efficacy and safety.

Some studies, especially those conducted in western countries, indicate that patients’ requirement for an international normalized ratio (INR) of 1.8 – 3, is generally 5 – 10 mg/day of warfarin. Many factors make these patients respond differently and, although it has been reported that a racial background or local geographical variables are important determinants of average warfarin dosage,2 – 4 little is known about Iranians regarding this matter.

The objective of the present study was to determine the optimal dose of warfarin according to PT and INR in patients with prosthetic heart valves in Kermanshah, North-West of Iran.

Patients and Methods

In a descriptive study, we examined warfarin dose requirements and their determinants in 115 outpatients on stable maintenance doses of warfarin with an INR of 2.0 – 2.5. All of the patients had either mitral or aortic prosthetic valves and they had been using warfarin for at least two months prior to enrollment into the study.

The patients were classified into four age
Optimal maintenance dose of warfarin

Table 1. Warfarin dosage (mg) based on sex

<table>
<thead>
<tr>
<th>Sex</th>
<th>n</th>
<th>Mean ± SD</th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>33</td>
<td>5.4 ± 2.0</td>
</tr>
<tr>
<td>Female</td>
<td>82</td>
<td>4.5 ± 1.81</td>
</tr>
<tr>
<td>Total</td>
<td>115</td>
<td>4.6 ± 1.9</td>
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</tbody>
</table>

groups: < 35, 36 – 44, 45 – 54, and > 55 yr. There were at least 25 patients in each age group.

All data were expressed as mean ± SD. The significance of the difference between variables was assessed using the Student's t-test and one way analysis of variance (ANOVA).

Results

A total of 115 patients including 82 women (20 – 47 yr) and 33 men (25 – 70 yr) were studied.

The mean ± SD warfarin requirement for these patients was 4.6 ± 1.8 mg. There was no significant difference between the two sex groups (Table 1).

There was a noticeable decline in the dose requirement between those aged < 35 and those > 55 years (Table 2).

The mean warfarin requirement in half of the patients was 4 (range: 2 – 4) mg/day and in 75% of patients this dose requirement was < 5 (range: 2 – 5) mg/day (Table 3).

Discussion

This study suggests that although the mean warfarin maintenance requirement in our patients is around 5 mg/day, the mean warfarin dose of 4 mg is optimal in 50% of patients. The study also suggests that, in the majority of patients (75%), a dose of < 5 mg/day is sufficient in achieving an INR of 2.0 – 2.5. In some studies from the United Kingdom and the United States, patients generally required 4 – 6 mg/day of warfarin to achieve an INR of 1.8 – 3. In a study from the UK by James et al, a small number of patients (5%) were even prescribed a dose of 10 mg or greater.

Meanwhile, as far as the dose requirement of warfarin was concerned, there was no significant difference between the two sex groups. However, age seemed to be an important factor in the maintenance dose requirement as warfarin requirement fell with increasing age, especially from the fifth decade of life. These results coincide with the findings from some other studies. On the other hand, some reports have indicated a possible ethnic basis for low warfarin requirements—3 mg in Chinese and 2.4 mg in Hong Kong populations.

To determine the optimal dosage of warfarin in Kermanshah population larger studies are needed.

References