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A Comparison of the Efficacy of Acenocoumarol and Warfarin in valve-replaced patients with Rheumatic Heart Disease

[1]Dr. Indranil Ray, [2]Prof.(Dr.) Ananya Chakraborty, [3]Dr. Eippa Matthan Kovoor, [4]Dr. Durga Prasad Reddy, [5]Dr Ankita Roy
[2]Medical Officer, West Bengal Health Service
[2,4]Professor and Head, [3]Ex. Associate Professor, [5]Post Graduate Trainee,
[2,3,5]Department of Pharmacology, [4]Department of Cardio-Thoraco- Vascular Surgery
[2,3,4]Vydehi Institute of Medical Sciences and Research Centre
[5]KPC Medical College and Hospital

***Corresponding Author:**
Dr. Ankita Roy
Post Graduate Trainee, Department of Pharmacology, KPC Medical College and Hospital

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Abstract

Background and Objectives

Rheumatic heart disease (RHD) damages heart valves requiring mechanical valve replacement entailing lifelong anticoagulation for which acenocoumarol or warfarin are often used. This study aimed to compare the efficacy of these two drugs in such patients.

Methods

It was a randomized, prospective, open-label, comparative study conducted among Cardio-Thoraco-Vascular Surgery (CTVS) inpatients and outpatients at Vydehi hospital, Bengaluru, from January to December, 2017, in 60 participants (30 per group). The participants were followed up monthly, for 3 months, to assess efficacy (PT & INR - target range 2 to 3.5).

Results

Comparing INR values of 1st, 2nd and 3rd months between study groups yielded p values of 0.568, 0.386 and 1.000 respectively. On comparing dose adjustments of 1st, 2nd and 3rd months, respective p values were 1.000, 0.476 and 0.353. Bleeding (ecchymosis, epistaxis, hematuria and g.i bleeding), alopecia, dermatitis, malaise and chest, leg and thigh, pain were the ADRs noted. Among 12 participants (24.48%) 7 receiving acenocoumarol (28%) and 5 assigned warfarin (20.83%), developed ADRs.

Interpretation & Conclusion

A comparison of severity of ADRs between groups, revealed superiority of acenocoumarol. ADRs were mild or moderate with warfarin but only mild for acenocoumarol.

Keywords: Rheumatic valvular heart disease; mechanical heart-valve replacement operation; oral anticoagulants; International Normalized Ratio.

Introduction

Rheumatic valvular heart disease is a long term sequela of rheumatic fever and also it's the most common cause is rheumatic fever worldwide. Prevalence of rheumatic valvular heart disease is 15.7 million persons, worldwide. Acute rheumatic fever (ARF) is believed to be an autoimmune disease following group A streptococcus infection, with multisystem involvement. Unless preventive measures are taken, episodes of ARF can recur in same person.

Its recurrence increases the chances of damaging the heart valves – called rheumatic heart disease (RHD).[1]

RHD primarily affects the mitral valve (in approximately 2/3 rd. of patients) & secondarily affects the aortic valve (in approximately 1/3 rd. of patients). Patients with valvular heart disease (VHD), with prosthetic heart valves (PHV) or with other comorbid conditions, are at high risk for thromboembolic complications & often require antithrombotic medications. Prothombin time (PT) guides treatment and varies across the world and among laboratories. Standardized PT is signified by International Normalized Ratio (INR). The therapeutic target range of INR for mechanical heart valve – should be maintained between 2 and 3.5.[1]

For management of ARF: NSAIDS (prevent progression to the stage of polyarthritis from initial disease stage), bed rest, fluid restriction, cardiac medications, echocardiography, cardiology assessment, diuretics, ACE inhibitors etc. are required. [2, 3]

Vitamin K antagonist Warfarin is the drug of choice as anticoagulation in prosthetic heart valves patients with both rheumatic and non-rheumatic valve disease. Diet affects the absorption of warfarin, so INR must be measured regularly, with adjustments of the dose as necessary. Newer anticoagulants (like Dabigatran) inhibit thrombin or activated factor X dose-dependently, but safety and efficacy of these drugs are still being studied and they are currently not recommended in patients with prosthetic valves.[2]

Acenocoumarol is more efficacious than warfarin and maintains INR within the therapeutic target range (TTR). Vitamin K antagonists like acenocoumarol and warfarin are preferred in India for oral anticoagulation.[4, 5]

Till date, there have been few comparative studies on the efficacy of Acenocoumarol and Warfarin. Hence, this study was undertaken to compare the efficacy of Acenocoumarol and Warfarin in valve replaced patients for Rheumatic heart disease.

Objective

To assess and compare the efficacy of Acenocoumarol and Warfarin in valve replaced patients with Rheumatic heart disease.

Materials And Methods

Source of data:

The study was conducted by the Department of Pharmacology in collaboration with Department of Cardio-Thoraco-Vascular Surgery (CTVS) .

Approval:

This study was approved by the Institutional Ethics Committee.

Study design :

This was a randomized, prospective, open label, comparative study.

Sample size:

Each study group included 30 participants. Total sample size was 60.

The participants were included in this study after obtaining written informed consent.

Inclusion criteria:

1. Age in between 18-60 years.
2. Aortic valve replaced patients for Rheumatic heart disease.
3. Mitral valve replaced patients for Rheumatic heart disease.
4. Double valve replaced patients for Rheumatic heart disease.
5. Patient undergone valve replacement surgery where mechanical valve prosthesis used.
6. Patient who are willing to provide full written informed consent.

Exclusion criteria:

1. Patient undergone any combined Cardio-Thoraco-Vascular Surgery procedure including Valve replacement surgery.
2. Patient with history of hypersensitivity to either drugs.
3. Patient with previous history of embolic episode or hemorrhagic tendency.

Methodology:

Each group comprised of 30 participants.

Group 1 or group A: Tablet Acenocoumarol, 1-4mg/day/oral for 3 months.

Group 2 or group B: Tablet Warfarin, 1-5mg/day/oral for 3 months.

Volume 8, Issue 5; September-October 2025; Page No 206-211

The initial & continuous doses of the drug was decided on the value of Prothombin time (P-time) & International normalized ratio (INR).

The participants were followed up monthly after starting the drug, for 3 months. Total study duration was 1 year. Venipuncture for blood study was done.

Outcome Measure:

Efficacy of both Warfarin and Acenocoumarol:-by testing;

1) Value of Prothombin time monthly (every month) for 3 months;
2) Value of International normalized ratio monthly (every month) for 3 months.

Statistical analysis:

Data collected were entered on Microsoft Office for Windows 2007 excel spread sheet. The baseline data like demography (IP/hospital number, age, sex etc.), efficacy, The categorical variables were compared using Chi-square test. Comparison of continuous variables between groups was carried out using Independent sample t- test (or unpaired student's t-test). Statistical significance was set at $p<0.05$.

Sample Size

Sample size was calculated by mean difference ($\sigma_{\bar{x}}$), pooled standard deviation (SP^2), standard deviation in group 1 (S_1^2), standard deviation in group 2 (S_2^2), power, scores in terms of standard deviation from their means (Z), precision (d) and significance level (α) of previous study.

$$n = \frac{Z^2_{(1-\alpha/2)}(2Sp^2)}{\alpha^2}; \quad Sp2 = (S_1^2 + S_2^2)/ d^2.$$

By this formula n = 22 in each group.

In this study each group was comprise 30 study subjects. The calculated sample size came to 22 in each group but, considering dropouts during the study a total of 30 subjects were enrolled in each group.

Results

60 participants were recruited for the study as per the protocol. 30 participants received Acenocoumarol (group A) and 30 participants received Warfarin (group B) according to randomization. 5 participants lost follow up in group A and 6 participants lost follow up in group B. So, remaining total 49 participants (81.66%) completed the study. 25 participants completed the study in group A (received Acenocoumarol) and 24 participants completed the study in group B (received Warfarin).

In group A (received Acenocoumarol) out of 30 participants, highest age was 58 years and lowest age was 22 years. In group B (received Warfarin) out of 30 participants, highest age was 60 years and lowest age was 20 years.

Out of 25 participants completed the study in group A (received Acenocoumarol) mean age ± SD was 44.44 ± 11.787; minimum age was 22 and maximum age was 58. Out of 24 participants completed the study in group B (received Warfarin) mean age ± SD was 37.71 ± 11.830; minimum age was 20 and maximum age was 60.

Mitral stenosis (MS), mitral regurgitation (MR), aortic stenosis (AS) and aortic regurgitation (AR) were the various diagnosis.(Table 1)

Total 207 numbers PT and total 207 numbers of INR were recorded. (Table 2)

The therapeutic target range (TTR) of INR values was between 2 and 3.5. Total number of INR values, recorded in both the groups, were evaluated as less than 2, between 2 and 3.5 and More than 3.5.(Table 3)

When INR values of 1st, 2nd and 3rd month were compared in both the study groups or between Acenocoumarol group and Warfarin group, all the p values were more than 0.05, so not significant. Statistical significance was set at $p<0.05$.

When 1st month INR values were compared in both groups p value was 0.568; so not significant.

When 2nd month INR values were compared in both groups p value was 0.386; so not significant.

When 3rd month INR values were compared in both groups p value was 1.000; so not significant.

So, both the drugs Acenocoumarol and Warfarin were equally efficacious.(Table 4,5,6)

Discussion

In present study, dose range of tablet Acenocoumarol was 1 to 4 mg orally and dose range tablet Warfarin was 1 to 5 mg orally. In other study conducted by

Volume 8, Issue 5; September-October 2025; Page No 206-211

Ghufran et al, same dose range was used for Acenocoumarol and Warfarin.[6]

In this study, for statistical analysis, chi-square test was used for comparing two groups (group A received Acenocoumarol and group B received Warfarin). This is comparable to a study done by Kulo et al, in which therapeutic INR values were compared among groups using the chi-square test.[7]

venipuncture for blood study was done for measuring INR, to compare the efficacy of Acenocoumarol and Warfarin. This findings are similar in other study by Kulo et al, in which the blood samples were taken by the venipuncture for measuring INR, to evaluate quality of treatment between warfarin and acenocoumarol groups.[7]

When INR values of 1st, 2nd and 3rd month were compared in both the study groups or between Acenocoumarol group and Warfarin group, p values were 0.568, 0.386 and 1.000 respectively; all the p values were more than 0.05, so not significant. This findings are similar in other study by Aida Kulo et al, in which no significant differences in the overall quality of the treatment in warfarin and acenocoumarol group were found, expressed by percentage of therapeutic INR values (51.77% vs. 53.62%, P = 0.548).[7]

Merits

This study is among the few studies evaluating the efficacy and safety profile Acenocoumarol and Warfarin in valve replaced patients with Rheumatic Heart Disease.

This study assessed multiple parameters like efficacy and safety profile of both oral anticoagulants.

Limitations

This was an open labelled randomised study. A double blind randomised study would have been better. The sample size was small because of time constraint. The study could have been done with a larger sample size. Longer duration of study will add more value. Follow up beyond 3 months would have been better to check efficacy more precisely.

Conclusion

The study therefore concluded that Acenocoumarol and Warfarin are equally efficacious.

This study showed that Vitamin K antagonists (VKAs) like Acenocoumarol or Warfarin must be administered as oral anticoagulants, after heart valve replacement surgery, in post-operative patients and both Acenocoumarol and Warfarin are equally effective in maintaining INR within therapeutic target range.

Counselling of patients by physicians on dietary habits & adherence to drugs can maintain INR within therapeutic target range and ensure patients' safety.

References

1. Fuster V, Harrington RA, Narula J, Eapen ZJ, editors. Hurst's the heart. Vol. 2. 14th ed. New York: McGraw-Hill; 2017.
2. Carapetis JR, Beaton A, Cunningham MW, Guilherme L, Karthikeyan G, Mayosi BM. Acute rheumatic fever and rheumatic heart disease. DISEASE PRIMERS. 2016;2:1-24.
3. Cilliers, A., Manyemba, J., Adler, A. J. & Saloojee, H. Anti-inflammatory treatment for carditis in acute rheumatic fever. Cochrane Database Syst. Rev. 2015;6(5):1-56.
4. Trailokya A. Role of patient education and counseling in Acenocoumarol management. InternMed. 2016;6(1):1-4.
5. Gopalakrishnan S. Oral Anticoagulants: Current Indian Scenario. Journal of the association of physicians of india. 2013;62:410-3.
6. Bryk AH, Plens K, Undas A. Prediction of unstable anticoagulation with acenocoumarol versus warfarin in atrial fibrillation. Cardiology Journal. 2017;24(5):477-83.
7. Kulo A, Kusturica J, Kapić E, Bečić F, Todić MR, Ristić LB, et al. Better stability of acenocoumarol compared to warfarin treatment in one-year observational, clinical study in patients with nonvalvular atrial fibrillation. Med Glas Ljek komore Zenicko-doboj kantona. 2011;8(1):9-14.

Table 1: Diagnosis wise distribution of participants in both the groups

Volume 8, Issue 5; September-October 2025; Page No 206-211

Diagnosis	Number of total subjects (n=60)	Number of subjects in Acenocoumarol group (n=30)	Number of subjects in Warfarin group (n=30)
MS, MR, AS and AR	14 (23.33%)	6 (20%)	8 (26.66%)
MS and MR	29 (46.66%)	17 (56.66%)	12 (40%)
AS and AR	17 (30%)	7 (23.33%)	10 (33.33%)

Table 2: Numbers of PT and INR recorded in both the groups

Time	Total numbers recorded in both groups		Numbers recorded in Acenocoumarol group		Numbers recorded in Warfarin group	
	PT	INR	PT	INR	PT	INR
Before Starting the drug	60	60	30	30	30	30
At 1st month	49	49	25	25	24	24
At 2nd month	49	49	25	25	24	24
At 3rd month	49	49	25	25	24	24

Table 3: INR values recorded in both the groups

INR values	In Acenocoumarol group (out of total 105 INR values)	In Warfarin group (out of total 102 INR values)
Less than 2	62 (59.04%)	71 (69.60%)
2 – 3.5	31 (29.52%)	25 (24.50%)
More than 3.5	12 (11.42%)	6 (5.88%)

Table 4: INR values recorded in both the groups at 1st month

INR values	In Acenocoumarol group (out of total 25 INR values)	In Warfarin group (out of total 24 INR values)
Less than 2	11 (44%)	15 (62.5%)
2 – 3.5	8 (32%)	6 (25%)
More than 3.5	6 (24%)	3 (12.5)

Table 5: INR values recorded in both the groups at 2nd month

Volume 8, Issue 5; September-October 2025; Page No 206-211

INR values	In Acenocoumarol group (out of total 25 INR values)	In Warfarin group (out of total 24 INR values)
Less than 2	14 (56%)	18 (75%)
2 – 3.5	8 (32%)	5 (20.83%)
More than 3.5	3 (12%)	1 (4.16%)

Table 6: INR values recorded in both the groups at 3rd month (For deciding continuous dose)

INR values	In Acenocoumarol group (out of total 25 INR values)	In Warfarin group (out of total 24 INR values)
Less than 2	12 (48%)	10 (41.66%)
2 – 3.5	12 (48%)	13 (54.16%)
More than 3.5	1 (4%)	1 (4.16%)

Volume 8, Issue 5; September-October 2025; Page No 206-211