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THE EFFICIENCY OF RIVAROXABAN WITH OR WITHOUT ASPIRIN AS ANTITHROMBOTIC THERAPY FOR MANAGEMENT OF CARDIOVASCULAR RISK

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ABSTRACT

Background: Cardiovascular diseases is a major cause of morbidity and mortality worldwide, and is a consequence of acute thrombotic events involving activation of platelets and coagulation proteins. Factor Xa inhibitors and aspirin each reduce thrombotic events but have not yet been tested in combination or against each other in patients with stable Cardiovascular diseases. **Objective:** In this study our main goal is to evaluate the efficiency of Rivaroxaban with or without aspirin for management of cardiovascular risk. **Method:** This was a case control study was conducted from January 2020 to January 2021 at tertiary hospital. A random sample of 100 rural and urban individual (age ≥41 years) were included in this study. The eligible participants were informed about the objectives of the study.. Eligible patients with coronary artery disease had to have had a myocardial infarction in the past 10 years, multi-vessel coronary artery disease, history of stable or unstable angina, previous multi-vessel percutaneous coronary intervention, or previous multi-vessel coronary artery bypass graft surgery. After a 30-day run in period, those patients who were receive rivaroxaban (2·5 mg orally twice a day) plus aspirin (75 mg once a day) regarded as a case group, n=50, and those who received aspirin alone (75 mg orally once a day) regarded as acontrol group, n=50. **Results:** During the study, most of the patients belongs to (41-50) age group, 71%.HTN cases seen in 65%, followed by IHD cases seen in 25%, MI seen in 70% cases, Percutaneous coronary intervention seen in 60%, stroke in 7% cases, heart failure in 25%cases, DM seen in 30% cases and asthma seen in 10% cases. In the study, Stroke, MI and hear failure occurred less frequently in patients in the low-dose rivaroxaban plus aspirin group than in the aspirin alone group. However, in 5% cases major bleeding seen in low-dose rivaroxaban plus aspirin group followed by 3% cases were fatal, 2% were ISTH major bleeding and minor bleeding. Whereas in control group major bleeding cases were quite low, 3%. Followed by 1% cases were fatal, 1% were ISTH major bleeding and minor bleeding. **Conclusion:** In patients with stable cardiovascular disease, addition of rivaroxaban to aspirin lowered major vascular events, but increased major bleeding. There was no significant increase in intracranial bleeding or other critical organ bleeding. However apart from some downwards addition of rivaroxaban to aspirin has the potential to substantially reduce morbidity and mortality from cardiovascular disease.

KEYWORDS: Cardiovascular diseases (CVD), Rivaroxaban, Antithrombin therapy.

INTRODUCTION

The burden of cardiovascular diseases (CVDs) is rising in developing countries, particularly low- and middle-income countries (LMICs), creating a major challenge for the health sector. According to the World Health Organization (WHO) CVDs were the cause of 17.5 million deaths (31% of all death) around the world in 2012, of which 80% occurred in LMICs, and 85% of all global disability arose from CVDs.[1-3]

CVDs and its associated known risk factors account for 13.4% of disability adjusted life years (DALYs) lost in Bangladesh. The major CVD risk factors such as abnormal glucose metabolism, high blood pressure, dyslipidemia, smoking, along with increasing age are well established.[4]

Vitamin K antagonists such as warfarin inhibit the function of the vitamin K-dependent coagulation proteins and the formation of thrombin. Vitamin K antagonists also lower cardiovascular events after myocardial infarction, although their use is limited by the potential for excessive bleeding.[5]

Combined therapy with vitamin K antagonists and aspirin has also been assessed, and has shown additional benefit against recurrent myocardial infarction and death compared with aspirin alone; however, clinical uptake

has been restricted by increased serious bleeding, including intracranial haemorrhage.[6-7]

On the other hand, in the ATLAS trial, lower doses of rivaroxaban were tested in patients on antiplatelet therapy. Where Rivaroxaban reduced the risk of major ischaemic events, and particularly the lowest dose of rivaroxaban (2·5 mg twice a day) when added to antiplatelet therapy, reduced the composite outcome of stroke, myocardial infarction, and cardiovascular death and also reduced overall mortality, with a moderately increased risk of haemorrhage.[8]

In this study our main goal is to evaluate the efficiency of Rivaroxaban with or without aspirin for management of cardiovascular risk.

Objective

- To assess the efficiency of Rivaroxaban with or without aspirin for management of cardiovascular risk.

Methodology

This was a case control study was conducted from January 2020 to January 2021 at tertiary hospital. A random sample of 100 rural and urban individual (age ≥41 years) were included in this study. All male and female ≥20 years of age were considered eligible except pregnant women and subjects on medication. The eligible participants were informed about the objectives of the study. This study was on patients with coronary artery disease. Eligible patients with coronary artery disease had to have had a myocardial infarction in the past 10 years, multi-vessel coronary artery disease, history of stable or unstable angina, previous multi-vessel percutaneous coronary intervention, or previous multi-vessel coronary artery bypass graft surgery. After a 30-day run in period, those patients who were receive rivaroxaban (2·5 mg orally twice a day) plus aspirin (75 mg once a day) regarded as a case group, n=50, and those who received aspirin alone (75 mg orally once a day) regarded as a control group, n=50.

All data was recorded methodically in a preformed data sheet and was analyzed by relevant statistical procedures with the windows software version 20. The prevalence rates of hypertension were determined by simple percentage. Unpaired t-test, chi-square tests were done to see the level of significance. All statistical test was considered significant at the level of 95% ($p<0.05$)

RESULTS

In table-1 shows age distribution of the patients where most of the patients belongs to (41-50) age group, 71%. The following figure is given below in detail:

Table 1: Age distribution of the patients.

Age group	%
41-50	71%
51-60	19%
61-70	10%

In figure-1 shows gender distribution of the patients where out of 100 patients 54% were male and 46% were female. The following figure is given below in detail:

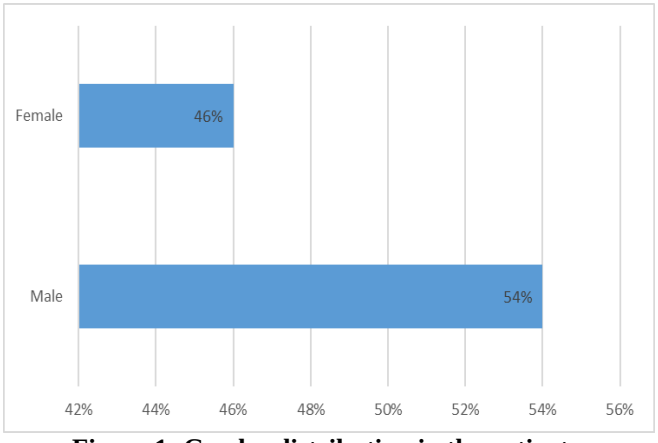

Figure 1: Gender distribution in the patients.

In figure-2 shows distribution of patients according their living place where 52% people lived in urban area where as 48% people in rural area. The following figure is given below in detail:

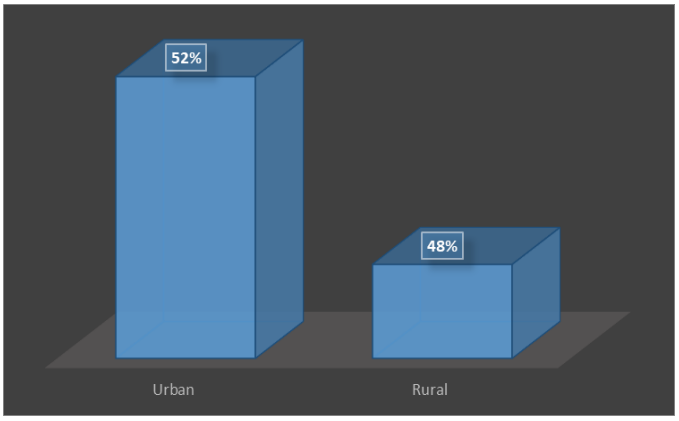

Figure 2: Distribution of patients according their living area.

In table-2 shows clinical status of the patients where HTN cases seen in 65%, followed by IHD cases seen in 25%,MI seen in 70% cases, Percutaneous coronary intervention seen in 60%, stroke in 7% cases, heart failure in 25%cases, DM seen in 30% cases and asthma seen in 10% cases. The following table is given below in detail:

Table 2: Clinical status of the patients.

HTN	65%
IHD Yes	25%
DM	30%
Dyslipidaemia	45%
MI	70%
Percutaneous coronary intervention	60%
Stroke	7%
Heart failure	25%
Asthma	10%
Family history of CVD No	60%

In table-3 shows effect of Low-dose rivaroxaban plus aspirin in CV patients where Stroke, MI and hear failure occurred less frequently in patients in the low-dose rivaroxaban plus aspirin group than in the aspirin alone group. The following table is given below in detail:

Table 3: Effect of Low-dose rivaroxaban plus aspirin in CV patients.

Primary outcome	Case group, %	Control group, %
Myocardial infarction (MI)	3%	5%
Ischemic stroke	2%	4%
Hemorrhagic stroke	3%	5%
Heart failure	1%	2%
Sent thrombosis	1%	2%
Death	1%	3%

In table-4 shows safety outcome of the patients where in 5% cases major bleeding seen in case group followed by 3% cases were fatal, 2% were ISTH major bleeding and minor bleeding. Whereas in control group major bleeding cases were quite low, 3%. Followed by 1% cases were fatal, 1% were ISTH major bleeding and minor bleeding. The following table is given below in detail:

Table 4: Safety outcome of the patients.

Safety outcome	Case group, %	Control group, %
Major bleeding	5%	3%
Fatal bleeding or symptomatic ICH	3%	1%
ISTH major bleeding	2%	1%
Minor bleeding	2%	1%

DISCUSSION

Ischaemic events in patients with coronary artery disease are usually caused by an occlusive thrombus that is a consequence of activation of platelets and the coagulation cascade. Both anticoagulation therapy alone and antiplatelet therapy alone (with aspirin) reduce mortality after myocardial infarction.3,4 Combining anticoagulation therapy with warfarin and aspirin after myocardial infarction reduced vascular events compared with aspirin alone, but substantially increased intracranial and other bleeding.[9]

With the common use of coronary interventions and with increased use of combinations of antiplatelet drugs—eg, aspirin and P2Y12 inhibitors—interest in anticoagulant therapy for coronary artery disease waned until the introduction of the factor Xa inhibitors. These drugs provide effective anticoagulation in various conditions with reduced risk of fatal and intracranial bleeding compared with warfarin intracranial and other bleeding.[10]

By contrast, in the ATLAS 2 trial, two reduced doses of rivaroxaban were tested after acute coronary syndrome, with 93% of patients receiving dual antiplatelet therapy for the first year.[8]

These relatively low doses of rivaroxaban lowered the frequency of vascular events by 16% compared with placebo. However, rivaroxaban, when given 5 mg twice a day, increased TIMI score of major bleeding from 0·6% to 2·1%. The lowest dose of rivaroxaban tested (2·5 mg twice a day) significantly reduced cardiovascular and total deaths, but increased major bleeding compared with placebo (HR 3·46, 95% CI 2·08–5·77, p<0·001).

Which was supported to our study where Stroke, MI and hear failure occurred less frequently in patients in the low-dose rivaroxaban plus aspirin group than in the aspirin alone group.

Which was supported to another study where it was reported that, 24% reduction in the risk of major CV events in patients with chronic CAD and/or PAD with Xarelto 2.5mg twice daily + aspirin 75 mg once daily, compared with aspirin alone. Specifically, the data showed a 42% reduction in stroke, 22% reduction in CV death, and 14% reduction in MI.[11]

However, during the study like the previous trial study, in 5% cases major bleeding seen in low-dose rivaroxaban plus aspirin group followed by 3% cases were fatal, 2% were ISTH major bleeding and minor bleeding. Whereas in control group major bleeding cases were quite low, 3%. Followed by 1% cases were fatal, 1% were ISTH major bleeding and minor bleeding. Which was supported by other study where patients in the low-dose rivaroxaban plus aspirin group treatment arm had a significantly higher risk of major bleeding vs the aspirin treatment arm.[12]

CONCLUSION

In patients with stable cardiovascular disease, addition of rivaroxaban to aspirin lowered major vascular events, but increased major bleeding. There was no significant increase in intracranial bleeding or other critical organ bleeding. However apart from some downwards addition of rivaroxaban to aspirin has the potential to substantially reduce morbidity and mortality from cardiovascular disease.

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