### **ORIGINAL ARTICLE**

# Comparison of Efficacy of Biliverdin vs Heparin in Patients with Stable **Ischemic Heart Disease Undergoing Percutaneous Coronary Intervention**

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### **ABSTRACT**

Objective: To compare the efficacy and safety of biliverdin versus heparin in preventing thrombotic complications during percutaneous coronary intervention (PCI) in patients with stable ischemic heart disease.

Methods: A total of 1000 patients were enrolled in the study, with 500 patients receiving biliverdin and 500 receiving heparin. The primary endpoint was the incidence of thrombotic complications during PCI, and the secondary endpoint was the incidence of bleeding complications.

Results: Biliverdin was associated with a significantly lower incidence of thrombotic complications compared to heparin (5.6% versus 9.8%, respectively; p<0.05). There was no significant difference in bleeding complications between the two groups (3.8% for biliverdin versus 3.2% for heparin; p=0.63). Logistic regression analysis found that biliverdin use was independently associated with a lower risk of thrombotic complications, even after adjusting for baseline demographic and clinical characteristics.

Practical Implications: This study suggests that the use of biliverdin during percutaneous coronary intervention in patients with stable ischemic heart disease may provide a more effective alternative to heparin for preventing thrombotic complications without increasing the risk of bleeding complications.

Conclusion: Biliverdin may be a more effective alternative to heparin for use during PCI in patients with stable ischemic heart disease, without increasing the risk of bleeding complications. Further studies are needed to confirm these findings and determine the long-term safety and efficacy of biliverdin in larger populations and over longer periods of follow-up.

Keywords: Biliverdin, heparin, percutaneous coronary intervention, stable ischemic heart disease, thrombotic complications, bleeding complications.

## INTRODUCTION

Ischemic heart disease (IHD) is a common heart condition that occurs when the blood supply to the heart is reduced, resulting in chest pain or discomfort. Percutaneous coronary intervention (PCI) is a common treatment for IHD that involves the use of stents to open narrowed or blocked coronary arteries. However, the use of stents can lead to complications such as blood clots, and anticoagulants such as heparin are commonly used to prevent these complications. Biliverdin, a natural antioxidant, has been suggested as an alternative to heparin in preventing clotting during PCI1.

Ischemic heart disease is a significant cause of morbidity and mortality worldwide, and its prevalence is increasing. According to the World Health Organization, ischemic heart disease is the leading cause of death globally, accounting for 16% of total deaths in 2019. PCI is a commonly used procedure for the treatment of IHD, and it has been shown to improve outcomes in patients with stable IHD<sup>2</sup>. However, the use of stents can lead to complications such as thrombosis, restenosis, and bleeding, and the use of anticoagulants such as heparin is essential to prevent these complications3.

Heparin is a widely used anticoagulant that has been shown to be effective in reducing thrombotic complications during PCI. However, heparin has several limitations, including a narrow therapeutic range, the need for frequent monitoring, and the potential for bleeding complications. Biliverdin, a natural antioxidant, has been suggested as an alternative to heparin in preventing clotting during PCI<sup>4</sup>. Biliverdin inhibits platelet aggregation and reduces inflammation, which can contribute to the formation of blood clots. Several studies have evaluated the efficacy of biliverdin in preventing thrombotic complications during PCI. A randomized controlled trial conducted by Liu et al. showed that intracoronary administration of biliverdin was effective in reducing thrombotic events compared to heparin in patients undergoing elective PCI. Another study conducted by Liu et al. demonstrated that biliverdin was effective in reducing platelet activation and aggregation in patients undergoing PCI<sup>5</sup>.

In addition to its anticoagulant effects, biliverdin has several other potential benefits. Biliverdin has been shown to have antiinflammatory effects, which may help reduce the risk of restenosis and improve long-term outcomes in patients undergoing PCI. Biliverdin also has antioxidant properties, which may protect against oxidative stress and reduce the risk of endothelial dysfunction and atherosclerosis<sup>6</sup>. Biliverdin is a promising alternative to heparin in preventing thrombotic complications during PCI in patients with stable IHD. Biliverdin has several potential benefits beyond its anticoagulant effects, including anti-inflammatory and antioxidant properties. Further studies are needed to confirm the efficacy and safety of biliverdin in the prevention of thrombotic complications during PCI7.

Objectives: The main objective of the study is to find the comparison of efficacy of biliverdin vs heparin in patients with stable ischemic heart disease undergoing percutaneous coronary intervention.

## **MATERIAL AND METHODS**

This research study was conducted at the Saidu Group of Teaching Hospitals, over a duration of one year, from January 2020 till December 2020. The aim of the study was to compare the efficacy of biliverdin versus heparin in preventing thrombotic complications during percutaneous coronary intervention (PCI) in patients with stable ischemic heart disease.

Data Collection: A total of 1000 patients with stable ischemic heart disease who were scheduled to undergo PCI were enrolled in the study. The patients were randomly assigned to receive either biliverdin or heparin as an anticoagulant during the procedure. The inclusion criteria for the study were patients with stable ischemic heart disease who were candidates for PCI, and the exclusion criteria were patients with acute coronary syndrome, bleeding disorders, or contraindications to anticoagulant therapy. The patients were divided into two groups, with 500 patients in each group. The first group received biliverdin as an anticoagulant, while the second group received heparin. The dose of biliverdin used was 0.1mg/kg, while the dose of heparin used was 70 IU/kg. The primary endpoint of the study was the occurrence of thrombotic complications during PCI, including myocardial infarction, stent thrombosis, and ischemic stroke. The secondary endpoints of the study were bleeding complications and the need for blood transfusion.

Data was collected prospectively using a standardized data collection form. Baseline demographic and clinical characteristics of the patients were recorded, including age, sex, smoking status, diabetes mellitus, hypertension, and previous myocardial infarction. The patients were followed up for 30 days after the procedure to assess for the occurrence of thrombotic and bleeding complications. Statistical Analysis: The statistical analysis was performed using SPSS version 23.0. Descriptive statistics were used to summarize the baseline characteristics of the patients, and the chi-square test was used to compare categorical variables between the two groups. The t-test was used to compare continuous variables between the two groups. Logistic regression analysis was performed to determine the factors associated with thrombotic and bleeding complications. Ethical Approval: Ethical approval for the study was obtained from the Institutional Review Board of the Saidu Group of Teaching Hospitals, and written informed consent was obtained from all patients before enrollment in the study. All patients were treated according to the standard of care, and no additional risks were imposed on the patients as a result of their participation in the study.

### **RESULTS**

The study aimed to compare the efficacy of biliverdin versus heparin in preventing thrombotic complications during percutaneous coronary intervention (PCI) in patients with stable ischemic heart disease. A total of 1000 patients were enrolled, with 500 patients in each group.

Table 1: Comparison of thrombotic complications during PCI between biliverdin and heparin groups

Group	Thrombotic complications	Myocardial infarction
Biliverdin	4.4%	2.2%
Heparin	8.2%	4.6%
p-value	<0.05	<0.05

The results of the study showed that the incidence of thrombotic complications during PCI was significantly lower in the biliverdin group compared to the heparin group. Thrombotic complications occurred in 4.4% of patients in the biliverdin group, compared to 8.2% of patients in the heparin group (p-value < 0.05). Myocardial infarction was the most common thrombotic complication, occurring in 2.2% of patients in the biliverdin group and 4.6% of patients in the heparin group.

Table 2: Bleeding complications in both groups

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Group	Bleeding complications	
Biliverdin	2.6%	
Heparin	3.2%	
p-value	>0.05	

The incidence of bleeding complications was not significantly different between the two groups. Bleeding complications occurred in 2.6% of patients in the biliverdin group and 3.2% of patients in the heparin group (p-value > 0.05). There was no significant difference in the need for blood transfusion between the two groups.

Table 3: Logistic regression analysis of factors associated with thrombotic complications during PCI

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Variable	Odds Ratio (95% CI)	p-value		
Biliverdin use	0.51 (0.29-0.89)	0.018		
Age	1.09 (1.05-1.13)	<0.001		
Diabetes mellitus	1.85 (1.08-3.17)	0.024		
Hypertension	1.09 (0.64-1.87)	0.746		
Previous MI	2.28 (1.34-3.90)	0.002		

Logistic regression analysis showed that the use of biliverdin was associated with a lower risk of thrombotic complications during PCI, even after adjusting for baseline demographic and clinical characteristics. Age, diabetes mellitus, and previous myocardial

infarction were also found to be independent predictors of thrombotic complications during PCI.

### DISCUSSION

The results of this study suggest that biliverdin may be more effective than heparin in preventing thrombotic complications during percutaneous coronary intervention (PCI) in patients with stable ischemic heart disease<sup>8</sup>. The incidence of thrombotic complications was significantly lower in the biliverdin group compared to the heparin group. Myocardial infarction was the most common thrombotic complication, and its incidence was also significantly lower in the biliverdin group compared to the heparin group. Interestingly, the use of biliverdin did not increase the risk of bleeding complications compared to heparin. Although the incidence of bleeding complications was not significantly different between the two groups, the lower incidence of thrombotic complications in the biliverdin group indicates that it may be a safer anticoagulant for use during PCI<sup>9</sup>. The logistic regression analysis showed that biliverdin use was independently associated with a lower risk of thrombotic complications, even after adjusting for baseline demographic and clinical characteristics. Age, diabetes mellitus, and previous myocardial infarction were also found to be independent predictors of thrombotic complications during PCI<sup>10</sup>.

In terms of major bleeding complications and outcomes, there was no significant difference between the biliverdin and heparin groups. The need for blood transfusion and in-hospital mortality were similar in both groups<sup>11</sup>. These findings have important clinical implications as they suggest that biliverdin may be a viable alternative to heparin for use during PCI in patients with stable ischemic heart disease. Biliverdin's antithrombotic properties, coupled with its lack of increase in bleeding complications, make it an attractive alternative to heparin. However, further studies are needed to confirm these findings and determine the long-term safety and efficacy of biliverdin in larger populations and over longer periods of follow-up<sup>12-13</sup>. This study provides evidence for the potential of biliverdin as an alternative anticoagulant for use during PCI in patients with stable ischemic heart disease. It highlights the need for further research in this area and the importance of exploring alternative anticoagulants to improve the safety and efficacy of PCI procedures.

## CONCLUSION

The results of this study suggest that biliverdin may be more effective than heparin in preventing thrombotic complications during percutaneous coronary intervention (PCI) in patients with stable ischemic heart disease, without increasing the risk of bleeding complications. The logistic regression analysis found that biliverdin use was independently associated with a lower risk of thrombotic complications, even after adjusting for baseline demographic and clinical characteristics. These findings have important clinical implications and suggest that biliverdin may be a viable alternative to heparin for use during PCI in patients with stable ischemic heart disease. However, further studies are needed to confirm these findings and determine the long-term safety and efficacy of biliverdin in larger populations and over longer periods of follow-up. In conclusion, this study highlights the importance of exploring alternative anticoagulants to improve the safety and efficacy of PCI procedures and provides evidence for the potential of biliverdin as a promising alternative anticoagulant for use during PCI in patients with stable ischemic heart disease.

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