Journal of Arrhythmia 32 (2016) 154–155

Contents lists available at ScienceDirect

Journal of Arrhythmia

journal homepage: www.elsevier.com/locate/joa

Rapid firing

# Successful intraprocedural anticoagulation with bivalirudin during pulmonary vein isolation in a patient with known heparin-induced thrombocytopenia type II

Barbara Bellmann, MD*, Patrick Nagel, MD, Bogdan G. Muntean, MD

*Department of Cardiology, Charité Berlin, Campus Benjamin Franklin, Hindenburgdamm 30, 12203 Berlin, Germany*

ARTICLE INFO

*Article history:*
Received 7 September 2015
Received in revised form
8 October 2015
Accepted 9 October 2015
Available online 19 November 2015

*Keywords:*
Pulmonary vein isolation
Atrial fibrillation
Heparin induced thrombocytopenia type II
Bivalirudin
Activated clotting time

ABSTRACT

We report the case of a 56-year-old female who presented with symptomatic paroxysmal atrial fibrillation. Anamnestic heparin-induced thrombocytopenia (HIT) type II was suspected, and a rapid diagnostic test showed antibodies against platelet factor 4. The heparin-induced platelet activation-assay was negative. Radiofrequency pulmonary vein isolation with intraprocedural anticoagulation using bivalirudin was ultimately performed. Dosing was controlled by monitoring the activated clotting time. Post-procedural blood tests were normal. There were no thromboembolic or bleeding events. Bivalirudin is a therapeutic option for anticoagulation during pulmonary vein isolation procedures in patients with a history of HIT type II.



## 1. Case report

### 1.1. History

We report the case of a 56-year-old female who presented with symptomatic paroxysmal atrial fibrillation. Anamnestic heparin-induced thrombocytopenia (HIT) type II was suspected, and a HIT diagnostic test was performed. The initial diagnosis of HIT II was made in 2006. A rapid test showed antibodies against platelet factor 4. The heparin-induced platelet activation assay was negative. The patient was on oral Apixaban (5 mg 1-0-1) for anticoagulation, and also metoprolol (95 mg 1-0-1). Relevant history included single-vessel coronary disease with moderately reduced systolic pump function, and a stroke without residual symptoms. After extensive consideration, radiofrequency pulmonary vein isolation with intraprocedural anticoagulation using bivalirudin was ultimately performed.

### 1.2. Treatment and course

Laboratory parameters normalized after the patient was hospitalized (Table 1). Oral anticoagulation with Apixaban was stopped the day before the planned procedure. At the beginning of pulmonary vein isolation after transseptal puncture, bivalirudin was administered as a 0.75 mg/kg intravenous bolus, followed by a 1.75 mg/kg/h infusion. The activated clotting time was subsequently closely monitored. The values tended to be high, but the infusion rate was maintained (Table 2). The planned radiofrequency pulmonary vein isolation was performed successfully without complications after 3-dimensional mapping of the pulmonary veins and left atrium. There was no post-interventional pericardial effusion. Bivalirudin was stopped immediately after the final radiofrequency application. No bleeding or clotting events were noted. The laboratory values remained stable before and after ablation (Table 1). After ablation, a direct and uncomplicated conversion to oral anticoagulation with Apixaban (5 mg 1-0-1) was performed. The patient was discharged home on the third postoperative day.

### 1.3. Discussion

Bivalirudin is a direct thrombin inhibitor that overcomes many limitations seen with indirect thrombin inhibitors, such as heparin. It is a short, synthetic peptide that is a reversible inhibitor

* Correspondence to: Department of Medicine-Cardiology, Charité Berlin Campus Benjamin Franklin, Hindenburgdamm 30, 12203 Berlin, Germany. Tel.: +49 30 8445 4782; fax: +49 30 8445 4648.
*E-mail address:* barbara.bellmann@charite.de (B. Bellmann).

http://dx.doi.org/10.1016/j.joa.2015.10.004
1880-4276/

**Table 1**
The laboratory values remained stable before and after ablation. The laboratory test results are consistently normal values without abbreviations.

| | One day before ablation | One day after ablation | Three days after ablation |
|---|---|---|---|
| **Hemoglobin (g/dl)** | 14.7 | 14.8 | 14.0 |
| **Hematocrit (l/l)** | 0.450 | 0.440 | 0.400 |
| **Platelets (/nl)** | 189 | 195 | 180 |
| **INR** | 1.14 | 1.08 | 1.08 |
| **Quick (%)** | 81 | 89 | 87 |

**Table 2**
The activated clotting time and infusion rate of bivalirudin during pulmonary vein isolation. The infusion of bivalirudin was started after uncomplicated transseptal puncture.

| Time (min) | Activated clotting time | Bivalirudin infusion rate |
|---|---|---|
| 0 | Eliminates | 0.75 mg/kg intravenous bolus, followed by a 1.75 mg/kg/h infusion |
| 10 | 607 s | 175 mg/kg/h |
| 20 | 463 s | 175 mg/kg/h |
| 40 | 595 s | 175 mg/kg/h |
| 60 | 496 s | 175 mg/kg/h |
| 80 | 528 s | 175 mg/kg/h |

of thrombin, and is potent and highly specific. Bivalirudin has a rapid onset of action with a plasma half-life of 25 min. It inhibits circulating and clot-bound thrombin, while also inhibiting thrombin-mediated platelet activation and aggregation. It does not bind to plasma proteins (other than thrombin) or to red blood cells. Therefore, it has a predictable antithrombotic response. It does not need a binding cofactor such as antithrombin. Bivalirudin does not activate platelets. Current studies recommend using bivalirudin as a preferred alternative to unfractionated heparin in patients with HIT for cardiac and vascular surgery as well as for percutaneous coronary intervention [1]. Anticoagulation for radiofrequency pulmonary vein isolation may be another potential use for bivalirudin in the setting of HIT. Ablation of pulmonary veins is an established therapeutic option for patients with symptomatic drug-refractory paroxysmal atrial fibrillation. Radiofrequency is currently the most widely used source of energy for pulmonary vein ablation. Our usual activated clotting time (ACT) values in radiofrequency procedures are above 350 s. The initial ACT value in this procedure was $>500$ s; we thought this was due to the initial bolus. Although the ACT value throughout the procedure was higher than the usual 350 s, we maintained the infusion rate to avoid fluctuations below 350 s. Despite lacking experience in the use of bivalirudin for radiofrequency pulmonary vein isolation, we tried not to undershoot our ACT target. We felt supported in this intraprocedural anticoagulation management by the fact that there were no bleeding or thrombotic complications. Anticoagulation is required during this procedure, since stroke risk is a feared complication of radiofrequency pulmonary vein isolation [2]. There are a few reports in the literature about the use of bivalirudin during electrophysiology procedures [3]; As in our case, bivalirudin was administered as a 0.75 mg/kg intravenous bolus, followed by a 1.75 mg/kg/h infusion. ACT was monitored closely during pulmonary vein isolation. There were no bleeding complications, although the ACT was intermittently increased (Table 2). To avoid fluctuations in a non-therapeutic range, the infusion rate was not lowered. The ACT is the most commonly used functional test to measure heparin anticoagulation. This test is based on the ability of whole blood to form a visible fibrin monomer within a glass tube. However, this procedure has known limitations. It is imprecise, and the sensitivity is in the lower range; thus, this method of measurement is of limited clinical use, in particular for the monitoring of hirudin and other direct thrombin inhibitors. Most recently, the direct prothrombin pathway has predominated for monitoring of direct thrombin inhibitors, as with determination of the ecarin clotting time. However, this is not always immediately and directly available. Moreover, Weeks et al. reported that hyper-ACT responses to bivalirudin therapy in percutaneous coronary intervention were not associated with elevated bleeding risk [4]. There were no thromboembolic events and the laboratory values remained stable before and after ablation (Table 1). After ablation, a prompt and uncomplicated conversion to oral anticoagulation with Apixaban (5 mg 1-0-1) was performed.

### 1.4. Summary

This case shows that the treatment of patients with rhythmological concerns who have actual or suspected HIT II can be very complex. Bivalirudin is a therapeutic option for anticoagulation during pulmonary vein isolation procedures in patients with a history of HIT.

## Conflict of interest

1. All authors contributed to the work and have reviewed and agree with the content of the article.
2. None of the article contents are under consideration for publication in any other journal or have been published in any journal.
3. No portion of the text has been copied.
4. I am aware that it is the authors' responsibility to obtain permission for any figures or tables reproduced from any prior publications, and to cover fully any costs involved.
5. All authors declare no conflict of interest related to this study.

## References

[1] Koster A, Spiess B, Jurmann M, et al. Bivalirudin provides rapid, effective, and reliable anticoagulation during off-pump coronary revascularization: results of the "EVOLUTION OFF" trial. Anesth Analg 2006;103:540–4.
[2] Linhart M, Bellmann B, Mittmann-Braun E, et al. Comparison of cryoballoon and radiofrequency ablation of pulmonary veins in 40 patients with paroxysmal atrial fibrillation: a case-control study. J Cardiovasc Electrophysiol 2009;20:1343–8.
[3] Baetz BE, Gerstenfeld EP, Kolansky DM, et al. Bivalirudin use during radiofrequency catheter ablation procedures in two patients with a history of heparin-induced thrombocytopenia. Pharmacotherapy 2010;30:952.
[4] Weeks PA, Alkhateeb HM, Michaud SE, et al. Evaluation of bivalirudin hyper- and hypo-ACT responses in the setting of percutaneous coronary intervention. J Invasive Cardiol 2013;25:250–3.