Thrombus Formation on Angioplasty Equipment During Primary Percutaneous Coronary Intervention for Acute ST Elevation Myocardial Infarction Despite Intravenous Enoxaparin Use: Case Report

ST Elevasyonlu Miyokard İnfarktüslü Hastada Primer Perkütan Koroner Girişim Esnasında İntravenöz Enoksaparin Kullanımına Rağmen Anjiyoplasti Ekipmanlarında Trombüs Formasyonu

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ABSTRACT Unfractionated heparin (UFH) has been traditionally used as the choice of antithrombin treatment during percutaneous coronary intervention. Increasing evidence suggests that treatment with the low molecular weight heparin enoxaparin during percutaneous coronary intervention (PCI) is safe and effective. Insufficient anticoagulation increases the risk of catheter thrombus formation during PCI. We report here a case with acute ST elevation myocardial infarction that periprocedural macroscopic thrombus formation on PCI equipment following antithrombin therapy with 0.75 mg/kg intravenously enoxaparin. All PCI equipments were removed and a bolus of intravenous UFH 100 U/kg was administered. New PCI equipments were inserted and the procedure was completed with stent implantation. Low molecular- weight heparin enoxaparin in the absence of a glycoprotein IIb/IIIa receptor blocker may be insufficient during percutaneous coronary intervention.

Key Words: Enoxaparin; thrombosis; angioplasty, transluminal, percutaneous coronary

ÖZET Anfraksiyone heparin (UFH), perkütan koroner girişimlerde antitrombotik yaklaşım için geleneksel olarak seçilen tedavi yöntemi olmuştur. Son yıllarda düşük molekül ağırlıklı heparin türü olan Enoksaparin'in perkütan koroner girişimlerde (PKG) kullanımının güvenli ve etkili olduğunu gösteren artan sayıda kanıtlar sunulmuştur. PKG sırasında yetersiz antikoagülasyon kateter trombüsü riski ile ilişkilidir. Biz bu olguda ST elevasyonlu miyokard infarktüslü (STEMI) hastada PKG esnasında 0,75 mg/kg dozda intravenöz Enoksaparin tedavisi altında kateterde makroskobik trombus formasyonu geliştiğini gözlemledik. Bütün PKG ekipmanları çıkarıldı ve bolus intravenöz UFH 100 U/kg dozunda verildi. Yeni PKG ekipmanları yerleştirilerek stent implantasyonu başarıyla uygulandı. Düşük molekül ağırlıklı heparin türü olan Enoksaparin glycoprotein IIb/IIIa reseptor blokerlerinin kullanılmadığı olgularda STEMI'de PKG sırasında kateter trombüsüne karşı yeterli koruma sağlamıyor olabilir.

Anahtar Kelimeler: Enoksaparin; tromboz; anjiyoplasti, translüminal, perkutan koroner

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Anti-thrombotic agents are needed during coronary angioplasty because of two potentially hazardous issues related to the procedure: (1) mechanical plaque disruption consequent to the dilatation process itself, which creates a local prothrombotic environment that is even more pronounced in acute coronary cases and (2) clot formation induced by the in-

terventional instruments (e.g., guiding catheters, metallic guidewires, dilatation balloons) utilized during the angioplasty (Figure 1). Unfractionated heparin (UFH) has been traditionally used as the choice of antithrombin treatment during percutaneous coronary intervention. However, although effective in reducing the risk of local thrombus and instrument related clotting, unfractionated heparin has several pharmacodynamic and pharmacokinetic limitations. Low molecular weight heparin (LMWH) enoxaparin has been increasingly reported as an alternative anticoagulant drug for coronary angioplasty.[1] However, in the setting of percutaneous coronary intervention (PCI) the efficacy of LMWH other than enoxaparin has not been extensively investigated. This issue is of interest as, due to the different ways of structural processing from UFH, each LMWH possesses a distinct pharmacokinetic and pharmacodynamic profile and therefore these agents cannot be used interchangeably for therapeutic purposes.[2,3]

Up to date the results of the studies designed to test the impact of antithrombin therapy using enoxaparin on catheter thrombi formation were controversial-reports from recent clinical studies range from sufficient antiplatelet only regimen without systemic anticoagulation for simple elective PCI to an superiority of UFH over enoxaparin-.

We report here a case that suggests that enoxaparin may provide insufficient protection against instrument-related clot formation.

CASE REPORT

A 59 year-old man presented to a community hospital emergency department complaining of squeezing chest pain during the previous three hours. On admission, his blood pressure was 130/80 mm Hg, and his heart rate was 74 beat/min. Physical examination was normal. His medical history was unremarkable. Electrocardiography showed a 3-5 mm ST-segment elevation in leads V1-V4. 300 mg aspirin, 600 mg clopidogrel, intravenous nitrate infusion and enoxaparin 0.75 mg/kg intravenously were administered before transfer to our center for primary PCI. Because enoxaparin had been given 40 minute before, the coronary intervention was continued without additional heparin. Diagnostic angiography showed that the infarct related artery (IRA) was left anterior descending artery. A subtotal stenosis was associated with a suspected lesion related thrombus with an initial Thrombolisis In Myocardial Infarction (TIMI) grade 1 distal flow. A guiding catheter (6 French) was inserted through the right femoral sheath. The first balloon inflation occurred 55 min after enoxaparin administration. Thereafter, an extensive adherent thrombus was noted on the catheter, guidewires and balloon shaft. All PCI equipment were removed and a bolus of intravenous UFH 100 U/kg was administered. New PCI equipment were inserted and the procedure was completed with stent implantation 72 min after initial intravenous enoxaparin administration.

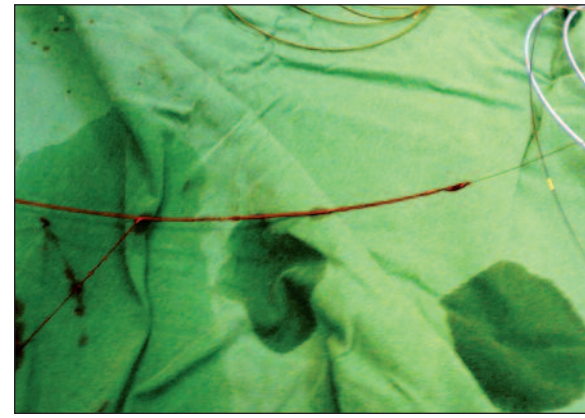

FIGURE 1: Thrombus observed on the surface of the deflated balloon at time of device retrieval.
(See color figure at http://cardivascular.turkiyeklinikleri.com/)

DISCUSSION

Low molecular weight heparins (LMWH) offer a variety of pharmacological advantages over UFH, such as better bioavailability and a more predictable anticoagulant response, rendering LMWH suitable for use in various indications. Enoxaparin is increasingly being given as an alternative to UFH in the anticoagulation treatment of acute coronary syndrome (ACS) with an early invasive strategy[4,5] and for elective procedures, too.[6,7] This development is underlined by recent guidelines correspondingly recommending the use of enoxaparin in the management of ACS.[1] The formation of material-related clots is of undisputable potential danger associated with the obvious embolic risk and to the need of complete retrieval of the instruments in the

midst of the interventional procedure. Curiously, enoxaparin has not been linked to an excess in major intra procedural complications in previous large clinical trials. Indeed, findings from the SYNERGY trial suggest that enoxaparin should be maintained as the sole antithrombotic agent during angioplasty for patients already on this drug.[5] Also, for elective patients, enoxaparin has been proposed in the STEEPLE trial as a valid anticoagulant option for coronary angioplasty.[6] It should be noted however, that instrument clotting may not be so readily apparent when examining the overall clinical results of randomized trials. Enoxaparin has been well demonstrated to protect against local thrombosis at the atherosclerotic plaque site. Raaz et al. demonstrated that enoxaparin is as effective as UFH in preventing catheter thrombus formation in an in vitro model.[8] However, instrument-related clots were observed in 5% of patients treated with enoxaparin in the series of Dana et al.[9] In theory, local coronary thrombus formation and instrument clotting may differ in their pathophysiological processes of activation of the intrinsic and extrinsic pathways and consequent generation of the haemostatic factors. One may question whether the vulnerability of enoxaparin for instrument clot formation but not for intra-coronary thrombosis could be explained by its higher anti-Xa/anti-IIa activity ratio (3:1) compared with unfractionated heparin (1:1). It is of note that fondaparinux, a specific inhibitor of factor Xa with negligible anti-IIa activity, have been previously shown to induce even more catheter-related clotting than enoxaparin.[10] Interestingly, in the study by Dana et al., the anti-Xa levels of patients with instrument clotting were within the therapeutic range at the beginning of the procedure.[7] It is therefore reasonable to assume that increased dosage might have not been effective to prevent or treat the complication, in which case crossing over to unfractionated heparin could be an alternative practical approach (not withstanding the risk of bleeding). It is clear that data from previous large randomized trials do support the use of enoxaparin as the sole antithrombotic regimen for coronary angioplasty and the findings shown by the outcome in our case must be further confirmed.[11] However, until additional information is available it is wise to keep alert and prepared to act promptly for catheter-induced thrombus formation when using enoxaparin in interventional procedures, particularly when IIb/IIIa receptor blockers are not being administered.

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