Currently taking metformin 850 mg twice a day with meals, glyburide 5 mg daily with breakfast, lisinopril 10 mg daily, and amlodipine 10 mg daily.

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Mrs S began to have pain in her upper back and left arm at 12 PM while grocery shopping. She ignored these symptoms and drove home. When she arrived home, her husband noticed that she was pale and out of breath from walking into the house. She told him about her pain, and he immediately called 911.

The paramedics arrived at 12:45 PM and found that Mrs S’s back and arm pains were intensifying. She reported the pain as 8/10, and her shortness of breath was making it difficult for her to talk. Her blood pressure was 98/52 mm Hg, heart rate was 112/min, respiratory rate was 29/min, and oxygen saturation was 90% on room air. Once in the ambulance, she chewed aspirin 325 mg and received oxygen at 4 L/min by nasal cannula and nitroglycerine 0.4 mg sublingually per protocol. En route to the hospital, the paramedics transmitted an electrocardiogram to the emergency department. The mismatch between oxygen supply and demand seen in acute coronary syndrome (ACS) can be altered. For those experiencing an ST-segment elevation myocardial infarction (STEMI), swift interventions with fibrinolytic agents, thrombin inhibitors, and antiplatelet agents can mean the difference between life and death.2

The purpose of this article is to review a case study and the drugs used to treat a patient with a STEMI. Mrs S, a woman with risk factors for coronary artery disease who had a myocardial infarction and underwent percutaneous coronary intervention (PCI), is discussed. Specifically, pharmacology as it relates to the hematologic system is reviewed.

Case Study

Mrs S is a 69-year-old woman who has hypertension and type 2 diabetes mellitus. She has a 30 pack per year smoking history, but she quit smoking 15 years ago. She is currently taking metformin 850 mg twice a day with meals, glyburide 5 mg daily with breakfast, lisinopril 10 mg daily, and amlodipine 10 mg daily. Mrs S weighs 179 pounds (81.4 kg) with a body mass index (calculated as weight in kilograms divided by height in meters squared) of 30.7.

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emergency physician alerted the emergency department staff that a STEMI patient was on the way. The electrocardiogram showed ST-segment elevation of 3 mm in leads I, aVL, and V3 through V6.

Mrs S arrived at the hospital at 1:00 PM. The emergency department nurses and physician were standing by with intravenous fluids and thrombolytic therapy. The 12-lead electrocardiogram was repeated, and evidence of ST-segment elevation was still apparent in leads I, aVL, and V3 through V6. The cardiologist on call was alerted that a patient with an anterolateral STEMI was in the emergency department. Mrs S’s blood pressure was now 112/65 mm Hg with a heart rate of 115/min; therefore, metoprolol 5 mg intravenous was given to decrease myocardial oxygen demand. Antiplatelet therapy, in the form of aspirin, had been started in the ambulance. In addition to the aspirin, Mrs S was given clopidogrel (Plavix) 300 mg by mouth.

At 1:15 PM, she reported her pain was still 6/10 and she received morphine 2 mg intravenously. The hospital did not have a cardiac catheterization laboratory, and because Mrs S’s symptoms had been present for less than 1.5 hours, fibrinolytic therapy was begun as no contraindications were present.2

Hematologic Pharmacology: t-PA and LMWH

In ACS, an unstable coronary plaque erodes and ruptures. Without pharmacologic intervention, the ruptured plaque in the endothelial wall begins to attract platelets, which adhere and aggregate. This forms a clot or thrombus, which limits or completely deprives an area of myocardium of oxygen. The ruptured plaque also causes the initiation of the clotting cascade and the release of clotting factors and mediators that further lead to the formation of thrombin and therefore fibrin (see Figure). The fibrin clot, directly or indirectly, is the target of many of the drugs used in patients with ACS, and specifically STEMI.2

Tissue plasminogen activator works to degrade fibrin and thereby dissolve clots. It exponentially accelerates the body’s natural process of fibrinolysis. As a plasminogen activator, t-PA binds to the fibrin in a thrombus and directly converts plasminogen to plasmin. Plasmin in turn breaks down the fibrin and disintegrates the clot. In the absence of fibrin or clot, t-PA has a minimal effect. This characteristic of being more clot-specific makes t-PA a safer fibrinolytic agent than some earlier generation drugs such as streptokinase or urokinase.4 Less systemic bleeding occurs, which accounts for the decrease in adverse reactions seen with t-PA compared with some of these other agents. One of the reasons that t-PA is widely used as fibrinolytic therapy for patients is the drug’s short initial half-life (5 minutes).4

To prevent severe adverse effects with t-PA, it is important to rule out any contraindications to fibrinolytic therapy before starting administration of the drug (Table 1).2

In hospitals where primary PCI is not available and the patient has had symptoms of ischemia for less than 12 hours with persistent ST-segment elevations, fibrinolytic therapy should be considered. For patients who are evaluated and found to be candidates for fibrinolytic therapy, this therapy should be administered as soon as possible after hospital arrival. The ideal time frame is within 30 minutes of arrival.3

Enoxaparin (LMWH) is an indirect thrombin inhibitor that is indicated for patients with ACS and STEMI.1 It does not directly produce anticoagulation; rather, LMWH works via antithrombin to inhibit factor Xa. Factor Xa is necessary to convert prothrombin to thrombin. When compared with unfractionated heparin (UFH), LMWH has increased bioavailability and a more
predictable pharmacokinetic profile across all patients. It is almost completely absorbed after subcutaneous injection, allowing less dose-dependent absorption, as is seen with UFH. The half-life is 4.5 hours, which permits daily or twice daily dosing.

As long as the creatinine level is less than 2.5 mg/dL in men and 2.0 mg/dL in women (to convert to micromoles per liter, multiply by 88.4), an intravenous bolus of 30 mg of LMWH should be followed by 1 mg/kg subcutaneous injections every 12 hours. If the patient is over the age of 75, the initial bolus should not be given and the dose should be decreased to 0.75 mg/kg every 12 hours. Because the drug is excreted by the kidneys,
patients with renal insufficiency (creatinine clearance <30 mL/min per 1.73 m²) should be given LMWH at a dose of 1 mg/kg every 24 hours to avoid build-up of the drug in the body.\(^3\)

A recent study showed the superiority of LMWH over UFH in STEMI patients who received fibrinolytic agents and then underwent PCI. The patients in the study treated with LMWH had a significantly lower chance of death or recurrent myocardial infarction with no change in the amount of major bleeding.\(^3\)

**Symptoms Persist: Time to Transfer**

Mrs S’s symptoms were initially relieved with the t-PA bolus and infusion. However, her arm and back pain returned nearly 50 minutes into the t-PA infusion. Her nurse also noticed the return of ST-segment elevations on her bedside monitor. The cardiologist and emergency department physician began the process of transferring Mrs S to a hospital 30 minutes away, where a cardiac catheterization laboratory was standing by and primary PCI was available.

Upon arrival, Mrs S was taken directly to the cardiac catheterization laboratory and was prepared for left-sided heart catheterization. Because she had been given LMWH at the outside hospital less than 12 hours earlier, no further indirect thrombin inhibitor was necessary.\(^3\) When the interventional cardiologist injected the left anterior descending (LAD) coronary artery, a 100% occlusion was noted in the midsection of the vessel. As expected, this was the culprit vessel given the anterolateral changes (in leads I, aVL, and V\(_3\) through V\(_6\)) seen on Mrs S’s previous electrocardiograms. Two drug-eluting stents were placed in the mid LAD with 0% residual stenosis in the vessel. Her other coronary arteries had only minor luminal irregularities. A left ventriculogram showed that Mrs S’s ejection fraction was 45%. She remained hemodynamically stable during the procedure but did have some bleeding in the groin at the site of the right femoral arterial sheath. A small hematoma of 4 cm diameter was present when the catheterization laboratory nurse brought Mrs S to the intensive care unit (ICU). On admission, the ICU nurse determined that the hematoma was not increasing, there was no further bleeding at the puncture site, and therefore close observation of the groin was indicated.

Mrs S’s ICU admission orders included metoprolol 25 mg every 12 hours, lisinopril 2.5 mg every 12 hours, simvastatin (Zocor) 80 mg every night at bedtime, aspirin 325 mg daily, and clopidogrel 75 mg daily (to start the morning after intervention). Her metformin was withheld for 48 hours given the dye exposure with the cardiac catheterization; withholding metformin is critical to avoid renal insufficiency because metformin is excreted by the kidneys. Her glucose levels were maintained between 110 and 140 mg/dL. (to convert to millimoles per liter, multiply by 0.0555) with a regular insulin subcutaneous correctional scale before each meal and every night at bedtime.

**Hematologic Pharmacology: Antiplatelet Agents**

Platelets become activated by thrombin and begin to aggregate at the site of plaque rupture in patients with ACS. Fibrinogen further aids in the production of the platelet plug, which is made up of the activated platelet cells. Activated platelets release adenosine diphosphate (ADP) and thromboxane A\(_2\) (TXA\(_2\)), potent chemical mediators that accelerate the formation of the clot. ADP and TXA\(_2\) recruit more platelets and the plug becomes a thrombus. The thrombus is created when a fibrin mesh surrounds the activated platelets.\(^2,4\)

The 2 critical antiplatelet agents used in this patient with ACS, aspirin and clopidogrel, work by blocking the release and effect of TXA\(_2\) and ADP, respectively.\(^2\) In doing so, these agents help to suppress the aggregation of platelets at the site of endothelial damage or plaque. Aspirin and clopidogrel are important for patients during the crisis of ACS because they help to minimize the size of the initial thrombus. Long-term use of these drugs in patients after a myocardial infarction is also crucial for the prevention of further platelet activation, stent restenosis or thrombosis, and possible adverse complications.\(^2,3\)

Aspirin is a cyclooxygenase-1 inhibitor. Cyclooxygenase-1 is an enzyme that converts prostaglandin G\(_2\) to TXA\(_2\) in platelets. Aspirin irreversibly inhibits platelets from producing TXA\(_2\) and therefore suppresses the aggregation of platelets at the site of vascular injury and throughout the body. Platelets cannot synthesize new cyclooxygenase-1 once aspirin has inhibited them; therefore, the effects of aspirin last for 7 to 9 days, the lifespan of a platelet cell.\(^6,7\)

Patients with STEMI should receive aspirin immediately at a dose of 162 to 325 mg by mouth
according to the 2009 updated STEMI guidelines from the American College of Cardiology. After PCI and placement of stents, patients should take aspirin 162 to 325 mg daily for 1 month (with bare metal stents), 3 months (with sirolimus-eluting stents), or 6 months (for paclitaxel-eluting stents). Then lifetime 75 to 162 mg daily aspirin should be prescribed. The exact dose prescribed is determined by each patient’s physician.

Clopidogrel is an ADP receptor blocker that works on platelet cell membranes. This drug irreversibly blocks the ADP receptor on platelets and obstructs platelet activation caused by ADP. Like aspirin, the effect of clopidogrel lasts for 7 to 9 days. Patients with STEMI should receive an oral loading dose of 300 to 600 mg of clopidogrel as soon as possible, regardless of whether they received fibrinolytic therapy. A daily dose of 75 mg should be continued for 1 year after placement of a bare metal stent or a drug-eluting stent. In patients who have an increased risk of bleeding or in whom significant complications may develop, the decision to discontinue clopidogrel earlier can and should be considered.

Although the antiplatelet drugs produce the desired effect of inhibiting platelets and preventing further sequelae at the site of endothelial damage, they can also cause unwanted bleeding. Aspirin and clopidogrel in combination significantly improve outcomes in patients with ACS; but major bleeding episodes have been reported to occur in as many as 2% with aspirin and 3% with the combination. It is important for nurses to educate patients with ACS not only about the importance of medication compliance with the antiplatelet drugs, but also about the possible adverse effects of bleeding. Nurses should advocate that their patients report all bleeding, even bleeding that is not life threatening, to their physician. Additionally, patients should be taught at hospital discharge that they should not discontinue aspirin or clopidogrel without discussing it with their physician.

### Hospital Course and Discharge

The small hematoma at the site of Mrs S’s right femoral sheath did begin to bleed again overnight in the ICU. Mrs S’s nurse decided to place a compression device to decompress the patient’s hematoma and control groin bleeding. The compression device was removed 4 hours later and the bleeding was completely resolved. The hematoma had also been reduced by the pressure and was 2 cm in diameter at the time of discharge. Mrs S was ambulating in the ICU on the morning after her procedure and did not have any additional bleeding at her right femoral sheath site.

She progressed well in the next 2 days on the cardiac telemetry unit. She had no further chest pain or shortness of breath. Her complete blood cell count and chemistry panel were unremarkable during her stay. Specifically, her creatinine level was 0.8 mg/dL on the morning after PCI and was 0.9 mg/dL on the morning of discharge. Her metformin dosage was resumed at the time of hospital discharge. Her blood pressure and heart rate were well controlled by metoprolol and lisinopril.

At discharge, the nurse educated Mrs S about her medications (Table 2). The amlodipine was discontinued because Mrs S had started treatment with a β-blocker (metoprolol). Her nurse informed her that the new β-blocker and her angiotensin-converting enzyme inhibitor (lisinopril) provide improved benefit for her after her ACS. These 2 classes of drugs are beneficial in preventing complications and recurrent events in patients with STEMI.

### Nursing Implications

It is important that nurses understand the pharmacology of these hematologic drugs in order to provide their patients with the best in evidence-based nursing care. The drugs reviewed in this article were used to treat Mrs S, but other important drugs can be used for patients with STEMI (Table 3). In STEMI patients who do not receive fibrinolytic therapy and proceed directly to PCI, antiplatelet drugs are often administered in the emergency department. Aspirin is given with either clopidogrel or prasugrel.
During the PCI, the cardiologist prescribes unfractionated heparin if LMWH has not been previously initiated. In addition, the cardiologist may decide to treat the patient in the catheterization laboratory with a direct thrombin inhibitor (eg, bivalirudin) or a glycoprotein IIb/IIIa inhibitor (eg, abciximab or eptifibatide).3

Nurses’ knowledge of these hematologic drugs is critical so that they can provide excellent patient education. Nurses play a vital role in educating their STEMI patients on the indications, mechanisms of action, and possible adverse effects of bleeding with the hematologic drugs.

Nurses can affect patients’ behavior by stressing the importance of medication compliance. When patients understand the indications for and importance of compliance with their medications, they are more likely to take them as prescribed. By educating their patients from the beginning of the hospital stay to the day of discharge, nurses can increase their patients’ knowledge base and prevent complications.

It is helpful to provide drug-related patient education handouts that are specific for each patient’s prognosis and diagnosis. These materials, when left at the bedside with the patient, can provide reinforcement of nursing education. Having educational material at the bedside can also allow the nursing staff to provide education when medications are being dispensed. The handouts also provide valuable education aids for the patients once they are home. Additionally, the stress of a hospital stay on a patient and his or her family can be significant. Education provided during this stressful time is vital, but handouts that the patient and family can review at home can often reinforce the nurses’ instructions.

**Summary**

Drugs that work on the hematologic system are a critical component in the care of patients with STEMI. The case of Mrs S may have resulted in a less favorable outcome if any of the 3 essential aspects of care of patients with myocardial infarction had been absent: rapid assessment, expert cardiac care, and appropriate drug selections that modulate the effects of the ruptured plaque and subsequent thrombus formation. Fibrinolytic agents, the indirect thrombin inhibitors, and antiplatelet drugs are all important in limiting morbidity and halting mortality in patients with STEMI.

**Table 3** Additional hematologic drugs used in care of patients with ST-segment elevation myocardial infarction (STEMI)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
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<tbody>
<tr>
<td>Prasugrel (Effient)</td>
<td>Antiplatelet agent</td>
</tr>
<tr>
<td></td>
<td>Effective for primary and nonprimary percutaneous coronary intervention (PCI)</td>
</tr>
<tr>
<td></td>
<td>Superior to clopidogrel in the inhibition of platelet aggregation; however, also increases the risk of major bleeding (when compared with clopidogrel)</td>
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<tr>
<td>Unfractionated heparin</td>
<td>Indirect thrombin inhibitor</td>
</tr>
<tr>
<td></td>
<td>Indirectly prevents the conversion of fibrinogen to fibrin via thrombin</td>
</tr>
<tr>
<td></td>
<td>Used in STEMI patients treated with primary PCI, nonprimary PCI, and fibrinolytic therapy</td>
</tr>
<tr>
<td>Bivalirudin (Angiomax)</td>
<td>Direct thrombin inhibitor</td>
</tr>
<tr>
<td></td>
<td>Bind thrombin and inhibit the formation of fibrinogen into fibrin</td>
</tr>
<tr>
<td></td>
<td>Added to the 2009 STEMI update as an acceptable anticoagulant for primary PCI</td>
</tr>
<tr>
<td>Abciximab (ReoPro)</td>
<td>Glycoprotein IIb/IIIa inhibitors</td>
</tr>
<tr>
<td>Eptifibatide (Integrilin)</td>
<td>Inhibit the glycoprotein IIb/IIIa receptor on activated platelets from binding with fibrinogen and von Willebrand factor; they reversibly block platelet aggregation</td>
</tr>
<tr>
<td>Tirofiban (Aggrastat)</td>
<td>Can be used in selected STEMI patients undergoing primary PCI (with or without stenting); used in conjunction with an indirect thrombin inhibitor at the time of PCI</td>
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References