On August 13, 2012, three cases of thrombotic thrombocytopenic purpura (TTP) were discovered in intravenous (IV) drug users in Tennessee. Further investigation identified 12 additional cases who reported non-medical, chronic IV Opana® ER use, which resulted in treatment using plasmaphoresis. Most had obtained the drug without a prescription. It was determined these TTP-like illnesses were due to dissolving and injecting oxymorphone HCl extended-release (Opana® ER) tablets into the vein.¹,²

TTP, a blood disorder characterized by microangiopathic hemolytic anemia and thrombocytopenia, is rarely observed, with an annual incidence rate of around 11 cases per 1,000,000 persons. The incidence is even higher in women, obese patients, patients of black race, and those in urban settings. Without treatment, TTP is associated with a high mortality rate.³,⁴ TTP may be associated with a variety of factors such as infection, pregnancy, cancer, drug therapies, autoimmunity, and deficiency of ADAMTS 13 (metalloproteinase also known as von Willebrand factor-cleaving protease).¹,⁴

There are no specific diagnostic criteria, which makes recognizing TTP difficult. TTP diagnosis is based on a “pentad of clinical features” - a presentation of fever, thrombocytopenia, microangiopathic hemolytic anemia, renal impairment, and neurologic deficits. A TTP diagnosis is suspected when laboratory testing reveals anemia and thrombocytopenia without leukopenia. Additionally, fragmented red cells (schistocytes) and immature red blood cells (reticulocytes) on the peripheral blood smear, elevated lactate dehydrogenase serum levels, indirect-reacting bilirubin, and a negative direct Coombs’ test suggest the presence of microangiopathic hemolytic anemia.³ Many present with nonspecific symptoms such as abdominal pain, nausea, vomiting, and weakness.⁵ The goal of management is to normalize the platelet count, which may be done through plasma exchange and high-dose corticosteroids. Other management options include rituximab or cyclosporine therapy, renal dialysis, or platelet transfusions.⁵
The FDA approved Opana® ER in 2006 for controlling moderate to severe pain. This compound is a semi-synthetic schedule II controlled substance that has selective affinity for the mu-opioid receptors.6 Due to the medication’s extended-release characteristics, the half-life is approximately 7 to 9 hours.7 Opana® ER only comes in tablet form, with doses ranging from 5 mg to 40 mg. The ER formulation contains polyethylene oxide and polyethylene glycol, but it is unclear if these components may prompt a TTP-like illness when Opana® ER is injected.8

Opioids are standard therapy for patients who have cancer pain or for non-cancer patients who have chronic pain, but many abuse these narcotics.9 Abuse may involve tampering or changing the original formulation to a powder, liquid, or vapor for use through a non-indicated route of administration, such as inhalation, injection, or smoking. The purpose of tampering is to allow faster drug release, which yields more rapid, pleasurable effects. For products such as Opana® ER, tampering compromises the extended-release mechanism. The pharmaceutical industry has created extended-release oxymorphone HCl tamper-resistant formulations to deter abuses from altering the dosage form to a more “favorable” route of administration.10 Endo Pharmaceuticals incorporated a “crush-resistant” formulation using INTAC technology in 2012 into their Opana® ER products.10 Emerging safety data have shown the new formulation is reducing abuse rates.12

Pharmacists who dispense Opana® ER should inform patients of the risks the drug may cause when not used as directed. IV drug abuse should be suspected in those patients presenting with TTP-like illness of unknown cause. The Centers for Disease Control and Prevention has recommended a drug test in patients with TTP-like illness of unknown cause to determine whether oxymorphone is identified in the urine; if present, this could indicate the patient has administered Opana® ER parenterally. Other recommendations include questioning patients about IV drug abuse, requesting a copy of the patient’s prescriptions to determine if their physician prescribed the medication, and referring patients to a substance abuse treatment program.1, 2, 13

References:


