Thrombotic Thrombocytopenic Purpura (TTP)—Like Illness Associated With Intravenous Opana ER Abuse—Tennessee, 2012


ON AUGUST 13, 2012, A NEPHROLOGIST REPORTED TO THE TENNESSEE DEPARTMENT OF HEALTH (TDH) THREE CASES OF UNEXPLAINED THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP), A RARE BUT SERIOUS BLOOD DISORDER CHARACTERIZED BY MICROANGIOPATHIC HEMOLYTIC ANEMIA AND THROMBOCYTOPENIA. THE ANNUAL INCIDENCE IS APPROXIMATELY 1 PER 100,000 POPULATION. KNOWN RISK FACTORS FOR TTP INCLUDE INFECTION WITH SHIGA TOXIN–PRODUCING ESCHERICHIA COLI (STEC) AND THE USE OF DRUGS, INCLUDING PLATELET AGGREGATION INHIBITORS, QUININE, AND COCAINE. THE THREE PATIENTS WERE INTRAVENOUS (IV) DRUG USERS WHO RESIDED IN A RURAL COUNTY IN NORTHEAST TENNESSEE. TO IDENTIFY OTHER CASES OF TTP-LIKE ILLNESS THAT MIGHT BE ASSOCIATED WITH INJECTION-DRUG USE, TDH CONDUCTED A WIDESPREAD INVESTIGATION. BY THE END OF OCTOBER, A TOTAL OF 15 SUCH CASES HAD BEEN REPORTED; NONE WERE FATAL. A CASE-CONTROL STUDY WAS CONDUCTED, AND INVESTIGATORS DETERMINED THAT THE CASES OF TTP-LIKE ILLNESS WERE ASSOCIATED WITH DISSOLVING AND INJECTING TABLETS OF OPANA ER (ENDO PHARMACEUTICALS), A RECENTLY FORMULATED OPIATE PAIN RELIEVER INTENDED FOR ORAL ADMINISTRATION.


THE 15 PATIENTS WERE FURTHER CATEGORIZED BY THE PRESENCE OR ABSENCE OF A CONCURRENT INFECTION (AS EVIDENCED BY SEPSIS) AND THE USE OF OPANA ER AS A POSSIBLE ETIOLOGY. CLINICAL CHARACTERISTICS WERE SIMILAR AMONG THE 15 PATIENTS. PATIENTS REPORTED SYMPTOMS SUCH AS ABDOMINAL PAIN, FATIGUE, FEVER, AND NAUSEA.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP) IS A RARE BUT SERIOUS BLOOD DISORDER CHARACTERIZED BY MICROANGIOPATHIC HEMOLYTIC ANEMIA AND THROMBOCYTOPENIA AND HAS NOT BEEN ASSOCIATED PREVIOUSLY WITH INTRAVENOUS ABUSE OF OPAHA ER. A CASE-CONTROL STUDY IDENTIFIED A STRONG ASSOCIATION (ODDS RATIO=35.0; 95% CONFIDENCE INTERVAL=3.9-312.1) BETWEEN TTP-LIKE ILLNESS AND INJECTION OF REFORMULATED OPAHA ER.

WHAT ARE THE IMPLICATIONS FOR PUBLIC HEALTH PRACTICE?

THE DISEASE MECHANISM AND EXTENT OF THE PROBLEM WITH OPAHA ER ABUSE ARE UNKNOWN. HEALTH-CARE PROVIDERS SHOULD ASK PATIENTS WITH TTP-LIKE ILLNESS ABOUT INTRAVENOUS DRUG ABUSE AND INFORM PATIENTS OF THE RISKS INVOLVED WHEN USED OTHER THAN AS PRESCRIBED.
TTP-like illness without infection (n = 8) | TTP-like illness with infection (n = 7) 
---|---
**Test result** |  |  |
Platelet count (per µL) | 20,000 | 26,000 |
Hematocrit (%) | 18.7 | 19.3 |
Hemoglobin (g/dL) | 6.0 | 6.5 |
Creatinine (mg/dL) | 1.1 | 2.5 |
BUN (mg/dL) | 28 | 52 |
LDH (units/L) | 1,080 | 768.5 |
ADAMTS13 activity level (%) | 90* | 64* |
Schistocytes present (no. patients) | 8 | 7 |
Symptom | No. (%) | No. (%) |
Nausea | 6 | 5 |
Abdominal pain | 5 | 6 |
Fever | 1 | 5 |
Fatigue | 5 | 5 |
Treatment |  |  |
Plasmapheresis | 6 | 6 |
Dialysis | 2 | 0 |
Other Illness |  |  |
Hepatitis C | 5 | 7 |
Sepsis | 0 | 0 |
Endocarditis | 0 | 3 |
Renal failure | 4 | 7 |
**Abbreviations:** BUN = blood urea nitrogen; LDH = lactate dehydrogenase; ADAMTS13 = the von Willebrand factor–cleaving protease. 
* Data not available for seven of the 15 cases.

The case-control study included 15 case-patients and 28 controls. All case-patients reported recent injection of reformulated Opana ER. Among the controls, 22 reported injecting oxycodone, and 18 reported injecting morphine. The odds ratio for case-patients with infection was undefined because all seven with infection reported recent injection of reformulated Opana ER. Public Health Response

TDH submitted an alert via CDC’s Epidemic Information Exchange (Epi-X) on August 23, 2012. The Food and Drug Administration (FDA) released a statement regarding the association of IV abuse of reformulated Opana ER and TTP-like illness on October 11. TDH submitted a second alert to Epi-X on October 24, and CDC released a Health Advisory on October 26 to warn against injection of Opana ER and to aid in case finding.


Editorial Note: TTP is a thrombotic microangiopathy, conditions characterized by thrombosis in arterioles and capillaries that manifest clinically with thrombocytopenia and microangiopathic hemolytic anemia. Patients with TTP require hospitalization and usually plasmapheresis. Without treatment, TTP is associated with a high mortality rate. TTP is more common among women. In addition to platelet aggregation inhibitors, other toxic chemotherapeutic and immunosuppressive drugs have been associated with TTP.
Hepatitis C and systemic infections often are associated with IV drug abuse as well as with thrombocytopenia, hemolytic anemia, and deficiency of the ADAMTS13 enzyme. Therefore, whether TTP was caused by infection or some noninfectious exposure has been unclear in certain previous cases. However, in the cases described in this report, injection of reformulated Opana ER was strongly associated (OR = 35.0; CI = 3.9-312.1) with the illness of the case-patients.

FDA approved Opana ER for oral use in 2006. However, like other opioid analgesics, the drug has been abused by some persons seeking its euphoria-inducing effects, including some who have crushed the tablets to snort them or dissolved them for injection. The new formulation, designed to inhibit crushing and dissolving tablets, was released into the market in February 2012. The new formulation contains inactive ingredients not found in the original formulation, including polyethylene oxide (PEO) and polyethylene glycol. Of note, in October 2010, the makers of OxyContin, another extended-release opioid analgesic, also launched a reformulated product designed to deter abuse that contained PEO. No cases of TTP-like illness following injection of reformulated OxyContin have been reported.

It is unclear what component or components of reformulated Opana ER might trigger TTP-like illness when injected and whether different methods of preparing the drug can increase or decrease the risk from injection. No human studies have evaluated the risk from injecting this new formulation, although in one study in rats, intravenous injection caused thrombocytopenia. It is also possible that the illness and bloodborne infection, but this is the first report of TTP-like illness associated with abuse of an opioid pain reliever by injection.

FDA has warned that Opana ER is meant to be taken orally and should only be taken when prescribed and as directed. CDC has recommended that clinicians treating patients with TTP-like illness with unknown etiology ask about IV drug abuse, perform a urine drug test to look for oxymorphone, and request a copy of the patient’s prescriptions for controlled substances from state prescription drug monitoring programs. Clinicians should counsel patients who report injection of reformulated Opana ER of the risk for recurrent TTP, bloodborne infections, and overdose with continued use; refer them to substance abuse treatment programs, and notify other clinicians who have prescribed the patient Opana ER. Cases can be reported to state or local health departments. A standardized case report form is available at e-mail, lbp4@cdc.gov.

Acknowledgments

Take-Home Lead Exposure Among Children With Relatives Employed at a Battery Recycling Facility—Puerto Rico, 2011

The recycling of lead has increased during the past 20 years, with more workers and their families potentially being exposed to lead from recycling facilities, including facilities that recycle lead-acid batteries. During November 2010-May 2011, four voluntary blood lead screening clinics for children of employees of a battery recycling facility in Puerto Rico were conducted. A total of 227 persons from 78 families had blood lead tests. Among 68 children aged <6 years, 11 (16%) had confirmed blood lead levels (BLLs) ≥10 μg/dL, the BLL at which CDC recommended individual intervention to reduce BLLs in 2010, and 39 (57%) children aged <6 years had venous or capillary BLLs ≥5 μg/dL, the reference value for elevated BLLs in children established by CDC in 2012. To determine whether take-home lead exposure contributed to the children’s BLLs of ≥10 μg/dL, vehicle

REFERENCES