

Most Acetaminophen Overdoses Don't Harm Liver

BY MITCHEL L. ZOLER
Philadelphia Bureau

Patients hospitalized for acetaminophen overdose had a 4.5% rate of acetaminophen-induced hepatotoxicity in a population-based study, Dr. Robert P. Myers and his associates said.

In a multivariate analysis of residents of Calgary and southern Alberta (Canada) during 1995-2004, significant risk factors for acetaminophen hepatotoxicity were al-

cohol abuse, preexisting liver disease, and unintentional ingestion, the authors said (Clin. Gastroenterol. Hepatol. 2008 August [Epub doi:10.1016/j.cgh.2008.02.053]).

In patients with none of these risk factors, 1.3% developed hepatotoxicity. In those with one risk factor, the hepatotoxicity rate rose to 5%. It was 19% in patients with two risk factors and 52% in those with all three risk factors, wrote Dr. Myers, who is from the liver unit in the department of medicine at the Uni-

versity of Calgary, and his colleagues.

The findings—based on 1,680 hospital admissions for acetaminophen overdose—also highlighted the clinical impact that acetaminophen-induced hepatotoxicity can have. Patients who developed this complication following an acetaminophen overdose were 2.5-fold more likely to be admitted to an ICU, and were 40-fold more likely to die while hospitalized, compared with patients who did not have hepatotoxicity following their overdose.

After case-mix adjustment, those who developed hepatotoxicity had a hospital length of stay that was 50% greater, and hospital costs that were double the level of patients without hepatotoxicity.

But the findings “reassuringly” showed that acetaminophen hepatotoxicity is uncommon following an overdose, supporting the “relatively benign” nature of most overdoses. More than 95% of the overdose episodes did not result in liver damage, the authors said. ■

PE resulting from DVT is the most common cause of preventable death among hospitalized patients.⁵ In the DVT FREE study funded by sanofi-aventis, which included 5451 patients with ultrasound-confirmed DVT, 71% did not receive any prophylaxis within 30 days of diagnosis.¹⁰ Moreover, nonsurgical patients were much less likely than surgical patients to receive appropriate DVT prophylaxis.¹⁰ The American College of Chest Physicians (ACCP) evidence-based clinical practice guidelines recommend that, for every general hospital, a formal, active strategy that addresses the prevention of VTE be developed (Grade 1A).⁵

“Providing preventive treatment (or primary prophylaxis) to these individuals can dramatically reduce the likelihood of a blood clot or PE.”¹¹

Recommendations for VTE Prophylaxis in Select Hospitalized Patients⁵ (Adapted From 2008 ACCP Guidelines)

Prophylaxis of DVT in medical patients with restricted mobility during acute illness^{5,11,a}

- For acutely ill medical patients admitted to hospital with congestive heart failure (CHF) or severe respiratory disease, or who are confined to bed and have one or more additional risk factors, including active cancer, previous VTE, sepsis, or inflammatory bowel disease: ACCP recommends thromboprophylaxis with low-molecular-weight heparin (LMWH) or low-dose unfractionated heparin (LDUH) (all Grade 1A)

Prophylaxis of DVT following abdominal surgery^{5,11,a}

- For higher-risk general surgery patients undergoing a major procedure for cancer: ACCP recommends thromboprophylaxis with LMWH or LDUH three times daily (each Grade 1A)
- For patients undergoing major general surgical procedures: ACCP recommends thromboprophylaxis continue until discharge from hospital (Grade 1A)

Prophylaxis of DVT following hip- or knee-replacement surgery^{5,11,a}

- For patients undergoing total hip replacement (THR) or total knee replacement (TKR): ACCP recommends routine thromboprophylaxis with LMWH (at the usual high-risk dose) or adjusted-dose vitamin K antagonist (VKA) (international normalized ratio [INR] target, 2.5; INR range, 2.0 to 3.0) for at least 10 days (all Grade 1A)
- For patients undergoing THR: ACCP recommends thromboprophylaxis be continued beyond 10 days and up to 35 days after surgery with LMWH (Grade 1A) or a VKA (Grade 1B)

Table 2. ACCP 2008 Guidelines: recommendations for VTE prophylaxis.

LOVENOX® (enoxaparin sodium injection) is indicated for the prophylaxis of DVT, which may lead to PE:

- In medical patients who are at risk for thromboembolic complications due to severely restricted mobility during acute illness
- In patients undergoing abdominal surgery who are at risk for thromboembolic complications
- In patients undergoing hip-replacement surgery, during and following hospitalization
- In patients undergoing knee-replacement surgery

Two Clinical Trials Showed LOVENOX® Provided Effective VTE Prophylaxis in Medically Ill Patients

MEDENOX (Prophylaxis in Medical Patients With Enoxaparin) was a multicenter, multinational, double-blind study that included 1102 acutely ill medical patients randomized to either LOVENOX® or placebo for 6 to 14 days during hospitalization.¹²

The incidence of DVT or PE was significantly lower in patients treated with LOVENOX® than placebo (5.5% vs 14.9%, respectively).¹² The use of LOVENOX® was associated with a 63% reduction in risk of VTE.¹²

There was no statistically significant difference in major bleeding events^{b,c} or thrombocytopenia comparing LOVENOX® with placebo.^{12,13}

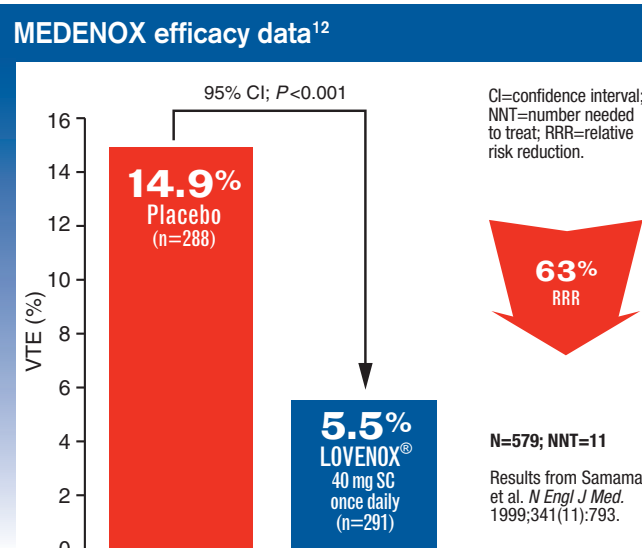


Figure 1. Short-term incidence and RRR of VTE in medical patients treated with LOVENOX® (40 mg) vs placebo. P values are for RRR.

^a Grades of recommendation – 2008 Guidelines: ACCP Evidence-Based Clinical Practice Guidelines (8th edition)—Grade 1A—strong recommendation based on high-quality evidence; Grade 1B—strong recommendation based on moderate-quality evidence; Grade 1C—strong recommendation based on low- or very low-quality evidence.¹¹

^b Based on the rate of major bleeding on LOVENOX® up to 24 hours after the last dose.¹³

^c Hemorrhage was classified as major if bleeding was overt and was associated with the need for transfusion of 2 or more units of packed red blood cells or whole blood, or with a decrease in the hemoglobin concentration of 2.0 g/dL or more from baseline, or if bleeding was retroperitoneal, intracranial, or fatal.¹²

Please see a brief summary of prescribing information, including boxed WARNING, at the end of the article.