Endocarditis as a Marker for New Epidemics of Injection Drug Use

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ABSTRACT

Background: We examined discharges for infective endocarditis (IE) at an academic teaching hospital for over 10 years to evaluate if an increase in hospitalizations for IE and increase in hepatitis C virus (HCV) in patients with IE could predict a new epidemic of injection drug use (IDU).

Materials and Methods: Retrospective medical record review of discharged patients with the diagnosis of IE as defined by the modified Duke criteria. Student's *t* test, chi-squared test and Fisher's exact test were used to calculate *P* values.

Results: There were 542 discharges among 392 unique patients with IE and 104 patients were readmitted 2-7 times. Of the total discharges, 367 (67.7%) were not screened for HCV, and of those tested, 86 (49.1%) were HCV+; 404 (74.5%) were not screened for HIV and of those tested, 28 (20.3%) were HIV+. Patients who self-identify as a person who injects drugs were more likely to be tested for HCV, 75 (69.4%) versus 12 (31.5%, $P < 0.0001$), and for HIV, 72 (66.6%) versus 13 (34.2%, $P < 0.0001$) compared with those who self-report no IDU. Those with a positive result for opiate or heroin toxicology test were more likely to be screened for HCV, 70 (66%) versus 22 (44.8%, $P < 0.0001$), and for HIV, 66 (62.2%) versus 25 (51%, $P < 0.0001$) than those with negative result for toxicology test. Over this period, there was a 2-fold increase in IE cases, a 3-fold increase in HCV antibody prevalence and a 6-fold increase in opiate toxicology screens showing positive result, but no increase in HIV.

Conclusions: Although IDU is a known risk factor for IE, the observation of a sharp increase in IE cases may signal a new epidemic of IDU and HCV.

Key Indexing Terms: Injection drug use; Human immunodeficiency virus; Hepatitis C virus; Endocarditis. **[Am J Med Sci 2016;352(6):609–614.]**

BACKGROUND

It is well known that injection drug use (IDU) is associated with infective endocarditis (IE)[1] because of using unsterile injection equipment and unsterile injection technique. The overall incidence of acute bacterial endocarditis is significantly higher among persons who inject drugs (PWID) compared to the non-IDU population, 150-2,000 cases per 100,000 person-years versus 1.7-6.2 cases per 100,000 person-years.[2-4] Previous studies demonstrating an increase in the rate of endocarditis, differences in the causative agents, affected valves and complications have all been directly linked to the increasing numbers of IDU-associated episodes of IE.[2,5,6] PWID also have an increased frequency of recurrent endocarditis.[7] It is estimated that PWID at some point during their lifetime comprise 2.6% of the U.S. population; thus, a significant number of individuals are then at risk for IE, and infection with hepatitis C virus (HCV), hepatitis B virus or human immunodeficiency virus (HIV) or with all these.[8] In contrast to non-IDU–associated IE, although PWID have typically been described as presenting with right-sided endocarditis, left-sided IE is not unusual.[9]

IDU is also a major risk factor for blood-borne viral infections, such as HIV, as well as the most common risk for HCV.[10,11] The Centers for Disease Control (CDC) tracks surveillance only for acute HCV; whereas the exact prevalence of chronic HCV in the United States is unknown, it is estimated at 3.4-5.3 million. HCV accounts for approximately 60-70% of all chronic hepatitis cases and up to 50% of cases of cirrhosis in the United States, and is the most important cause of chronic liver disease, end-stage liver disease, hepatocellular carcinoma and liver transplantation.[11,12] An estimated 4.1 million Americans (1.65%), have antibody to HCV (anti-HCV), indicating either ongoing or previous infection.[13] Chronic HCV causes estimated 16,627-19,659 deaths annually in the United States.[13] It is estimated that at least 20% of patients with chronic HCV would develop cirrhosis approximately 20-30 years after infection and 5% would die of HCV-related liver disease.[10,14] Disease progression is faster among those with both HIV and chronic HCV, with progression to cirrhosis occurring approximately 10-15 years after infection.[10] Unlike HIV, HCV can remain infectious in a used syringe, filter, cooker and injection equipment surfaces for 2-9 weeks depending on factors such as temperature and humidity.[15,16]

The CDC estimates that more than 1 million people are living with HIV in the United States but 12.8% are unaware of their infection.[17] In 2010, PWID represented 8% of new HIV infections and in 2011, 15% of those

living with HIV.[17,18] It is difficult to estimate the precise transmission of HIV through IDU as it is dependent on the caliber of the needle, the HIV burden of the infected individual and the blood residue in a cooker, filter or the syringe hub itself.

At the University of Cincinnati Medical Center, we began seeing an increase in the number of IE cases in the mid-2000s, including patients transferred from outlying community hospitals, many of whom reported opioid IDU, which had not previously been a problem in southwest Ohio. We decided to examine all hospitalizations for IE at a tertiary care teaching hospital over a 10-year span to evaluate whether an increase in hospitalizations for IE could be verified and whether it was associated with an evidence of opioid IDU. We looked at infection with HCV and HIV, a history of IDU and toxicology screen results to see if an increase in IE cases and blood-borne chronic viral infections in patients with IE could be used to predict a new epidemic of IDU.

METHODS

This study was conducted at the University of Cincinnati Medical Center, a 605-bed tertiary teaching hospital with more than 31,600 yearly admissions. We performed a retrospective medical record review of all discharged patients ($n = 660$) with an ICD-9 diagnosis of IE from January 1, 1999 to December 31, 2009. Each medical record was reviewed for notes (emergency department, admitting team, infectious diseases consultation [IDC] and discharge summary), echocardiography results and all laboratory and microbiologic results. Only cases that met the modified Duke Criteria for IE were included in the final analysis.[19] We also reviewed whether screening for HCV antibody and HIV was performed during the current hospitalization for IE, or whether it was documented from prior evaluation. *P* values were calculated using the Student's *t* test; chi-squared test and Fisher's exact test where appropriate. We also were able to obtain the hospital charges for most cases.

We used data from the Hamilton County Coroner's crime laboratory that serves all police departments in the greater Cincinnati area. All confiscated substances and drug-related items at a crime scene or arrest were tested for controlled and illegal substances. Specifically, "heroin confiscations" are drugs seized by law enforcement, which test positive for heroin in the crime laboratory. These data can be used as a proxy estimate of the heroin supply in greater Cincinnati from 2000-2010.[20]

This study received institutional review board approval from the University of Cincinnati.

RESULTS

There were 542 discharges among 392 unique patients with IE and 104 patients were readmitted 2-7 times for suspected IE. The number of discharges for IE associated with HCV antibody prevalence and positive result for opioid toxicology screens increased over the 10-year period (Figure 1). Most patients were male (308, 56.8%) and white (319, 58.9%), with a mean age of 50.6 years (standard deviation [SD] = 15.8 years) and a similar median age of 50 years. Overall, there was a 20% (111 patients) in-hospital mortality rate and the mean length of stay was 14.6 days (SD = ±12 days). Most had public insurance, traditional or emergency Medicaid or Medicare (414, 76.4%), whereas 18 (3.3%) had no insurance (Table 1). However, these data do not represent the true proportion without insurance on admission, as hospital social workers aggressively pursue traditional or emergency Medicaid as soon as possible for those who may qualify. The 18 patients without insurance either died too quickly or were transferred to other hospitals before qualifying for either traditional or emergency Medicaid.

Only 138 (25.4%) discharges were screened for HIV, and 28 (20.2% of those screened) were infected with HIV. For HCV, 175 (32.2%) discharges were screened and 86 (49% of those screened) had a positive result for antibody test (Table 2). Among those with positive result versus negative result for opioid toxicology screens, 70 (66%) versus 22 (45%), $P = 0.01$, were screened for HCV, whereas screening for HIV was similar between these 2 groups 66 (62.2%) and 25 (51%), $P = 0.22$ (Table 3). Of those who self-reported IDU versus those who self-reported no IDU at their initial interview, 75 (69%) versus 12 (31.5%), $P < 0.001$, were screened for HCV antibody and 72 (66.6%) versus 15 (39.5%), $P = 0.004$, were screened for HIV.

Among the 138 discharges screened for HIV, 15 (54%) of the HIV-positive and 82 (75%) of the HIV-negative discharges were also screened for HCV ($P = 0.05$), and of those HIV-positive discharges screened for HCV antibody, 7 (47%) were positive (Table 4). Of the 12 (43%) HIV discharges with a positive result for opioid toxicology test, most (9, 75%) were screened for HCV.
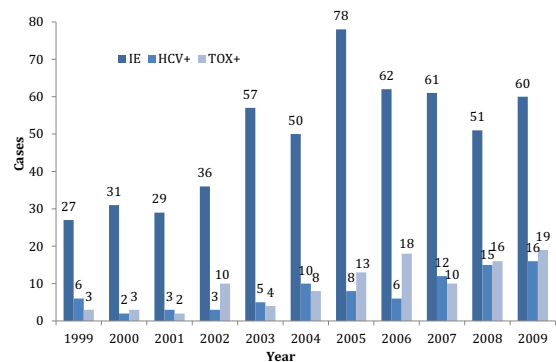
FIGURE 1. The number of admission for infective endocarditis (IE), number testing positive for HCV, and number with a positive result for opiate or heroin toxicology test from 1999-2009. HCV+, those testing positive for hepatitis C virus antibody; IE, infected endocarditis; Tox+, those with positive result for opiate or heroin toxicology tests.