CLINICAL INVESTIGATION

Opiate Injection-associated Infective Endocarditis in the Southeastern United States

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ABSTRACT

Background: Opiate pain reliever (OPR) misuse by injection is increasing in the United States. Infective endocarditis (IE), a devastating complication of injection OPR use, has been understudied.

Methods: We conducted a retrospective chart review of IE cases at an academic tertiary care hospital in North Carolina. Hospital admissions from 2009-2014 were screened for cases of definite IE. Subjects reporting injection drug use (IDU) were classified as IDU-IE, and compared to those without reported IDU, classified as No IDU-IE. Rates of IDU-IE and No IDU-IE, patient demographics, microbiologic data and outcomes were compared between the groups.

Results: A total of 127 incident admissions for IE were identified, 48 (37.8%) were classified as IDU-IE and 79 (62.2%) as No IDU-IE. IDU-IE cases increased from 14% of hospitalizations for IE in 2009 to 56% in 2014; reporting of OPR injection increased in 2012 and continued through the study period. IDU-IE subjects were younger (32.6 ± 11.7 versus 54.4 ± 13.1, $P < 0.0001$), more likely to be single ($n = 33$ [68.8%] versus $n = 23$ [29.1%], $P < 0.0001$) and to reside in rural communities ($n = 36$ [75.0%] versus $n = 25$ [31.6%], $P < 0.0001$) than No IDU-IE subjects. Hospital length of stay (26 days versus 12 days, $P < 0.0001$) and intensive care unit length of stay (2 days versus 1 day, $P = 0.04$) were longer for IDU-IE patients and hospital mortality did not differ (10.4% IDU-IE versus 8.9% No IDU-IE, $P = 0.77$).

Conclusions: IDU-IE rates increased over time, and OPR injection use in rural communities appears to be a major contributor. Interventions to reduce IDU-IE and OPR misuse are needed to halt this growing epidemic in at-risk rural communities.

Key Indexing Terms: Injection drug use; Oxymorphone; Critical care; Infection; Opana. [Am J Med Sci 2016;▮(▮):▮▮▮–▮▮▮.]

INTRODUCTION

Opiate pain reliever (OPR) prescribing has increased substantially over the past 15 years in the United States, and OPR overdoses and deaths in this country have outpaced those from heroin and cocaine.[1-3] OPR overdoses and injection drug use (IDU; via subcutaneous or intravenous injection of crushed pills or other substances) began to rise in the early 2000s, particularly in rural communities.[4,5] More recently, OPR IDU has received significant attention because of its association with a community outbreak of human immunodeficiency virus (HIV) and hepatitis C virus (HCV) infections in rural communities in the Midwest and Southeast U.S.[6,7] At our tertiary care academic medical center in north central North Carolina, we anecdotally observed an increase in the frequency of hospitalizations related to OPR IDU.

One of the most devastating consequences of IDU is the development of infective endocarditis (IE). IE is an infection of the endocardial surface of the heart in which an infected thrombus, or vegetation, forms on the native or prosthetic valve in the setting of bacteremia and endothelial damage. IE is associated with organ failure, prolonged hospitalization, high cost and death in up to a quarter of patients.[8,9] Unsterile practices during preparation and injection of OPRs that introduce skin and oral bacteria into the bloodstream may be one mechanism for the increased risk of IE in this population.[10,11] Although HIV and HCV outbreaks among OPR injection drug users have received significant media attention, studies examining IE in these patients are lacking. Therefore, to identify temporal trends, demographics and outcomes of IE at our hospital and to examine the temporal association of IE with IDU, we performed a retrospective chart review of hospitalizations related to IE at our medical center from 2009-2014.

METHODS

Study Location

The study was conducted at Wake Forest Baptist Medical Center (WFBMC), an 850-bed academic medical center with approximately 42,000 hospital admissions per year located in Winston-Salem, NC, U.S.A. It serves as a tertiary care medical center for the surrounding north-central region of North Carolina and rural areas of western Virginia, West Virginia, and eastern Tennessee.

Study Design

This study was approved by the Wake Forest School of Medicine Institutional Review Board. Subjects were identified initially by screening the hospital database for admissions to WFBMC for patients aged 18 years or older hospitalized with primary ICD-9 codes for IE from January 1, 2009 to August 31, 2014. ICD-9 codes used to screen hospital records were 421.0, 421.1, 421.9, 424.90, 424.91 and 424.99. Cases of IE identified by ICD-9 were verified by individual chart review. Patients were only classified as having IE if they met the modified Duke Criteria for definite IE.[12] For patients with recurrent admissions to WFBMC for IE, only the initial hospitalization during the study period was recorded. IDU-IE was defined if IDU was acknowledged by the patient and documented in the medical record during that hospitalization. For those cases in which there was high clinical suspicion for IDU though denied by the patient, the hospitalization was classified as IDU-IE if the patient had a history of IDU and associated bacteremia documented in the year before index hospitalization at our medical center. The definition of IDU-IE was determined *a priori* individual chart review. Cases without IDU criteria were classified as No IDU-IE. The incidence of total IE cases during the study period was normalized to hospital admissions over each interval to determine if new IE cases represented a change in IE incidence or the overall rate of hospital admissions.

Study Variables

Patient demographics and clinical data were obtained from the medical chart for each case of IE meeting the above criteria during the study period. Counties of residence were classified as rural or nonrural based on delineations from the United States Office of Management and Budget from 2013 (http://www.census.gov/population/metro/).

Statistical Analysis

Data are reported as mean ± standard deviation or *n* (%) or Kaplan Meier estimated median and interquartile range as indicated. Comparisons of groups were made using a two-sample *t* test or a chi-square test for continuous and categorical variables respectively. In determining discharge location, those who died in the hospital were censored. Hospital LOS and intensive care unit (ICU) LOS were compared by the log-rank test. Hospital mortality was a dichotomous variable compared using a chi-square test.

RESULTS

A total of 127 incident admissions to our hospital for IE were identified between January 2009 and August 2014. Of them, 48 (37.8%) were classified as IDU-IE. The remaining 79 (62.2%) were classified as No IDU-IE. Incident IDU-IE cases increased over the study period, with IDU-IE accounting for 14%t of hospitalizations in 2009 and increasing to 56% in the last 4 quarters of our study period (Figure A). We also found an upward trend in both IDU-IE and No IDU-IE cases over the 2013 calendar year, with a doubling of total IE rates compared to other time periods (Figure A). During the study period from 2009 through the third quarter of 2012, we identified only one reported case of OPR injection (oxycodone) in the IDU-IE group. During the fourth quarter of 2012 through 2014, we identified an increase in reporting of OPR injection use, primarily oxymorphone (Opana) and oxycodone (Figure B). The increase in cases of IE beginning in late 2012 coincided simultaneously with the increased reporting of OPR injection use.

Baseline characteristics of the study cohort are reported in Table 1. IDU-IE patients were younger than those without identifiable IDU (32.6 ± 11.7 versus 54.4 ± 13.1 years, $P < 0.0001$). No differences were found in sex and race or ethnicity between the groups, though IE patients were more likely to be male (68.5%) and white

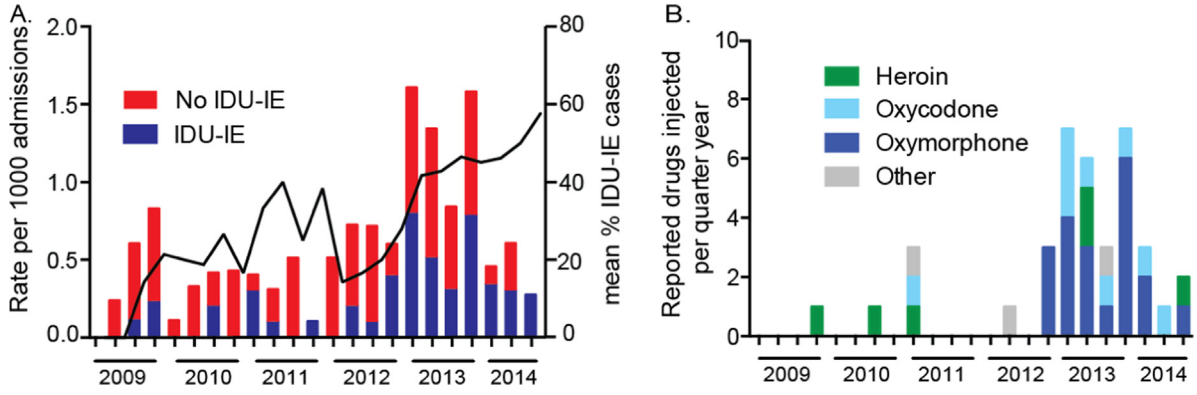

FIGURE. Trends in infective endocarditis and injection drug use. (A) Rates of injection drug use infective endocarditis (IDU-IE) and noninjection drug use infective endocarditis (No IDU-IE) were calculated per 1000 hospital admissions over each quarter year (left *y* axis). Yearly percentages of IDU-IE to No IDU-IE cases over the study period were calculated (right *y* axis). The line represents a 4-quarter moving average of IDU-IE to No IDU-IE. (B) Type of drugs that patients reported injecting in the IDU-IE cohort over the study period. The "Other" category included 1 case each of morphine extended release, methadone and cocaine. Some patients reported injecting more than one drug. In 13 subjects with IDU-IE, a specific injection drug was not identified.