

What's New in the Patient Safety World

July 2017

Antibiotics and Adverse Events

In our November 2015 What's New in the Patient Safety World column “[Medications Most Likely to Harm the Elderly Are...](#)” we cited a study from New Zealand that found medications to be the number one cause of harm to ambulatory patients age 65 and older and antibiotics the most common offenders ([Wallis 2015](#)). The antibiotic category accounted for 51% of all medication injuries and 39% of serious or sentinel injuries.

That was on the outpatient side. Now a new study on almost 1500 patients hospitalized on four general medicine services at Johns Hopkins Hospital ([Tamma 2017](#)) found that 20% of hospitalized patients experienced at least 1 antibiotic-associated ADE (adverse drug event). For non-clinically indicated antibiotic regimens, 20% were also associated with an ADE, including several cases of C difficile infection. Every additional 10 days of antibiotic therapy conferred a 3% increased risk of an ADE. The most common ADEs were gastrointestinal, renal, and hematologic abnormalities, accounting for 42%, 24%, and 15% of 30-day ADEs, respectively.

Importantly, this study followed patients not only through hospital discharge but also following discharge. 27% of the antibiotic related ADE's occurred after hospital discharge. So they recorded ADE's as either 30-day or 90-day ADE's. Many of the antibiotic-related ADE's occurred later. 43% of all the ADE's were found in their 90-day follow up period. 39% of those were C. diff infections and 61% were multiple drug resistant organism infections. The median time to development of a 90-day ADE was 15 days.

The most frequently prescribed antibiotics were third-generation cephalosporins, parenteral vancomycin, and cefepime and 79% of patients received more than one antibiotic. Notable differences were identified in the incidence and types of ADEs associated with specific antibiotics. For example, aminoglycosides, parenteral vancomycin, and trimethoprim-sulfamethoxazole were associated with the highest rates of nephrotoxic effects, QTc prolongation occurred with azithromycin and ciprofloxacin, and neurotoxic effects, including encephalopathy or seizures, occurred with cefepime.

Perhaps the most striking finding is that these rates were seen at Johns Hopkins Hospital, which already has a very robust antibiotic stewardship program. One would anticipate the rates to be even higher at hospitals not having such robust programs.

Avoidability was defined as occurring when antibiotic therapy was considered to be not indicated after review by infectious disease expert reviewers. The rate of potentially avoidable ADE's may have been even higher, since they did not include excessively prolonged durations of antibiotic therapy or inappropriately broad antibiotic use in their calculation of avoidable antibiotic associated ADEs.

In our November 2015 What's New in the Patient Safety World column "[Medications Most Likely to Harm the Elderly Are...](#)" we also noted a US study ([Shebab 2008](#)) that found an estimated 142,505 visits annually were made to US EDs for drug-related adverse events attributable to systemic antibiotics. Antibiotics were implicated in 19.3% of all ED visits for drug-related adverse events. Allergic reactions accounted for 78.7% of visits. Those authors suggested that minimizing unnecessary antibiotic use by even a small percentage could significantly reduce the immediate and direct risks of drug-related adverse events in individual patients.

And, of course, inappropriate antibiotics are not limited to ambulatory and acute care settings. Up to 75% of nursing home patients are also inappropriately given antibiotics ([CDC 2015a](#)) and CDC has recommended that all nursing homes implement its "Core Elements of Antibiotic Stewardship for Nursing Homes" ([CDC 2015b](#)).

Antibiotic related ADE's can lead to prolongation of hospital stays and, given that some of the ADE's occur later, can also lead to rehospitalizations or emergency room visits. Hence, not only are antibiotic related ADE's harmful to patients but they also can add considerable cost to our healthcare system. This provides increased emphasis on the need for effective antibiotic stewardship programs.

Some of our prior columns on antibiotic stewardship:

- October 14, 2014 "[Antibiotic Stewardship](#)"
- November 2015 "[Medications Most Likely to Harm the Elderly Are...](#)"
- July 2016 "[NQF/CDC Guideline on Antibiotic Stewardship](#)"
- August 2016 "[Some Reassurance on Antibiotic Stewardship](#)"
- November 2016 "[C. Diff and Your Predecessor's Room](#)"
- December 2016 "[Update on Ambulatory Antibiotic Stewardship](#)"

References:

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