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Adverse events associated with fluoroquinolone and macrolide therapy in adult outpatients treated for community-acquired pneumonia

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Background: Community-Acquired Pneumonia (CAP) is a significant cause of morbidity and mortality across the U.S. Due to voluntary adverse event (AE) reporting systems, it is anticipated that AEs are underreported among outpatients with CAP. There are also sparse published real-world data on the frequency of certain AEs with antibiotics used among outpatients with CAP. This study sought to quantify and compare select AEs of interest among adult outpatients with CAP who received fluoroquinolone or macrolide monotherapy.

Material/methods: Study design: U.S. retrospective claims analysis of MarketScan® Commercial & Medicare Supplemental Databases. Inclusion criteria: (1) ≥18 years old, (2) ICD-9-CM codes for CAP in the outpatient setting from 2011 to 2015, and (3) received a macrolide or fluoroquinolone as monotherapy. Patients were excluded if any antibiotic prescription claim was filled in the 30 days prior to the CAP episode. Data on patient demographics, insurance source, comorbid conditions, healthcare resource utilization, pharmacy claims, vital status, and antibiotic treatment failure were collected. Incidences of ventricular tachycardia, tachycardia, jaundice, elevated liver enzymes, liver failure, tendonitis, tendon rupture, peripheral neuropathy, neuritis, and *Clostridium difficile* were identified by ICD-9-CM codes and compared between treatment groups.

Results: Of the 221,233 in the included population, 112,054 (50.7%) unique patients received macrolide monotherapy (mean age 49.1 years old, 46.4% male, 16.8% Medicare), and 109,179 (49.3%) received fluoroquinolone (mean age 55.1 years old, 49.1% male, 25.4% Medicare). The incidence of AEs by these index drug class are shown in the table. Overall, 1.62% of macrolide patients and 2.22% of fluoroquinolone patients (OR=1.38 [1.30-1.46]; p<0.0001) experienced a selected AE of interest. Among the AE examined, tachycardia, jaundice, elevated liver enzymes, and peripheral neuropathy were more pronounced among fluoroquinolone patients than macrolide patients. Notably, the incidences of tendon related AEs (OR=1.54 [1.30-1.82]; p<0.0001) and *Clostridium difficile* (OR=2.02 [1.44-2.82]; p<0.0001) were greater among patients on fluoroquinolones vs. macrolides.

Adverse Drug Events Among CAP Patients on Antibiotics by Index Drug Class - Age 18 and Above				
Adverse Event	Macrolide	Fluoroquinolone		
	Total N= 112,054	Total N= 109,179		
	N (%)	N (%)	OR [95% CI]	P-Value
Cardiac	973 (0.87%)	1192 (1.09%)	1.26 [1.16-1.37]	<.0001
Ventricular tachycardia	232 (0.21%)	300 (0.27%)	1.33 [1.12-1.58]	0.0001
Tachycardia	762 (0.68%)	926 (0.85%)	1.25 [1.14-1.38]	<.0001
Hepatic	228 (0.20%)	324 (0.30%)	1.46 [1.23-1.73]	0.0002
Jaundice	31 (0.03%)	56 (0.05%)	1.86 [1.20-2.88]	0.0129
Elevated liver enzymes	181 (0.16%)	255 (0.23%)	1.45 [1.20-1.75]	0.0012
Liver failure	22 (0.02%)	26 (0.02%)	1.21 [0.69-2.14]	0.8265
Musculo-skeletal	220 (0.20%)	329 (0.30%)	1.54 [1.30-1.82]	<.0001
Tendonitis	132 (0.12%)	211 (0.19%)	1.64 [1.32-2.-4]	<.0001
Tendon rupture	90 (0.08%)	129 (0.12%)	1.47 [1.13-1.93]	0.0252
Neuropathy	384 (0.34%)	532 (0.49%)	1.43 [1.25-1.63]	<.0001
Peripheral neuropathy	205 (0.18%)	357 (0.33%)	1.79 [1.51-2.13]	<.0001
Neuritis	182 (0.16%)	181 (0.17%)	1.02 [0.83-1.26]	0.5822
Clostridium Difficile	51 (0.05%)	100 (0.09%)	2.02 [1.44-2.82]	<.0001

Conclusions: Adverse events are common in adult outpatients treated for CAP. Significant and serious AEs occur more frequently among patients who receive fluoroquinolone vs. macrolide therapy. Consideration of AE risk potential should be a priority for physicians managing adult outpatients with CAP.