WASHOE COUNTY HEALTH DISTRICT
ENHANCING QUALITY OF LIFE

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EPI-NEWS

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ANTIBIOTIC RESISTANCE THREATS

- The 2nd Year Surveillance Findings of Carbapenem Resistant Organisms (CROs) in Washoe County

Introduction

On October 21, 2011 and March 31, 2017, the Washoe County Health District (WCHD) issued two issues of Epi-News addressing one of the top antibiotic resistance threats, i.e., carbapenem resistant Enterobacteriaceae (CRE). In those two issues, local surveillance data on CRE were published. In 2017, WCHD expanded surveillance from MDRB-CR (Multi-Drug Resistant Bacilli-Carbapenem Resistant) to CRO (Carbapenem Resistant Organisms). This included making CRO a reportable condition in Washoe County for hospital laboratories. This expansion also included investigating cases with carbapenemase-producing organisms (CPO), identifying contacts, and preventing further spread of CPO.

A primary mechanism of carbapenem resistance in Gram-negative bacteria is acquired carbapenemases, enzymes that hydrolyze these antibiotics to make them ineffective. There are five major carbapenemases which pose the largest public health risks. They are: *Klebsiella pneumoniae* carbapenemase (KPC), New Deli Metallo-β–lactamase (NDM), OXA-48 like enzymes, Verona Integron-encoded Metallo-β-lactamase (VIM), and Imipenem Metallo-β-lactamase (IMP). This means resistance genes that code for carbapenemases can be exchanged between different Gram-negative bacteria via genetic packets called plasmids. Resistance can then be spread between different bacteria among patients.

CRO surveillance findings for the first year were published on January 26, 2018 (See here.) The purpose of this issue is to: 1) Share major findings from the CRO surveillance in 2018; 2) Share major achievements in CRO prevention in the community.

Methods

Surveillance is primarily laboratory-based. However, a case having a CPO infection or colonization triggers an individual epidemiological investigation. A case of CRO is defined as an infection or colonization with a carbapenem resistant organism of one individual per year regardless of their resident status. Infection or colonization with a second species of CRO organism or isolation of the same CRO organism in a new site in the same individual is counted as a separate case. Cases of CRO are first identified at local hospital laboratories through antibiotic susceptibility testing (AST). Specimens shown to be resistant to carbapenem drugs are then forwarded to the Nevada State Public Health Laboratory (NSPHL) for further testing. NSPHL performs its own AST, along with the modified carbapenem inactivation method (mCIM) to identify if the organism produces carbapenemase. If it does, this means the organism is positive for CPO. A PCR will then be performed to determine which carbapenemase is produced. The positive laboratory result will be reported by NSPHL to WCHD and to the hospital that submitted the specimen. If indicated, WCHD and the hospital will then work together to implement control measures.

Highlights of Findings

Morbidity of CROs and CPOs

In 2018, there were a total of 134 CRO cases and 17 CPO cases reported. Of 134 CRO cases, 43 (32%) had CRE; 87 (65%) had carbapenem resistant *Pseudomonas aeruginosa* (CRPA), and 4 (3%) had carbapenem resistant *Acinetobacter* (CRA) or other CROs. Of 43 CRE cases, 15 (35%) were CPO cases. Of 87 CRPA cases, one (1.1%) was a CPO case. The 17 CPO cases by organism and type of carbapenemase are listed in the table below.

Organism	Types of Carbapenemase			
	KPC	NDM	OXA-48-Like	VIM
E. coli	5	1	1	
E. cloacae	1			
K. pneumonia	5	1		
K. Oxytoca			1	
P. aeruginosa				1
Not isolated	1			

The non-KPC cases reported in 2018 were either associated with hospitalizations in foreign countries or seeking medical care in foreign countries. A total of 47 contacts associated with these 17 CPO cases were identified and tested. Of 12 KPC cases, six KPC cases were associated with an outbreak in a group home.

Demographics & Descriptive Characteristics

Of 134 CRO cases, the median age was 70 years (range: <1-95 years). The youngest patient was a one-month-old baby who had an underlying condition which required surgery and had CRE but not CPO. The source of CRE was unknown. Fifty-seven percent (57%) of cases were male and 76% were White, non-Hispanic. Twenty-seven (27%) were not Washoe County residents but were hospitalized in Washoe County. The specimen sources included: urine (44%), wound (20%), respiratory (17%), rectal (11%), invasive sites (4%), surgical sites (1%), and other (2%). Patient settings included: inpatient (45%), outpatient (34%), long-term acute care (10%), skilled nursing facility (6%), and intensive care unit (4%).

Severity by Number of Antibiotic Classes

Of the reported CRO cases, 66% (86/130) were resistant to three classes of antibiotics and 48% (62/130) were resistant to four or more classes of antibiotics. Pan-resistance was defined as non-susceptible to all tested drugs at the clinical lab and 3.8% (5/130) were pan-resistant. The organisms identified as pan-resistant were *Acinetobacter* (2), *Pseudomonas aeruginosa* (2), *K. pneumoniae* (1).

Antibiotic Susceptibility among CROs

Generally, when the bacteria are resistant to the carbapenem class, it is also resistant to multiple antibiotic classes. The following table describes the antibiotic susceptibility among 43 cases of CRE and 87 cases of CRPA in 2018. CRA cases are not included in this table because of the very small number reported.

Table 1. Antibiotic Susceptibility (AS) (%) for CRE and CRPA, Washoe County, 2018

Antibiotic*	CRE (%S)	CRPA (%S)
Ampicillin	3	5
Piperacillin	13	89↑
Cefepime	32	60↑
Cefotaxime	28↑	0
Cefotetan	17↑	
Ceftazidime	21	69↑
Ceftriaxone	15	0
Cefuroxime	3	5
Cephalothin	0	
Ampicillin-sulbactam	0	0
Piperacilin-tazobactam	19	63
Ciprofloxacin	65↑	45
Levofloxacin	69	37
Amikacin	100↑	91
Gentamicin	81	83
Tobramycin	68	90
T/S	61	0
Aztreonam	24	91
Tigecycline	91↑	
Nitrofurantoin	50↑	
Imipenem	30	1
Meropenem	37↓	31
Ertapenem	13	Intrinsic resistance

*If the number of tests is under 10 it is not included in this table.
↑ An increase of 10% or more compared to AS% in 2017
↓ A decrease of 10% or more compared to AS% in 2017

Novel Treatment Strategies for CPOs

Based on Table 1, it is known that there are not very many antibiotics that are effective against CROs. Treatment of CPO remains very difficult. According to a recently published review article[1], combination chemotherapies seem to be effective against KPC-producing bacteria. Novel combinations (ceftazidime-avibactam paired with aztreonam) are also being explored. Some local clinical laboratories started performing antibiotic susceptibility for this type of novel combination drugs and data are being collected at WCHD. Such data will be shared in a future issue of Epi-News.

[1] Robert A. Bonomo, et. al. Carbapenemase-Producing Organisms: A Global Scourge. Clinical Infectious Disease. 2017;XX(00):1-8.

Coordinated Intervention to Combat CROs

CDC recommended five CRO containment strategies in its recent publication [2], i.e., rapid detection, infection control assessments, colonization screenings, coordination between healthcare facilities, and continued vigilance until spread is controlled. Since January 2017, WCHD has been working closely with local hospitals and state agencies by conducting bimonthly teleconferences. As of March 2019, all hospitals in Washoe County have implemented a screening question about foreign hospitalization history within the past six months during the hospital admissions process. If the newly admitted patient has a history of hospitalization in a foreign country in the past six months, the patient will be placed into contact precautions, a CPO colonization screening test will be ordered and a specimen will be collected. Testing is performed at the state lab. By doing this, Washoe County will quickly identify colonized cases and prevent further spread. A new publication[3] demonstrated that a centrally coordinated intervention is an essential public health tool in reducing CRE in healthcare facilities.

Recommendations for Healthcare Providers

WCHD strongly recommends that healthcare providers (HCPs) in Washoe County take the following actions in terms of combating CROs:[4]

1. Stay aware of facility specific CRO rates (CRE, CRPA, CRA) and community-wide CRO rates by reading WCHD's annual antibiogram at www.tinyurl.com/WashoeAntibiogram.
2. Ask if a patient has received medical care somewhere else, including in another country within the past six months.
3. Place patients currently or previously colonized or infected with CPO on Contact Precautions. Whenever possible, dedicate rooms, equipment, and staff to CPO patients.
4. Wear a gown and gloves when caring for patients with CPO.
5. Perform hand hygiene – use alcohol-based hand rub or wash hands with soap and water before and after contact with the patient or their environment.
6. Alert the receiving facility when you transfer a CPO patient, and find out when a patient with CPO transfers into your facility.
7. Make sure labs immediately alert clinical and infection prevention staff when CPO are identified.
8. Prescribe and use antibiotics wisely.
9. Discontinue devices like urinary catheters as soon as no longer necessary.
10. Please always report CPO cases to WCHD at 775-328-2447 or fax to 775-328-3764.

Acknowledgement

We are grateful to all hospitals, infection control practitioners and laboratory staff for their reporting and collaboration to make this surveillance work possible.

[2] https://www.cdc.gov/mmwr/volumes/67/wr/mm6713e1.htm?s_cid=mm6713e1_w
[3] Debby Ben-David, et. al. Success of a National Intervention in Controlling Carbapenem-resistant Enterobacteriaceae in Israel's Long-term Care Facilities. Clinical Infectious Diseases. 2019;68(6):964-71.
[4] https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html