

Effect of Piperacillin/Tazobactam shortage on hospital associated *Clostridium difficile* infection at a large teaching hospital

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Overview:

Following the global shortage of Piperacillin/Tazobactam, many hospitals have adopted new empirical antibiotics guidelines.

Consequent increased reliance on quinolone and cephalosporin antibiotics may increase rates of *Clostridium difficile* infection (CDI).

Rates of CDI were explored at a large UK teaching hospital.

Following formulary change, CDI increased from 28 to 38 cases per 6 months. Quinolone exposure was notably higher in patients with CDI following the formulary change.

An ongoing Piperacillin/Tazobactam shortage may negatively impact CDI rates.

Introduction:

Since March 2017 there has been a shortage of Piperacillin/Tazobactam subsequent to an explosion at a factory producing its raw materials.

Many hospitals globally have adopted new empirical antibiotic guidelines.

Piperacillin/Tazobactam may inhibit *Clostridium difficile* colonisation during therapy.

Methods:

All cases of hospital acquired CDI April 2016 to October 2017 from a large teaching hospital in Merseyside.

Data collected from CDI post-infection reviews including indication and duration for all in-patient antibiotics prescriptions.

Hospital antibiotic consumption data was collated and compared before and after the formulary change.

Trust antibiotic consumption data:

Antibiotic:	Defined daily doses per six months:	
	Pre-formulary change	Post-formulary change
Ciprofloxacin	12,000	22,000
Tazocin	11,700	2,100

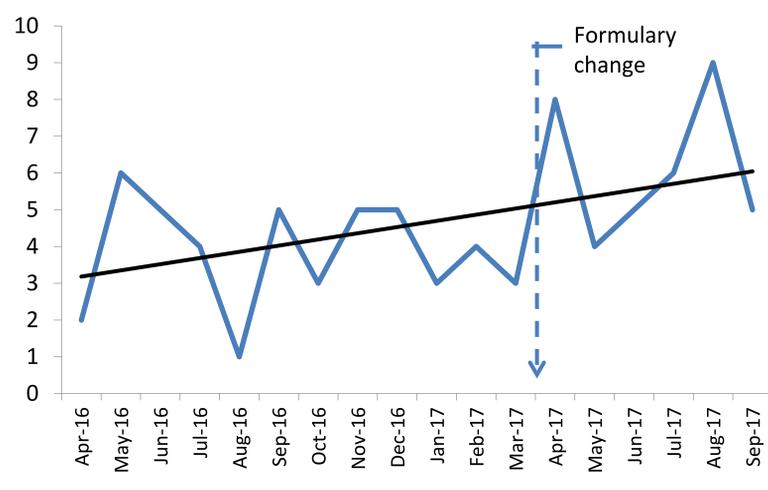
CDI rate pre-formulary change:

Average 28 case/month

CDI rate post-formulary change:

Average 38 cases/month

Graph: CDI cases per month



Characteristics and antibiotic exposure before and after formulary change:

	Pre shortage	Post shortage
Age	76.3 years	72.9 years
Time admission -> symptom onset	15.2 days	19.4 days
Antibiotic exposure prior to symptoms:		
• Piperacillin/Tazobactam	69% (38/55)	16% (5/31)
• Cephalosporin	44% (24/55)	35% (11/31)
• Quinolone	7% (4/55)	39% (12/31)
• Aminoglycoside	2% (1/55)	23% (7/31)
• Meropenem	19% (6/55)	7% (4/31)

Results:

Antibiotic consumption data following the formulary change: quinolone use almost doubled.

On average, 28 cases of hospital acquired CDI per 6-month period before the Piperacillin/Tazobactam shortage.

38 cases per 6-months subsequent to formulary review.

Amongst patients with CDI, formulary change was associated with a significant reduction in exposure to Piperacillin/Tazobactam (53% reduction) and an increased exposure to quinolones (35% increase) and aminoglycosides (21% increase).

No identified changes in infection control practices coincided with increased rates of CDI.

CDI ribotyping did not identify a predominant strain and did not support cross-transmission of ribotypes in clinical areas.

Conclusions:

Increased rate of CDI in the 5 month period following Piperacillin/Tazobactam shortage.

Similar to recent multi-centre research in the USA identifying association between formulary changes to higher risk regimens, and increased rates of CDI. (1)

Piperacillin/Tazobactam may inhibit *C. difficile* colonisation. (2)

Increased reliance on quinolones in the absence of Piperacillin/Tazobactam may be implicated in the increase in CDI rates.

Numbers are small and follow-up is ongoing to monitor this potential emerging challenge for control of CDI.