Changes in the use of broad-spectrum antibiotics after withdrawal of Cefepime from the market : an interrupted time series analysis

C. Plüss-Suard, A. Pannatier, G. Zanetti
University Hospital, Lausanne, Switzerland
ESCP, Geneva
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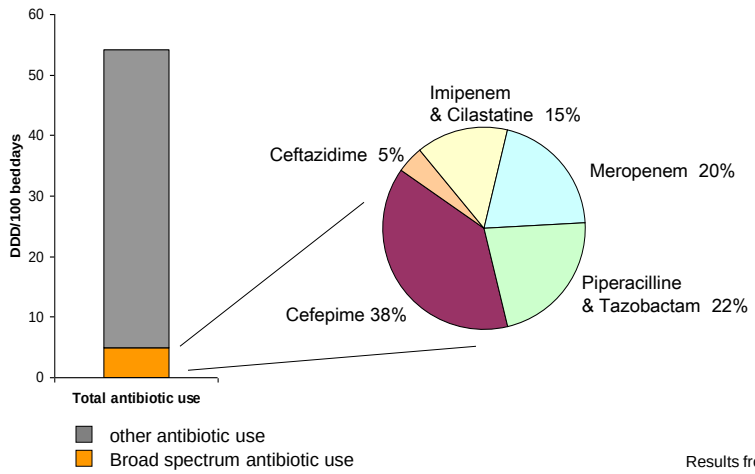
Background and Objective

Cefepime was the most used broad-spectrum antibiotic in Swiss public acute care hospitals in 2006



Results from anresis, 2006

Background and Objective

Cefepime was withdrawn from market in January 2007, and then replaced by a generic since October 2007.

The goal of the study was to evaluate changes in the use of broad-spectrum antibiotics after the withdrawal of the cefepime original product.

Design

How much did the withdrawal change the monthly use of other selected broad-spectrum antibiotics with anti-*Pseudomonas* activity :

Ceftazidime
Imipenem & Cilastine
Meropenem
Piperacilline & Tazobactam

in DDD/100 beddays from January 2004 to December 2008

through a generalized regression-based interrupted time series model

Setting

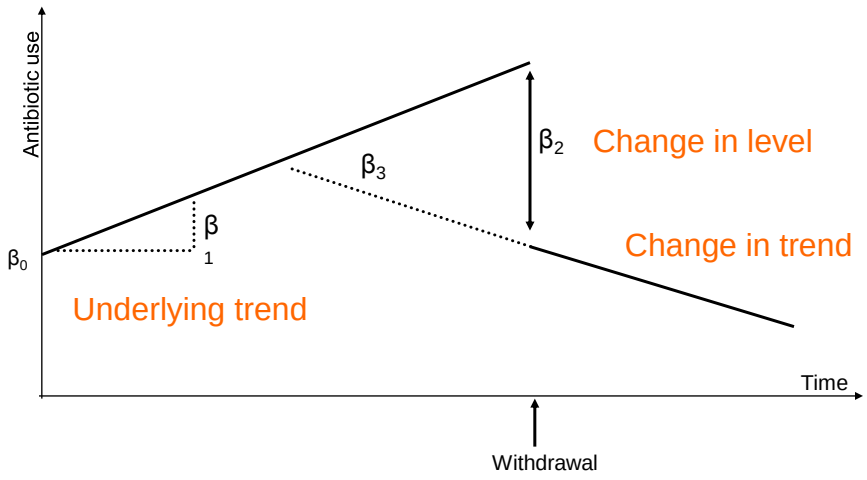
10 Swiss public acute care hospitals

- 7 with < 200 beds
- 3 with 200 – 500 beds

9 hospitals had a shortage of cefepime

1 hospital had no shortage thanks to importation of cefepime from abroad

Main outcome measures



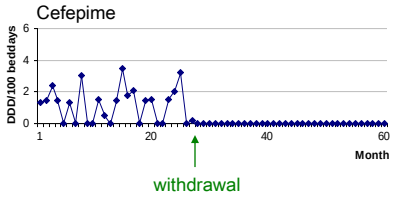
$Y_t = \beta_0 + \beta_1 \times time_t + \beta_2 \times event_t + \beta_3 \times time\ after\ event_t + e_t$

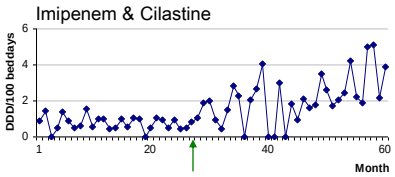
Ansari, JAC, 2003, 52: 842-848; Wagner, J Clin Pharm Ther, 2002, 27: 299-309

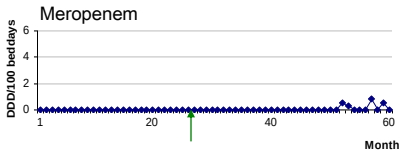
Results

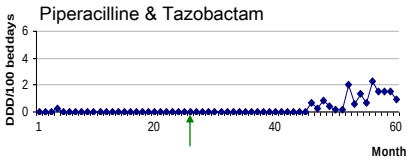
Visual inspection of the series

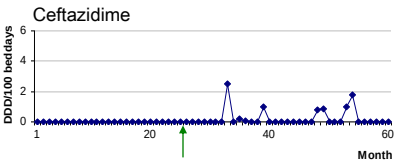
Example of Hospital A





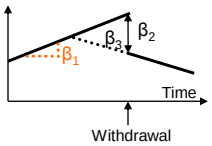






Results II

① Underlying trend β_1



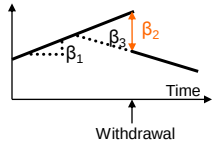
Average decrease by – 0.05 DDD/100 beddays per month

Cefepime

Hospital	Coefficient β_1	p Value
A	-0.0049275	0.850
B	-0.0473721	**0.000**
C	-0.1544024	0.099
D	-0.0000699	0.986
E	-0.1309812	**0.000**
F	-0.0048357	0.952
G	-0.047456	0.348
H	-0.0453755	0.212
I	-0.0147802	**0.001**
J	-0.0336172	0.487

Results III

② Change in level β_2

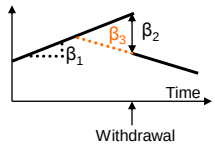


Significant increase of
imipenem & cilastine in 5 hospitals
piperacilline & tazobactam in 1 hospital

	Imipenem & cilastine		Piperacilline & tazobactam	
Hospital	Coefficient β_2	p Value	Coefficient β_2	p Value
A	0.2827179	0.479	0.00426159	0.300
B	-0.1250277	0.400	-1.591833	0.000
C	1.861201	**0.000**	-0.1753089	0.681
D	0.316672	0.182	0.2262886	**0.016**
E	1.265777	**0.006**	-1.069847	0.037
F	3.369909	**0.000**	-1.260862	0.099
G	0.5631727	**0.034**	0.116857	0.519
H	1.138991	**0.025**	0.1666248	0.427
I	-0.51518	0.049	-0.0317878	0.791
J	0.0634558	0.236	0.08244287	0.125

Results IV

③ Change in trend β_3



Greatest for piperacilline & tazobactam

+0.043 DDD/100 beddays per month [95% CI -0.001, 0.089]

Significant in 4 hospitals ($p < 0.05$)

	Piperacilline & tazobactam	
Hospital	Coefficient β_3	p Value
A	0.546144	**0.000**
B	0.0962737	**0.000**
C	-0.0013912	0.964
D	-0.0038368	0.395
E	0.156795	**0.000**
F	0.1046336	**0.027**
G	-0.0390074	0.000
H	-0.0204324	0.141
I	0.0110235	0.216
J	0.1067304	0.136

Conclusion

1. The decrease in cefepime use before its withdrawal was possibly due to pre-existing difficulty in drug supply
2. The withdrawal of cefepime resulted in :
   - an increase in level for Piperacilline & Tazobactam and Imipenem & Cilastine in 6/10 hospitals
   - an increase in trend for Piperacilline & Tazobactam in 4/10 hospitals thereafter
   - no change in the hospital without shortage

⇨ As these changes generally occur at the price of lower bacterial susceptibility, a manufacturers' commitment to avoid shortages in the supply of their products would be important

Future prospects

Measure the impact of the changes :

in cost

in susceptibility rates to these antibiotics

Thanks