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

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Background and Objective

Cefepime was one of the most used broad-spectrum antibiotics in Swiss public acute care hospitals. The drug was withdrawn from market in January 2007, and then replaced by a generic since October 2007.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

A generalized regression-based interrupted time series model1,2 incorporating autocorrelated errors assessed how much the withdrawal changed the monthly use of other broad-spectrum antibiotics (cefazidime, imipenem/clastatine, meropenem, piperacilline/tazobactam) in defined daily doses (DDD)/100 bed-days from January 2004 to December 2008.

Setting

10 Swiss public acute care hospitals (7 with < 200 beds, 3 with 200 – 500 beds). 9 hospitals (group A) had a shortage of cefepime and 1 hospital had no shortage thanks to importation of cefepime from abroad.

Main Outcome Measures

Underlying trend of use before the withdrawal, and changes in the level and in the trend of use after the withdrawal (Fig. 1).

Results

Before the withdrawal, the average estimated underlying trend (coefficient β1) for cefepime was decreasing by – 0.047 (95%CI –0.086, -0.009) DDD/100 bed-days per month and was significant in 3 hospitals (group A, p < 0.01) (Fig. 2,3). Cefepime withdrawal was associated with a significant increase in level of use (β3) of piperacilline/tazobactam and imipenem/clastatine in respectively 1 and 5 hospitals from group A.

After the withdrawal, the average estimated trend (β2) was greatest for piperacilline /tazobactam (+0.043 DDD/100 bed-days per month; 95% CI -0.001, 0.089) and was significant in 4 hospitals from group A (p < 0.05). The hospital without drug shortage showed no significant change in the trend and the level of use. The hypothesis of seasonality was rejected in all hospitals.

Conclusions

The decreased use of cefepime observed before its withdrawal from the market could be explained by pre-existing difficulty in drug supply. The withdrawal of cefepime resulted in change in level for piperacilline/tazobactam and imipenem/clastatine. Moreover, an increase in trend was found for piperacilline/tazobactam thereafter. 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. As perspectives, we will measure the impact of the changes in cost and sensitivity rates of these antibiotics.

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