

Susceptibility of VTEC to antibiotics and antibiotic influence on verotoxin as a VTEC major virulence factor

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Background:

The clinical and public health importance of infection by verotoxin-producing *Escherichia coli* (VTEC) have become increasingly recognized internationally since the early 1980s. VTEC are associated with human disease including mild diarrhea, severe bloody diarrhea and hemolytic uremic syndrome (HUS). They cause HUS mostly in children. Children are hospitalised at Intensive Care Units where they are given antibiotics prophylaxis. However, it has been recognized that certain antimicrobial drugs have capacity to enhance the release of verotoxin. Because antimicrobial agents may play a role in the pathogenesis of severe VTEC disease, chemotherapy for VTEC infections or complications remains controversial.

We report four cases of HUS caused by verotoxin2-positive VTEC. The three patients were treated by cephalosporins because of complications (respiratory tract infection), the last patient was treated by quinolone antibiotic (imminent sepsis). In both cases we detected that given antibiotics *in vitro* were able to enhance production of verotoxin 2 (VT2).

Methods:

MIC test was performed for all clinical VTEC strains associated with HUS. The four clinical VTEC strains (three with serotype O157 and one O26) were incubated with ampicillin/sulbactam, meropenem, cefepime, piperaciline, piperacilline/tazobactam, cefotaxime, ceftazidime, gentamycine, amikacin, ciprofloxacin and trimethoprim/sulfamethoxazole using dilution method. After incubation, the verotoxin was separated and the presence of verotoxins was confirmed by ELISA with monoclonal antibodies against VT2. We used Mann-Whitney U test for statistical analysis.

Results:

All tested strains were susceptible to used antibiotics.

On the basis of ELISA tests we have found that ciprofloxacin, trimethoprim/sulfamethoxazole ($p < 0.001$), amikacin, gentamycine and cefepime ($p < 0,01$) and cefotaxime, ceftazidime, piperaciline, piperacilline/tazobactam ($p < 0,05$) significantly induce the production of verotoxin 2 in case of VTEC O157. In case of VTEC O26, we have found that ciprofloxacin ($p < 0,05$) significantly induces the production of verotoxin 2.

Conclusions:

Antimicrobial drugs play role not only as inhibitors of the bacterial growth but some of them can activate the production of important virulence factors during the SOS response. Our opinion is that it is important to not only isolate VTEC from HUS patients but also to detect the influence of antibiotics which are used in hospitals (and were given in cases reported in this study) to verotoxin production.