The PAE was calculated by the following equation:

\[ \text{PAE} = T - C \]

where \( T \) is the time to achieve 1 log \(_{10}\) cfu/mL growth for the antibiotic-exposed sample and \( C \) is the time to achieve 1 log \(_{10}\) cfu/mL growth for the untreated control sample (Table 1).

In summary, DW-224a showed very potent and dose-dependent bactericidal effect against all strains tested. The clinical usefulness of DW-224a should be established by further studies.

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Transparency declarations

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References


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First description of \( \text{bla}_{\text{CTX-M-1}} \)-carrying Escherichia coli isolates in Danish primary food production

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Sir,

Escherichia coli is a common commensal of the intestinal tract of animals and humans, but can also be an important pathogen. \( E. \) coli isolates resistant to oxyiminocephalosporins due to the production of extended-spectrum \( \beta \)-lactamases (ESBLs) have emerged worldwide and a number of different ESBL genes such as the \( \text{bla}_{\text{SHV}}, \text{bla}_{\text{TEM}}, \text{bla}_{\text{CTX}} \) and \( \text{bla}_{\text{CMY}} \) genes have been identified in \( E. \) coli.\(^1\)\(^–\)\(^3\) The same genes have been shown to encode resistance in different countries, which could indicate a global spread of these genes. The first ESBL-producing bacterium from food animals in Denmark was found in August 2003. This was a \( \text{bla}_{\text{CMY-2}} \)-containing Salmonella Heidelberg isolate obtained from the intestine of a boar imported from Canada.\(^4\) In the same year in October the Danish Institute for Food and Veterinary Research (DFVF) received three Salmonella Virchow isolates found in quails imported from France, which were found to contain \( \text{bla}_{\text{CTX-M-9}} \).\(^5\)

In Denmark ESBL-producing isolates of \( E. \) coli have not previously been isolated from animals in primary food production. However, in July 2005 two \( E. \) coli isolates from infections in pigs showing resistance to cephalosporins were identified during the routine diagnostic testing at the Laboratory for Pig Diseases in Kjellerup, Denmark. The isolates were from two different farms, and one was from a case of diarrhoea (isolate A) and the other one from septicaemia (isolate B).

Isolate A was haemolytic and serogrouped as O149, while isolate B was non-haemolytic and serogrouped as O20. Both isolates were examined for antimicrobial susceptibility by MIC determinations using a commercially dehydrated panel Sensititre (Trek Diagnostic Systems, UK). The following antimicrobials were assayed: ampicillin, apramycin, cefalotin, cefotin, cepodoxime, chloramphenicol, ciprofloxacin, co-amoxiclav, florfenicol, gentamicin, nalidixic acid, neomycin, spectinomycin, streptomycin, sulfamethoxazole, tetracycline and trimethoprim.
In addition, the presence of ESBL genes was determined as described previously. Both isolates were resistant to ampicillin, cefalotin, cefetium and cefpodoxime, and had reduced susceptibility to co-amoxiclav; they both contained blaCTX-M-1 and the ESBL resistance was transferable to nalidixic acid-resistant E. coli MT102 recipients. Isolate B was also resistant to apramycin, gentamicin, neomycin and tetracycline, but resistance to these antimicrobials was not co-transferred with the ESBL resistance. Plasmid purification and hybridization to undigested and PsI-digested plasmids from the donors and transconjugants revealed that the blaCTX-M-1 gene was located on a plasmid with a size of >70 kb and on a band of ~4.5 kb in both isolates and their transconjugants. This could indicate that the plasmids from the two E. coli isolates are related.

The origin of the ESBL genes in the two farms is not known. Contacts to the veterinarians visiting the two farms did not reveal any indication of connections between the farms or trading contacts with other countries. Data from the continuous monitoring of drug usage in Denmark showed that a fourth-generation cephalosporin, cefquinome, had been used for three individual treatments in farm A in 2004, while a third-generation cephalosporin, cefetium, had been widely used in farm B in 2004 and 2005.

E. coli with blaCTX-M-1 have also been reported from both animals and humans in other countries. Thus, there are several international reservoirs from where the resistance could have spread to these two Danish farms.

The present observation showed that ESBL-producing isolates have also emerged in the primary food production in Denmark. Thus, it must be expected that these genes will spread further among food-producing animals and thereby constitute a reservoir of resistant strains and resistance genes that can transfer to and cause treatment problems for humans. The global spread of ESBL-mediated resistance in E. coli and other Enterobacteriaceae is one of the emerging problems we are currently facing. Thus, studies determining the way in which the spread occurs are urgently needed. This is to our knowledge the first report of blaCTX-M-1 from pigs.

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References


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Sir, Klebsiella pneumoniae produces species-specific class A chromosomal β-lactamases that confer resistance to ampicillin, amoxycillin, carbenicillin and ticarcillin. Three families of chromosomal β-lactamases, including SHV, LEN and OKP, have been identified in clinical K. pneumoniae isolates. Plasmid-mediated SHV-type extended-spectrum β-lactamases (ESBLs) are widespread in K. pneumoniae isolates, and there has been a predominance of SHV-12 in south-east Asia. In this study, we investigated the diversity of chromosomal β-lactamase genes in clinical K. pneumoniae isolates from Korean hospitals and the incidence of SHV-12 according to genotypes of chromosomal β-lactamases.