Göteborg, 2020

Recurrent infection with Extended-Spectrum Beta-Lactamase (ESBL)-producing Enterobacteriaceae

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, torsdagen den 4 juni kl. 9.00

av Anna Lindblom

Fakultetsopponent:
Professor Niels Frimodt-Møller
Århus Universitet, Danmark

Avhandlingen baseras på följande delarbeten

I. Lindblom A, Karami N, Magnusson T, Ahrén C. **Subsequent infection with extended-spectrum β-lactamase-producing Enterobacteriaceae in patients with prior infection or fecal colonization.** Eur J Clin Microbiol Infect Dis. 2018; 37: 1491-1497

II. Lindblom A, Kk S, Müller V, Öz R, Sandström H, Ahrén C, Westerlund F, Karami N. **Interspecies plasmid transfer appears rare in sequential infections with extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae.** Diagn Microbiol Infect Dis. 2019; 93: 380-385

III. Karami N, Lindblom A, Yazdanshenas S, Lindén V, Ahrén C. **Recurrence of urinary tract infections with ESBL-producing *Escherichia coli* are caused by homologous strains among which clone ST131-O25b is dominant.** J Glob Antimicrob Resist. 2020, epub ahead of print

IV. Lindblom A, Karami N, Kristiansson E, Yasdanshenas S, Kiszakiewicz C, Kamenska N, Henning C, Ahrén C. **Recurrent urinary tract infections with ESBL-producing *Escherichia coli* are caused by isolates of specific phylotypes and clones.** *Manuscript*

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Recurrent infection with Extended-Spectrum Beta-Lactamase (ESBL)-producing Enterobacteriaceae

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Abstract

Infections with Extended-Spectrum Beta-Lactamase (ESBL)-producing Enterobacteriaceae (EPE) are increasing globally. The most common EPE are the gut pathogens *Escherichia coli* (ESBL-*E. coli*) and *Klebsiella pneumoniae* (ESBL-*K. pneumoniae*). The spread of antimicrobial resistance (AMR) in these organisms is due both to the spread of high-risk bacterial clones and to the transfer of AMR-genes via easily transmissible plasmids. This thesis focuses on factors of importance for recurrent EPE- infection. In **paper I,** the frequency of subsequent EPE-positive clinical cultures in an unselected patient group with a fecal screen or clinical culture positive for EPE was investigated. It was uncommon with a following clinical culture in patients with a positive fecal screen, but a new EPE-infection was common (almost 30%) in patients with a previous EPE-positive clinical culture (>90% urine cultures). In **paper II**, the rate of a change of species and possible ESBL-carrying plasmid transfer between clinical ESBL-*E. coli* and ESBL-*K. pneumoniae* isolates in subsequent infections was investigated by a novel plasmid typing technique, Optical DNA mapping (ODM). The rate of a change of species was shown to be low (<3%). Possible transfer of plasmids was found in a few cases. ODM in these cases rendered valuable information of plasmid numbers, plasmid sizes and the location of resistance genes. **Paper III** was a retrospective study of bacterial factors of importance for recurrent ESBL- *E. coli* UTI in 123 patients. Almost all isolates causing recurrences were of the same phylogroup as the index isolate. PFGE of a subset of isolates showed strain homology in 98%. Phylogroup B2 dominated, and within this phylogroup, presence of the subclone ST131- O25b-*fimH*30Rx was associated with multiple recurrences. In **paper IV**, ESBL-*E. coli* isolates from recurrent and sporadic UTI were prospectively collected. A comparison of bacterial characteristics with focus on ST131-O25b and its subclones showed an increase in risk of recurrence in patients infected with the virulent subclone. In conclusion, this thesis provides valuable new knowledge about factors influencing recurrences of EPE-infection.

Keywords: ESBL, *E.coli*, recurrent infection, UTI, AMR, phylogroup, *fimH*30Rx

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