MCR-1 plasmid-mediated colistin resistance in hospital outbreak in China

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The correspondence by Tian G-B et al. provides details of an outbreak of colistin-resistant Escherichia coli and Klebsiella pneumoniae in a Chinese pediatric oncology unit. The outbreak included six patients of which five had K. pneumoniae and one E. coli. All colistin-resistant isolates were sensitive to carbapenems.

Further background data on colistin resistance in China is found in the paper by Wang Y et al. (Lancet Infect Dis 2017;17:390-9), which analyzed more than twenty thousand Gram-negative isolates and found mcr-1 in 76 (1%) of 5,332 E. coli, 13 (<1%) of 3,480 K. pneumoniae, one (<1%) of 890 E. cloacae, and one (1%) of 162 Enterobacter aerogenes. The risk factors for finding the mcr-1 gene was use of antibiotics before hospital admission, and in the report by Tian G-B et al. also immunosuppression. In both studies the sequence types (ST) were varied and a variety of resistance genes were found and that the mcr-1 gene was found on different plasmids.

The conclusion from these two studies is that colistin resistance is widespread in China also outside hospitals. Hospital outbreaks are not surprising giving that hospitals concentrate severe ill individuals often in need of antibiotics and being immunosuppressed. Once in the hospitals, these multidrug-resistant bacteria are very difficult to get rid of illustrated by the fact that the five K. pneumoniae were clonally related.

Both studies did not look for colistin resistance if the mcr-1 gene was not present, which is a clear limitation.

Interestingly, all six E. coli in the report by Tian G-B et al. were sensitive to meropenem and in the study by Wang Y et al. all 75 isolated with the mcr-1 plasmid were also meropenem sensitive indicating that using meropenem susceptibility as a proxy for colistin resistance will not identify colistin resistance isolates.

The prevalence figures are very high, especially as all types of clinical specimens were included. Furthermore, the high rate of intestinal colonization among healthy volunteers and in particular among hospitalized patients is alarming. The variety of sequence types suggest that mcr-1 plasmids did spread into several lineages of E. coli proving their considerable transmission capacity. These ST types include such well known global clones as ST131 (of which the authors wrongly state that beyond their isolates it was earlier reported from Denmark, only. In fact, it was also reported from a bloodstream isolate from the Arabian Peninsula (Sonnevend A et al. 2016 IJID 50:85-90).

Although systemic colistin use in human medicine is mainly restricted to infections due to carbapenem-resistant isolates, the low rate of carbapenem resistance among the Chinese colistin-resistant E. coli isolates is of concern. Most laboratories restrict colistin susceptibility testing (considerably hindered by the technical difficulties involved, i.e. being restricted to broth dilution) to isolates with decreased susceptibility to carbapenems.

This dangerously leaves colistin resistance (with the possibility of being encoded on easily transmissible plasmids) in these carbapenem susceptible, i.e. the majority of the strains, unnoticed facilitating its spread. The presence of multiple resistance genes on mcr-1 plasmids will provide multiple options to maintain these colistin resistance-coding plasmids in the flora.

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