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Susceptibility of ESBL-producing Escherichia coli to commercial bacteriophage coctails originated in Georgia

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Background: *Escherichia coli* is the leading bacterial pathogen responsible for intestinal as well as extraintestinal infections, including urinary tract infections, bacteremia, and meningitis. ESBL-producing *E. coli* (ESBL-EC), known to be resistant to β-lactams, their combinations and non-β-lactam antibiotics, might lead to infections with limited antibiotic therapy in clinical practice as well as unsuccessful treatment. Due to global emergence of these type of multi drug resistant strains, alternative therapies for their infections are in seach worldwide. Bacteriophage therapy is among the alternatives, since bacteriophages have hight host specificity and actions unrelated of antibiotic targets. They also have self-propogating and self-limiting activities allowing low dosing and bacteriophage elimination following infection resolution.

Material/methods: The *in vitro* susceptibilities of non-replicating 142 ESBL-EC isolated from adults and children with infections in urinary tract and blood were examined using four different bacteriophage cocktails. ESBL production by ESBL-EC was confirmed according to EUCAST criteria and clonality were done using Php-typing method. *In vitro* spot tests were performed to determine the activities of four bacteriophage cocktails (Pyophage, Intestiphage, Enko and Ses) against each isolate. Observing confluent, semi-confluent, opaque lysis or individual plaques determined the isolate susceptibility. When the lysis was not possible, the corresponding isolates were determined to be resistant.

Results: A great majority (131/142, 92.3%) of ESBL-EC strains were determined to be susceptible to at least one commercial bacteriophage cocktail. Enko, Intestiphage and Pyophage preparations were active against more isolates than Ses (87.3%, 81.7%, 81.7% and 59.2% of isolates were susceptible to Enko, Intestiphage, Pyophage and Ses, respectively). 11 of the ESBL-EC isolates were resistant to all commercially available bacteriophage cocktails. Of these, three isolates (18% of resistant to the commercial preparations, 2.1% of entire isolates) were susceptible to specifically prepared bacteriophages isolated from sewage water by an enrichment technique using the commercial phage-resistant ESBL-EC as the host strain.

Conclusions: In this study bacteriophage preparations, that are used as part of standard clinical practice in the Republic of Georgia, were observed to have in vitro activity against ESBL-EC isolated from children and adults in Kayseri, Turkey. Although bacteriophage therapy has been a successful part of standard healthcare practice for decades, the other countries has been sceptical to accept bacteriophages as alternative anti-infectives. However, in this study an in vitro confirmation of their success on a well-characterized isolate collection is reported as an initial action, which is encouraging for their clinical use.