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THE EFFICACY OF MANIPULATING INTESTINAL MICROBIOTA IN ERADICATION OF MULTIDRUG RESISTANT ORGANISM

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Relevance. Antibiotics have benefitted human healthcare, however acquired antimicrobial resistance (AMR) mechanisms in bacteria greatly affects the utility of antibiotics and is a global healthcare burden. In modern healthcare settings, AMR and lack of effective modalities to combat with AMR has made the risk of colonization and infection by multidrug resistant organisms (MDRO) inevitable for hospitalized individuals who are severely immunosuppressed or immunocompromised thus increasing the rate of morbidity, therapeutic failure, relapses, hospitalization duration, mortality and hospital readmissions. At present, validate treatments for multidrug resistant infections (MDRI) or pan-drug resistant infections (PDRI) are scarce and still in trial. Studies on intestinal microbiota and their significant role in human health have been emerging in the recent past. Dynamic composition of intestinal microbiota including unculturable bacteria is a reservoir for antibiotic resistant genes (resistomes), thus helping to maintain homeostasis by colonization resistance. The re-establishment of healthy microbiota as if to manipulate the antibiotic resistant gene against endogenous infections and infection transmission is a viable approach for limiting MDRO. Contemporary studies and development pipelines which focus on non-antibiotic strategies against AMR consider microbiota mediated mechanisms like fecal microbiota transplantation (FMT), probiotics, prebiotics, bacteriophages and synbiotics very promising.

Aim: the objective of this study is to present existing evidence on the assessment of safety and the efficacy of fecal microbiota transplant, probiotics and bacteriophages for therapeutic restoration of colonization resistance thus treating or preventing MDRO infection.

Materials and methods. Herein, this narrative review discusses microbiota mediated current strategies for the control of MDRO and AMR. An organized literature search was undertaken to find studies discussing FMT, probiotics, synbiotics and bacteriophages in treatment for MDRI or decolonisation of MDRO. PubMed, clinical trials.gov, Web of Science, and Google scholar database were used as main search tools. The search was filtered with keywords and timeframe starting from January 2016 to date. 32 studies were found in compliance with the searched criteria and these studies were carefully summarized and reviewed.

Results and their discussion. The administration of FMT, probiotics, synbiotics or bacteriolytic phases were found to have varying degrees of impact against MDR pathogens and reduce resistome abundance and MDRO in the gut. These mechanisms were safe in general and didn't cause AMR as in case of antibiotic therapy, thus can potentially reduce the risk of endogenous infection as well as transfer of resistomes or pathogens to others. Among these mechanisms, FMT was proven the most efficient in decolonizing MDRO and it was also evident that the efficacy of FMT significantly varied with the route of administration, frequency and bowel wash. However probiotics, synbiotics and bacteriophages require more evaluation for their potential efficacy. This presents the need for further studies which will evaluate these mechanisms with proper detail.

Conclusion. Though manipulation of the gut microbial community is well functional in immunocompetent individuals, safety of these mechanisms on immunocompromised individuals should be evaluated. In FMT, specificity is required to be developed for microbes that reside in distinct metabolic niches within the gut and possess different physiology. Though spontaneous eradication of MDRO with time in absence of treatment is not entirely uncommon, availability of adequate treatment options will definitely aid in prevention, control and eradication of MDRO and therapeutic interventions for treatment resistant global outbreaks.