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Editorial

Infective Endocarditis — Time to Switch to Per Oral Antibiotics?

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Few trials in clinical cardiology and infectious disease medicine during the past year have provided such interesting results as the Partial Oral Endocarditis Trial (POET) [1]. By challenging the established notion that antibiotic treatment in infective endocarditis must be administered intravenously, the trial opens up the possibility of a switch to per oral antibiotics in patients who have been deemed stable. This represents a paradigm shift in the treatment of this severe disease, with far-reaching implications for individual patients and society alike.

infective endocarditis (IE) is a rare but significant condition, with an incidence of 1.7 - 6.2 cases per 100,000 patient-years [2]. First recognized in the 17th century, it has been called by many names over the years. Data from the pre-antibiotic era depict a disease with near 100% mortality. After the arrival of penicillin and its derivatives in the decades following World War II, IE became a curable disease. Since then, advances in diagnostics, monitoring, surgical techniques, the establishment of endocarditis teams, and an increased awareness in the medical community have further improved results. The backbone of treatment, namely a prolonged course of intravenous antibiotics, has all the while remained intact [3].

However, modern pharmacokinetic and pharmacodynamic models suggest the possibility of attaining sufficient drug exposure through per oral administration, providing the patient is not critically ill. Hence, the assumption can be made that oral treatment of IE should be equally as efficacious as intravenous treatment in stable patients. Some clinical data exist to support this, but the studies are mainly retrospective. The POET trial is noteworthy for its size and prospective design. One thousand nine-hundred and fifty-four patients with supposed left-side IE were screened for inclusion, of whom 400 were ultimately included and randomized. Patients in the oral group were given two antibiotics of different classes to account for unforeseen individual uptake variations. They were subsequently monitored carefully for clinical signs and lab test results indicating therapeutic failure. Plasma concentrations of the administered antibiotics were also monitored. Results were defined from a composite endpoint of all-cause mortality, unplanned thoracic surgery, septic embolism, and bacteremia relapse. The results were a slight and statistically insignificant advantage in favor of per oral treatment, thereby demonstrating non-inferiority.

While this is certainly promising, some questions remain. The study only pertains to left-side endocarditis. Furthermore, the size of the study allows for conclusions to be drawn only regarding the most common pathogens (namely *Staphylococcus aureus*, coagulase-negative *Staphylococci, Streptococci,* and *Enterococcus faecalis*). While not a major drawback, this does slightly limit clinical applicability. Furthermore, the oral treatment regimen requires administration of two antibiotics, as opposed to the standard intravenous regimen which generally consists of only one drug. This may have an adverse effect on the microbiological ecology of the patient and on the population level. As for the fraction of patients excluded between initial screening and final inclusion (approximately 80%), it goes to show that this new treatment option currently is to be reserved for only a small subpopulation of endocarditis patients.

For these selected patients, however, the advantages are numerous and important, the most obvious of which is the freedom and improved quality of life for individuals not tethered to a hospital. Beyond the purely subjective benefits, early discharge will reduce risks connected to hospitalization, such as immobilization-associated complications and colonization with multidrug-resistant bacteria. Furthermore, frequent skin penetration needed for intravenous drug administration is painful and carries the risk of complications of its own. As for resource management, shortened intravenous treatments result in shorter hospital stays and/or less resource-intensive outpatient care. This, in turn, lowers costs, as well as freeing valuable hospital beds for other purposes.

All in all, the POET trial results are welcome and provide the potential for improving the treatment of thousands of individuals each year. As always, it will be interesting to see how these new recommendations are received by clinicians worldwide and the extent to which they will be implemented in real-world clinical practice. Ideally, the trial will also inspire further research. Right-side endocarditis seems an obvious subject to tackle next, as does endocarditis caused by more unusual pathogens. And surely, the stage is set for a trial that directly compares different lengths of antibiotic treatment.

Conflict of Interest

The authors have no conflicts of interest.

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