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Commentary

Novel and Adjunct Treatment for Drug Resistant Tuberculosis: A Public Health Imperative

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DESCRIPTION

Conventional multi- and extensively-drug resistant TB (MDR/XDR-TB) treatment regimens lack efficacy, are protracted, toxic, resource intensive and are plagued by poor patient adherence. It is therefore no surprise that treatment success rates are dismal. Despite considerable economic investment, South African data show that standardized treatment for MDR-TB resulted in an overall treatment success rate of just 46%. Treatment success rates are even lower in XDR-TB, with two independent studies reporting successful treatment outcomes in just 22% and 16% of patients. The limitations of current MDR/XDR-TB regimens account for the large proportion of unfavourable treatment outcomes. Clinical outcomes for XDR-TB remain poor irrespective of HIV status. Our quantitative and qualitative studies suggest that the adverse effects associated with the XDR-TB drugs and cumulatively high pill burden compared to anti-retroviral therapy (ART) may lead to preferential ART adherence and consequently improved survival, however this did not translate into more favourable XDR-TB treatment outcomes. In addition, treatment failure and mortality rates are high with 19-23% of patients with XDR-TB remaining unresponsive to therapy and 42%-46% dying within two years of treatment initiation. Furthermore, Pietersen and colleagues found that after 5 years of follow-up 73% of XDR-TB patients had died. Alarmingly, 42% of patients with XDR-TB that were discharged had failed treatment. The median survival time of these patients was 19.84 months from the time of discharge. Genotypic methods later showed evidence of disease transmission, from a discharged patient who failed treatment, to another family member. Similarly, a 19 year old HIV negative female was treated for MDR-TB in 2011. She was appropriately treated at an MDR-TB facility, culture converted, remained cultured negative for 18 months and deemed cured.

Nine months later she presented to the same facility with recurrent MDR-TB infection. It later emerged that she resides with her aunt and best friend, both of whom have MDR-TB infection and are poorly adherent to treatment. These circumstances highlight inadequacies in current MDR/XDR-TB treatment and management strategies and their greater public health significance, especially in vulnerable populations. Clinical trials have shown that bedaquilin, delaminid and linezolid improve sputum culture-conversion rates in MDR/XDR-TB patients with attendant adverse events of a predominantly mild to moderate nature. While these scientific advances are encouraging, their long-term epidemiological effect may be limited; these recently available drugs are expensive, are yet to be freely available to all patients and their efficacy in pragmatic, overburdened and resource limited settings is still to be evaluated. Gradually however, genomic mutations in mycobacterium tuberculosis bacilli may render these drugs vulnerable to acquired resistance. Adjunct TB therapies in combination with standard drug regimens offer some promise in the fight against drug resistant forms of TB. A recent open-label phase 1 safety trial found that autologous mesenchymal stromal cell infusion, in combination with standard chemotherapy, in patients with MDR/ XDR-TB resulted in improved radiology at 6 months in 70% of patients with no serious adverse events. Adjunct therapies may additionally improve treatment success rates, shorten treatment regimens, enhance immunity and prevent recurrence. These data suggest that adjunct therapeutic options need to be further explored if we are to achieve better clinical outcomes and accelerate the control of drug-resistant TB.

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