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High prevalence of bedaquiline and linezolid resistance in extensively drug-resistant tuberculosis patients in a Médecins Sans Frontières clinic, Mumbai, India

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Introduction

Bedaquiline (BDQ) and linezolid (LZD) are Group A drugs and form part of shorter and longer BDQ-based regimens under India's National Tuberculosis (TB) Programme. A systematic review including some data from India on acquired BDQ resistance reports 2.2% phenotypic and 4.4% genotypic resistance in patients treated with BDQ-based regimens. The pooled frequency of LZD resistance among drug-resistant tuberculosis (DR-TB) isolates was 4.2% in a different study. The emergence of resistance to BDQ is concerning as it results in difficulties in constructing regimens, and is associated with unsuccessful treatment outcomes among DR-TB patients. Since 2015, Médecins Sans Frontières (MSF) has provided treatment for TB patients in Mumbai with extensive resistance patterns, who need newer drugs and have limited treatment options under India's National TB Elimination Programme.

Methods

We carried out a descriptive retrospective study of routinely collected programmatic data from December 2020 to February 2022. The study population consisted of culture-positive DR-TB patients with BDQ and LZD exposure for over one month, referred to the MSF clinic with 1) suspected or confirmed treatment failure; 2) DR-TB diagnosed household contacts of BDQ-exposed DR-TB patients.

Ethics

This research fulfilled the exemption criteria set by the MSF Ethics Review Board (ERB) for a posteriori analyses of routinely collected clinical data, and thus did not require MSF ERB review.

Results

88 culture-positive samples were subjected to BDQ and LZD drug susceptibility testing (DST). Of these, 27 showed resistance to BDQ, LZD, or both. 22.7% (20/88) showed BDQ resistance, 17% (15/88) LZD resistance, and eight patients (9%) were simultaneously resistant to BDQ and LZD. Of 88 samples, two were DR-TB diagnosed contacts of BDQ-exposed index cases, and the remaining were BDQ-exposed patients (> one month). In the resistant cohort of 27, equal proportions were male and female, and mean exposure to all Group A drugs was 14 months. 74% (20/27) patients had bilateral disease; 26% (7/27) had unilateral disease, of which 67% (18/27) had lung cavities. Simultaneous resistance to clofazimine and fluoroquinolones was found among 30% (8/27) and 78% (21/27) patients respectively. Within the resistant cohort, two patients refused treatment and 25 started on treatment. Out of 25 patients starting treatment, 8% (2/25) successfully completed treatment, 48% (12/25) died, 20% (5/25) failed, 4% (1/25) were lost to follow-up, and 20% (5/25) were still on treatment at the time of analysis. Of the five patients still on treatment patients, two culture-converted and three are still culture-positive after three months of treatment.

Conclusion

We observed a high proportion of BDQ and LZD resistance in patients who previously failed on BDQ and LZD-based regimens. We observe high mortality and unsuccessful outcomes in treating such cases. Designing effective treatment regimens for patients with retreatment episodes and a history of BDQ and LZD exposure is extremely challenging. We urgently recommend increased programmatic access to DST for LZD and BDQ, to ensure early access to effective regimens.

Conflicts of interest

None declared.