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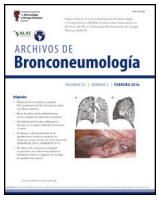

Editorial

Challenges and Outlooks in Multi-drug Resistant Tuberculosis☆

Retos y posibilidades ante la tuberculosis multirresistente

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Drug-resistant tuberculosis (TB) has become one of the major obstacles currently encountered in the control of this disease worldwide.[1] The widespread and sometimes inappropriate use of rifampicin in the last 40 years has generated a growing number of cases of rifampicin-resistant TB (RR-TB). Rifampicin resistance is the most decisive factor in the prognosis of TB patients.[2] If this drug cannot be used, treatment must continue for at least 21–24 months, and combinations of less effective, more toxic drugs[3] are required, leading to cure rates of only 50%.[1] Moreover, more than 90% of RR-TB cases are also carriers of isoniazid (H)-resistant strains[3]; these patients make up the so-called multidrug-resistant TB (MDR-TB) group.

The problem is further compounded by the appearance and spread of cases of extensively drug-resistant TB (XDR-TB), which is MDR-TB that is also resistant to the fluoroquinolones (FQ: levofloxacin and/or moxifloxacin) and second-line injectable drugs (SLID: amikacin and/or capreomicin and/or kanamicin), the 2 most active groups of second-line drugs available, which are the last resort in patients with RR/MDR-TB.[3] It is already estimated that around 10% of cases of MDR-TB are XDR-TB.[1]

The situation surrounding RR/MDR-TB has worsened in recent years. In 2015, 10.4 million cases of TB were diagnosed, of which 580 000 were RR/MDR-TB.[1] Of these, more than half occurred in patients not previously treated for TB,[1] demonstrating that these forms of TB are already being actively transmitted in the community. Studies have shown that, globally, 3.9% of untreated cases of TB (initial or primary MDR-TB) and 21% of previously treated cases have RR/MDR-TB, leading to 250 000 deaths.[1]

The situation is even more worrying if one considers that only 25% of these patients are receiving effective treatment, and among those that do, only 52% are achieving cure (30% in XDR-TB). In other words, only about 10% of cases of MDR-TB worldwide are being cured.[1] It is clear that these numbers only represent individual benefits, while the epidemiological impact remains practically zero and the epidemic continues unchecked.

Fortunately, the RR/MDR-TB situation in Spain is much more encouraging, thanks in particular to the good clinical management of cases of TB in the past.[2] So, while the problem is difficult to quantify due to under-recording of TB cases and no systematic determination of resistance profiles, it seems that primary MDR-TB occurs at a rate of around 0.1% in Spanish natives and 2.2% in immigrants.[4] In 2015, only 42 cases were reported to the WHO, and no follow-up information on the progress of these patients was provided.[1]

If the global MDR-TB epidemic is to be controlled, at least 90% of patients must be detected and offered treatment, and 90% must be cured.[5] To improve detection and to reduce the time to diagnosis, all suspected TB cases must be tested with rapid molecular detection, using GeneXpert or another similar technique.[6] GeneXpert is a real-time PCR that not only greatly increases the sensitivity of the sputum smear in the initial diagnosis of TB, but also detects rifampicin resistance in the same process, all in the space of less than 2 hours.[7]

Patients with rifampicin-sensitive TB will be easily cured with the initial TB treatment regimen used worldwide (2 HRZE/4 HR).[3] Patients with RR-TB, however, must also undergo molecular testing that will detect resistance to H, FQs and SLIDs, so that they can be offered the best treatment possible from the word go. Standardized, conventional PCRs are now available which provide results in only 1–2 days, and are marketed under the names GenoType or LPA (Line Probe Assay).[8] This is only way to improve detection of RR/MDR-TB and XDR-TB and offer patients the most appropriate treatment.

To improve the lamentably low cure rates among these patients, cases of RR/MDR-TB which remain sensitive to FQs and SLIDs must receive a protocolized short treatment (9–12 months) of second-line drugs.[9] Cure rates of around 85%-90% have been achieved with these short regimens only, compared to the mean 52% cure achieved with the conventional 21- to 24-month regimens used to date.[1,9]

Cases in whom MDR-TB plus resistance to FQs or SLIDs or both (XDR-TB) is detected require an individualized regimen aimed at administering at least 4 drugs not previously used in that patient.[3] Of particular interest are the highly potent linezolid, and the new drugs bedaquiline and delamanid, both of which are already approved by the WHO.[9] These 3 drugs, along with others, such as the carbopenems (imipenem, meropenem, ertapenem) and clofazimine,[10] are achieving cures in a large majority of XDR-TB patients.

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Despite major concerns regarding the current global situation surrounding MDR-TB, important diagnostic and therapeutic advances have been made in the last 5–10 years that are of great help in achieving early diagnoses and high cure rates in this form of the disease. The next challenge may be to apply these advances on a worldwide level, although admirable efforts are being made in recent years to ensure the worldwide implementation within the next 2–3 years of all these strategies, even in the most disadvantaged countries.

Finally, it is important to note that all cases of TB, even in patients with very extensive resistance profiles, have a high possibility of cure if the currently available diagnostic and therapeutic tools are employed.

References

1. Organization WH. Global tuberculosis report 2016. World Health Organization Document; 2016. WHO/HTM/TB/2016.13:1–204.
2. Caminero Luna JA. Origen, presente y futuro de las resistencias en tuberculosis. Arch Bronconeumol. 2001;37:35–42.
3. Caminero JA, van Deun A, Fujiwara PI, Monedero I, Chiang CY, Rieder HL, et al. Guidelines for clinical and operational management of drug-resistant tuberculosis. Paris: International Union Against Tuberculosis and Lung Disease; 2013.
4. García-García JM, Blanquer R, Rodrigo T, Caylà JA, Caminero JA, Vidal R, et al. Social, clinical and microbiological differential characteristics of tuberculosis among immigrants in Spain. PLoS ONE. 2011;6:e16272, http://dx.doi.org/10.1371/journal.pone.0016272.
5. World Health Organization. Implementing the End TB Strategy: the essentials. World Health Organization Document; 2015. WHO/HTM/TB/2015.31:1–113.
6. Caminero JA, Migliori GB. Automated digital microscopy in new tuberculosis diagnostic algorithms. Can it boost case finding? Am J Respir Crit Care Med. 2015;191:1352–3.
7. World Health Organization. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB in adults and children. Policy update. World Health Organization Document; 2013. WHO/HTM/TB/2013.16:1–79.
8. World Health Organization. The use of molecular line probe assays for the detection of resistance to second-line anti-tuberculosis drugs. Policy guidance. World Health Organization Document; 2016. WHO/HTM/TB/2016.07.
9. World Health Organization. WHO treatment guidelines for drug-resistant tuberculosis. 2016 update. World Health Organization Document; 2016. WHO/HTM/TB/2016.04:1–59.
10. Caminero JA, Scardigli A. Classification of antituberculosis drugs: a new proposal based on the most recent evidence. Eur Respir J. 2015;46:887–93.