The widespread and sometimes inappropriate use of rifampicin (R) over the past 40 years has given rise to a growing number of rifampicin-resistant tuberculosis (RR-TB) cases, which has become the most decisive factor in the prognosis of TB patients. Treating TB without rifampicin involves long-term therapy over several months with less effective and more toxic drugs, resulting in a cure rate of just 50%. In addition, more than 90% of RR-TB patients are also resistant to isoniazid (H), and this condition is known as multidrug-resistant TB (MDR-TB). More and more cases of RR-TB/MDR-TB are being identified each year. Of the 10.4 million cases of TB diagnosed worldwide in 2015, 580,000 were RR-TB/MDR-TB. Of these, more than half had not previously been treated for TB, thus showing that there is active community transmission of these forms of TB. Globally, 3.9% of previously untreated TB cases (initial or primary MDR-TB), and 21% of previously treated cases are identified as RR-TB/MDR-TB. The mortality rate has risen to 250,000 cases. The problem further intensifies with the onset and spread of what is known as extensively drug-resistant TB (XDR-TB), which is characterised by MDR-TB plus extensive resistance to fluoroquinolones (FQs), levofloxacin and/or moxifloxacin and second-line injectables (SLIs, amikacin and/or capreomycin and/or kanamycin). These are the two most active second-line drug groups currently available and the only ones to offer a potential cure to patients with RR-TB/MDR-TB. It is estimated that around 10% of MDR-TB cases are XDR-TB.

The situation is further exacerbated by the fact that only 25% of MDR-TB patients have access to effective treatment and only 52% of these are successfully cured (30% of XDR-TB patients). In other words, only around 10% of all MDR-TB cases worldwide are being cured. With these outcomes it is clear that any benefit achieved will only affect individual patients with a practically negligible epidemiological impact, thus giving rise to an uncontrolled epidemic.

In Spain, however, the RR-TB/MDR-TB outlook is fortunately much more favourable, thanks in large part to the historical effective clinical management of TB cases.

To attempt to control the worldwide MDR-TB epidemic, at least 90% of patients must be correctly identified and have access to appropriate treatment, and a cure rate of 90% must be achieved. To increase detection and prevent delayed diagnosis, rapid molecular tests must be conducted in all suspected TB cases using GeneXpert or a similar test. GeneXpert uses real-time PCR, which not only offers significantly greater sensitivity than sputum smear microscopy in the initial TB diagnosis, but also detects resistance to rifampicin in the same process. What is more, the entire test takes less than 2 hours.

Patients who test positive for RR-TB or MDR-TB must also undergo molecular testing for resistance to H, FQs and SLIs in order to offer the most appropriate treatment from the outset. To improve the extremely low cure rate, patients with RR-TB/MDR-TB who are not resistant to FQs and/or SLIs should be administered a standardised and shortened (9-12-month) second-line treatment regimen. Only these shortened regimens have achieved cure rates approaching 85-90%, compared with a mean cure rate of 52% for the conventional regimens of 21-24 months prescribed to date.

For MDR-TB patients who are also resistant to FQs, SLIs or both (XDR-TB), personalised regimens comprising at least 4 new drugs not previously administered to the patient must be prescribed. Where possible, these should include the potent drug linezolid and the new drugs bedaquiline and delamanid, which have already been approved by the WHO. These 3 drugs, together with other agents like carbapenems (imipenem, meropenem, ertapenem) and clofazimine, are successfully curing the vast majority of XDR-TB patients.
Although the current MDR-TB situation worldwide is a cause for grave concern, notable diagnostic and therapeutic advances have been made in the past 5-10 years that have significantly contributed to earlier diagnosis and higher cure rates for this disease subtype.

References


