Editorial

Evaluating the efficiency of polymerase chain reaction in diagnosing pulmonary tuberculosis in indigenous and non-indigenous patients

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The DOTS strategy was proposed by the World Health Organization (WHO) in 1993 with the objective of containing the global expansion of tuberculosis (TB).

This strategy emphasizes the decentralization of diagnosis and treatment in order to increase the access of the population to the health system, while maintaining the quality of health care through supervision, quality control and monitoring.

The goals of the WHO have been the detection of 70% of the patients with active TB, in addition to the treatment success of at least 85% of the cases detected.

In countries that have achieved high levels of implementation of the DOTS strategy, the overall rate of treatment success has increased from 60% to 82%. However, case detection remained stable at 43%.[1]

Therefore, the increase in the case detection of pulmonary TB has come to be considered an additional worldwide strategy for the 2006 to 2009 period.[2] The majority of studies that evaluate molecular biology techniques for the diagnosis of TB have been carried out in industrialized countries, and few studies have evaluated the clinical usefulness of such techniques as routine procedures.[3-5] In developing countries, the analysis of molecular biology techniques in the diagnostic field has not been prioritized, due to its elevated costs, technical and operational difficulties of implementation, even in reference laboratories, and due to the lack of information on its clinical relevance and/or the cost-effectiveness ratio in different clinical scenarios. Among the few reports described in these regions, most of those evaluating new molecular methods for the diagnosis of TB are based on laboratory diagnostic criteria or on the use of clinical information to evaluate conflicting results.[6-7] In addition, laboratories do not consistently employ the necessary quality or biosafety controls.[8] Data on the cost-effectiveness ratio of these methods as routine procedures were only recently described in a study carried out in an African country. According to this study, the use of PCR was cost-effective when compared to traditional methods.[9]

Based on these facts, a study on the accuracy of PCR in the diagnosis of pulmonary TB, such as the one carried out in the Brazilian state of Amazonas by Salem et al. and published in this issue of the Brazilian Journal of Pulmonology, is highly relevant and pertinent.[10]

The authors comment on the possible alternatives to an ancient problem: the low diagnostic yield of smear microscopy in the diagnosis of pulmonary TB in indigenous populations in Brazil.[11]

In this study, in selected respiratory samples, using culture as the gold standard, the accuracy (sensitivity and specificity) of PCR was compared with in natura and concentrated smear microscopy, as well as with mycobacteria culture.

The authors emphasized some important aspects: less sensitivity of direct and concentrated smear microscopy in sputum samples among indigenous (ranging from 0 to 1.2%) than among non-indigenous subjects (ranging from 25% to 44.7%); greater incidence of atypical mycobacteria in indigenous (11%) than in non-indigenous patients (3.3%); a high rate of false-positive PCR results (14%), principally in clinical samples of indigenous patients containing atypical mycobacteria.

These results suggest the existence of mycobacteria species with DNA regions homologous to the Mycobacterium tuberculosis *IS*6110.

Unfortunately, Salem et al. did not employ additional molecular biology techniques in the nontuberculous mycobacterial strains, since those samples were discarded after their correlation with

the M. tuberculosis complex had been ruled out.

Such an analysis could confirm or refute the results mentioned by some authors regarding false-positive PCR results with *IS*6110 in atypical mycobacteria isolates;[12] and, in case they are present in this population in Amazonas, it could define which atypical mycobacteria present DNA regions homologous to the *M. tuberculosis IS*6110.

Nevertheless, the following positive aspects are of note: this is one of the rare manuscripts with appropriate scientific methodology on the accuracy of PCR in the diagnosis of pulmonary TB in indigenous or immunocompetent individuals and residents in regions of high prevalence of infection by atypical mycobacteria; this study used PCR with primers that amplify the *IS*6110 sequence, recently described in a meta-analysis as the most accurate sequence in the diagnosis of tuberculosis;[13] the findings of this study were correctly commented upon in the discussion of its limitations.

Therefore, these findings call for the implementation of routine mycobacteria culture, and not only sputum smear microscopy, in the diagnosis of pulmonary TB in indigenous patients, rather than, as recommended by the Ministry of Health, only in patients infected by the human immunodeficiency virus or suspected of suffering from drug-resistant TB.

In addition, in developing countries such as Brazil, there is an urgent need for other studies on the accuracy and performance of new diagnostic technologies for neglected diseases. Such studies should analyze laboratory results, as well as sociodemographic, clinical and radiological variables, which are rarely included in studies conducted by researchers working in referral laboratories.

Furthermore, researchers, as well as by those responsible for public policies, should prioritize pragmatic clinical trials in cooperation with the Brazilian Agência Nacional de Vigilância Sanitária (ANVISA, Health Products Oversight Agency), the organization that regulates these studies, in order to define the clinical usefulness of these new technologies, as well as their cost-effectiveness ratio, for further implementation by the Unified Health Care System.

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