INAHTA Brief 2017/038

Title Assessment of biological tests for Pneumocystis Pneumonia (*Pneumocystis jirovecii* infections) diagnosis.

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Reference ISBN number: 978-2-11-151498-0, link to full report in French: https://www.has-sante.fr/portail/jcms/c_2680246/fr/evaluation-des-actes-de-diagnostic-biologique-de-la-pneumocystose-pneumocystis-jirovecii?xtmc=&xtcr=1

Aim

The aim of this work is to evaluate the accuracy of biological techniques for the diagnosis of *Pneumocystis* Pneumonia (bilateral pneumonitis caused by human-specific fungus Pneumocystis jirovecii) in immunosuppressed individuals. It focuses on direct identification of specific fungal organisms by microscopic methods (immunofluorescence -IF, staining methods) and Pneumocystis-specific DNA detection by polymerase chain reaction (PCR) in respiratory fluid samples. In addition, it evaluates the dosage of the soluble antigen β -(1-3)- D -glucane (BG) in blood.

This study was conducted with a view to inclusions in the List of Procedures in Laboratory Medicine reimbursed by the National Health Insurance System in France.

Conclusions and results

The analysed data (from five good practice guidelines, an health technology assessment (HTA) report, two meta-analyses, the points of view of three relevant professional bodies and of the National Reference Centre for Invasive fungal Infections and antifungal Medicines) allow us to conclude that:

I- For the specific research by examination under a microscope:

- Direct microscopic examination of bronchoalveolar lavage fluid (BAL) is currently the first-line examination for the diagnosis of pneumocystosis.
- This research should be carried out by two complementary tests, -IF and a tinctorial staining or two tinctorial stainings - to detect the two fungus life stages called trophic forms and cysts in order to increase the sensitivity. The standard staining methods could allow for identification of other infectious microorganisms responsible for opportunistic infections in these immunocompromised patients.

II- Quantitative real-time Polymerase chain reaction (q-PCR) on BAL can be used to detect Pneumocystis DNA when microscopic examinations have failed despite a high suspicion of Pneumocystis infection with radiological and clinical criteria.

Its use in non-invasive respiratory specimens (sputum, aspirates, rinses) is possible but P. jirovecii Pneumonia cannot be ruled out in the event of a negative result because this test is less sensitive than on BAL.

III- The detection of the pan-fungal β-(1-3)-D-glucane (BG) soluble antigen (Ag) in blood is indicated:

- When differential diagnosis for a febrile pneumonia in an immunocompromised patient is difficult, the BG test on serum is interesting especially when a pulmonary sample cannot be collected. A negative BG result makes it possible to exclude an invasive fungal disease; conversely if positive, other diagnosis data are needed to identify the fungal organism species.
- The BG is tested by a colorimetric assay (modification of the Limulus Amebocyte Lysate pathway).
- This research for BG in serum is not indicated in the therapeutic follow-up.

Methods

The method consisted of:

- Performing a critical analysis of the identified summary literature (good practice guidelines, HTA reports, general/systematic reviews and meta-analyses) after a systematic and selective document research based on methodological quality.
- Then collecting the views of the professional health bodies concerned (Hematology, Infectious Biology, Infectious Diseases (AIDS) and the National Reference Centre).

This material was summarised in a proposal, submitted to the HAS Board for validation.

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