Introduction

Molds from the genus Aspergillus are ubiquitous. Some of them, mainly A. fumigatus, are opportunistic pathogens. They can affect either immunocompetent and immunosuppressed host with a wide range of diseases, some of them lethal without treatment, and are affecting millions of people over the world. Diagnosis of these diseases challenging and relies on multiple criteria. For the immunocompetent host, proof of exposure to Aspergillus with serology, mainly IgG response, is a major criteria of the diagnosis. Many serological techniques are available, however they are not suited for resource-poor settings, being too expensive and/or relying on a stable electric supply. We present here the evaluation of a lateral flow immunochromatographic (ICT) technique for the detection of anti-Aspergillus antibodies in the serum or plasma. This technique produces result in less than 30 minutes with minimal laboratory equipment needed.

Materials and methods

The evaluation was composed of two studies:

- A 4 month single center prospective study (Marseille, France): 44 cases and 210 controls.
- A multicentric retrospective study (Bordeaux, Marseille, Montpellier, Rennes and Toulouse, France): 262 cases and 188 controls

Case definition was based on consensus conference:

- Allergic BronchoPulmonary Aspergillosis (ABPA)
- Chronic Bronchopulmonary Aspergillosis (CPA)
- Chronic colonization in CF
- Acute and Sub-Acute Invasive Aspergillosis (IA-SAIA)
- All other proven localized aspergillosis (abcesses, sinusitis, …)

Controls definition: patients who underwent aspergillus serology testing but did not matched with the above definitions.

Sero logical techniques used to detect anti-Aspergillus antibodies were as follow : Elisa Biorad (Rennes, Bordeaux, Montpellier), WB Aspergillus LDBIO (Montpellier, Bordeaux), Elisa Serion (Toulouse, Marseille), IEP (Toulouse, Marseille, Rennes).

Aspergillus ICT was used by dispensing 15µL of serum or plasma sample then 4 drops of the eluating solution. Results were read with naked eye 20 to 30 minutes later. Positivity of the test was give by the presence of a grey or black line under the “T” sign (see fig).

For all centers where WB was not done as part of the routine follow-up of patients it has been made retrospectively expect for 7 samples from the prospective study (insufficient volume, 2 cases and 5 controls), WB was used according to manufacturer’s instruction. Example of positive WB is shown (see fig).

For both test, Sensibility (Se), Specificity (Sp) and their 95% confidence intervals (95CI – Wilson’s method with correction of continuity) were calculated using clinical status as gold standard. Agreement between both test was given using Cohen’s kappa.

Results

- Prospective study:
  ICT was positive for 40/44 cases and negative for 211/219 controls
  Se = 90.9%
  Sp = 96.3%

- Retrospective study:
  ICT was positive for 232/262 cases and negative for 181/188 controls.
  Se = 88.5%
  Sp = 96.3%

- Total : (disease per disease results for ICT and WB)
  ICT was positive for 272/306 cases and negative for 392/407 controls.
  Se = 88.9%
  Sp = 96.3%

Table 1 : disease per disease results for ICT and WB

<table>
<thead>
<tr>
<th>Aspergillus disease</th>
<th>ICT</th>
<th>WB</th>
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<tbody>
<tr>
<td>ABPA</td>
<td>68/73 (93%)</td>
<td>72/73 (99%)</td>
</tr>
<tr>
<td>APC</td>
<td>72/78 (92%)</td>
<td>77/78 (99%)</td>
</tr>
<tr>
<td>Colonization</td>
<td>84/94 (89%)</td>
<td>81/92 (88%)</td>
</tr>
<tr>
<td>IA-SAIA</td>
<td>16/24 (67%)</td>
<td>19/24 (79%)</td>
</tr>
<tr>
<td>Others</td>
<td>32/37 (86%)</td>
<td>34/37 (92%)</td>
</tr>
<tr>
<td>Total positive (Se)</td>
<td>[94,3-95,6%]</td>
<td></td>
</tr>
<tr>
<td>Total positive (Sp)</td>
<td>[98,3-98,7%]</td>
<td></td>
</tr>
<tr>
<td>Controls (SP)</td>
<td>392/407 (96%)</td>
<td>379/402 (94%)</td>
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</tbody>
</table>

• ICT/WB comparison
  Agreement between both technique was considered to be very good : 657/706 samples gave the same results (93%). Cohen’s kappa: 0.858 [0.819-0.896].

Table 1 : disease per disease results for ICT and WB

Conclusions

The new Aspergillus ICT kit showed excellent performances with 89% sensitivity and 96% specificity. Those performances were very closed of those of the WB (93% sensitivity, 94% specificity). Agreement between both techniques was very good (Kappa 0.858). Due to its ease of use, the ICT brings new diagnostic opportunities in resource-poor settings.

References


Evaluation of new lateral flow device for the detection of anti-Aspergillus antibodies and comparison to the Western Blot

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ICT was positive for 272/306 cases and negative for 392/407 controls.

Se = 88.9%
Sp = 96.3%

ICT was positive for 283/304 cases and negative for 379/402 controls.

Se = 93.1%
Sp = 94.3%