Implementation of the BioFire FilmArray® Respiratory Panel 2 plus as a syndromic approach for diagnosis of respiratory infections

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Objectives

1) Characterize clinical performances of the BioFire FilmArray® Respiratory Panel 2 plus (RP2plus) assay (IUO version) in comparison with FilmArray® Respiratory Panel (RP) and our standard of care (SOC) PCR technique (Respiratory panel MWS R-GENE, bioMérieux®).

2) Define the added value of this complete panel including 22 respiratory pathogens (18 viruses and 4 fastidious bacteria).

Samples tested

Fresh nasopharyngeal swab clinical samples from 190 patients suspected of respiratory infection prospectively collected during 2 months (from 20th of September to 16th of November 2016 = weeks 38 to 46).

Main results

**Global positivity rates:**

<table>
<thead>
<tr>
<th>SOC</th>
<th>Percentage (value of pathogens detected)</th>
<th>Positive samples (%)</th>
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<tbody>
<tr>
<td>RP2plus</td>
<td>35 (including 1 coinfection)</td>
<td>18.4%</td>
</tr>
<tr>
<td>RP</td>
<td>98 (including 3 coinfections)</td>
<td>51.6%</td>
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</table>

**Better performance for rhinovirus and enterovirus detection:**

- RP2plus detected 85 rhinovirus type and enterovirus type.
- SOC detected 28 SOC positive cases.
- ROC detected 21 SOC negative cases.
- RP2plus detected 36 SOC tested.

For samples tested by both SOC and RP2plus, pathogen detection was concordant for 109/112 (92.6%) pathogens.

Molecular detection techniques

- Biofire FilmArray® RP and RP2plus assay, bioMérieux® (third generation of the FilmArray® RP assay including 2 additional pathogens: Bordetella pertussis and Middle East Respiratory Syndrome Coronavirus MERS-CoV; IUO version of the panel, which was identical to the CE-IVD version commercially available).
- SOC routine test (Respiratory Multi Well System MWS R-GENE, bioMérieux®): performed according to viral epidemiology (rhino/enterovirus detection performed on 129/190 (67.9%) samples) and/or specific clinical requests.

Discussion

- Added value of RP2plus versus RP:
  - Improvement on RV&EV, ADV, PIV and CoV detection.
  - No difference could be seen on Influenza and RSV due to the study season.
  - **14.7%** RP2plus positive / RP negative results that could be found in a 3rd PCR technique.

- Added value of RP2plus versus SOC:
  - Clear increase in positivity rate: RP2plus detected 54 additional viruses not detected by SOC. 36 hrRV&EV, 14 PIV and 4 CoV. The same increase was previously reported with RP compared to classical real-time PCR [1-5].

- For Pconivirus detection, RP2plus showed a sensitivity of 93.94% with a negative percent agreement of 89.7%. However, RP2plus did not detect 2 SOC-positive (RP-negative) samples with threshold cycle values of 30.06 and 34.4, but, RP2plus detected 20 SOC-positive (RP-positive) samples with Ct between 30.55 and 43.68. The genotyping of these two viruses is currently under further investigation in the Centre National des Entérovirus, Lyon.

- Identification of 11 coinfections (5.8%) with 2 pathogens not detected by SOC, among those:
  - For a 0.5 year old female patient, RV&EV SRC SOc PCR was positive, however, RP2plus detected a coinfection with M. pneumoniae, requiring antibiotic therapy.
  - For a 68 years old female patient with severe asthma, RV&EV SRC SOc PCR was negative, however, RP2plus detected an influenza A H3-CoV 229E coinfection, requiring patient’s isolation to prevent influenza nosocomial spread.

- None of the patients with RP2plus negative results presented with obvious clinical suspicion of viral infection.

Limit: No semi-quantification data available → switch to a classic real time PCR technique for viral excretion follow-up.

Conclusion

The RP2plus panel showed excellent performances for viruses and fastidious bacteria detection. Its use should improve diagnosis of respiratory infections. The **added value** compared to our SOC is clear (+46% positivity rate) and could be valuable in critical clinical situations as it can detect in a single assay, 22 respiratory pathogens on 300 μl of nasopharyngeal swab samples, the RP2plus is an easy (2 mins hands-on time) and rapid (45 mins of analysis time) tool for 24 hours / 7 days respiratory diagnostic. This test could have an added important value in severe cases (ICU, immunocompromised, cystic fibrosis...).

References


Acknowledgments

BioFire Diagnostics, LLC, Kevin BOURZAC, PhD.

bioMérieux®: Martina HINATOVA, PhD. Hansjoerg SCHWAGGER