Impact of the Implementation of a Rapid Meningitis/Encephalitis Panel on Clinical Outcomes: Multicenter, Retrospective Cohort of Adult and Pediatric Patients

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Background

- Meningoencephalitis is relatively rare and current guidelines recommend empiric use of intravenous (IV) acyclovir for suspected encephalitis[1,2]
- In 2015, the first rapid multiplex polymerase chain reaction (PCR) panel was approved for the detection of central nervous system (CNS) pathogens, the FilmArray® BioFire® Meningitis/Encephalitis (ME) panel[3]
- The FilmArray® BioFire® ME panel detects 6 species of bacteria, 7 viruses, and 2 fungi with a positive percentage of agreement of 100% for 9 of the 14 pathogens[4]
- In clinical trials, the ME panel had a specificity of 99.2% for all analytes except *S. agalactiae* and a sensitivity of ≥95.7% for all targets except human herpes virus 6 (HHV-6) and group B streptococcus, with results available in approximately 1 hour[4]

Initiative Details

Study Purpose

To determine the impact on clinical outcomes of the FilmArray® BioFire® ME panel compared to previously utilized cerebrospinal fluid (CSF) studies (i.e. CSF culture, viral PCR)

Study Design

- Multicenter, quasi-experimental, retrospective cohort of 7 hospitals in a community and academic hospital system
- Adult and pediatric patients aged 0 days to 89 years
- Receipt of empiric IV acyclovir pre- and post-implementation of ME panel
- Pre-ME cohort: April 1, 2016-December 1, 2016
- Post-ME cohort: April 1, 2017-December 1, 2017

PRIMARY OBJECTIVE

To compare the duration of IV acyclovir (hours) for presumed meningoencephalitis pre- and post-implementation of the ME panel

Analyzed by Wilcoxon rank-sum

SECONDARY OBJECTIVES

- Duration of empiric ME antibacterials
- In-hospital mortality
- Hospital length of stay (LOS)
- Intensive care unit (ICU) LOS
- Incidence of acute kidney injury (AKI)
- Test-turnaround time (TAT)

Analyzed by Wilcoxon rank-sum, Chi-square or Fisher's exact test

SUBGROUP ANALYSES

- TAT by number of daily courier trips to the central laboratory
- TAT by distance from the central laboratory

Analyzed by Kruskal-Wallis

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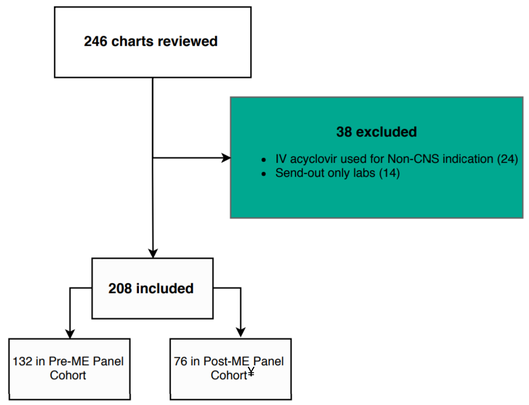
Figure 1. Study Inclusion Algorithm



¥ 76 patients needed in each cohort to achieve 80% power (alpha = 0.05)

Table 1. Patient Demographic Data

Characteristic	Pre-ME Cohort (n = 132)	Post-ME Cohort (n = 76)
Male sex, n (%)	70 (53.0)	44 (57.9)
Age <18 years, n (%)	62 (47.0)	25 (32.8)
Ethnic Group		
Not Hispanic/Latino, n (%)	94 (71.2)	50 (65.8)
Hispanic or Latino, n (%)	35 (26.5)	23 (30.3)
Unknown/other, n (%)	3 (2.3)	3 (3.9)
Facility where lumbar puncture performed		
Non-centralized lab, n (%)	104 (78.8)	62 (81.6)
Centralized lab, n (%)	28 (21.2)	14 (18.4)
Median dose of IV acyclovir (IQR*)		
Pediatric (mg/kg)	19.9 (18.6-20.2)	19.8 (10.1-20.1)
Adult (mg/kg of IBW§)	10.0 (9.5-10.2)	10.0 (9.7-10.2)
Median baseline SCr¥ (mg/dL), (IQR)	0.7 (0.4-0.9)	0.8 (0.4-1.1)
Median baseline CSF WBC/mm³ (IQR)	9.0 (2.0-91.8)	9.0 (2.0-73.5)
Admitted to ICU, n (%)	75 (56.8)	37 (48.7)
CSF tests ordered "stat", n (%)	89 (67.4)	59 (77.6)

* IQR – Interquartile range
§ IBW – Ideal body weight
¥ SCr – Serum creatinine

Table 2. Microbiological Data

Positive Test Results	Pre-ME Cohort n (%)	Post-ME Cohort n (%)
CSF culture	5/132* (3.8)	5/76§ (6.6)
Herpes Simplex Virus (HSV)-1	0/127 (0)	1/76 (1.3)
HSV-2	1/127 (0.8)	2/76 (2.6)
Enterovirus	6/55 (10.9)	9/76 (11.8)
Varicella Zoster Virus (VZV)	2/31 (6.5)	1/76 (1.3)
Cytomegalovirus (CMV)	0/13 (0)	0/76 (0)
HHV-6	0/1 (0)	1/76 (1.3)

*Positive cultures: *Cryptococcus neoformans* (1), gram-positive cocci, unspeciated (1), gram-variable cocci, unspeciated (1), *Streptococcus salivarius* (1), *Haemophilus influenzae* (1)
§Positive cultures: *Staphylococcus aureus* (2), *Streptococcus pneumoniae* (1), *Streptococcus agalactiae* (1), *Streptococcus anginosus* (1)

Results

Figure 2. Primary Outcome Data

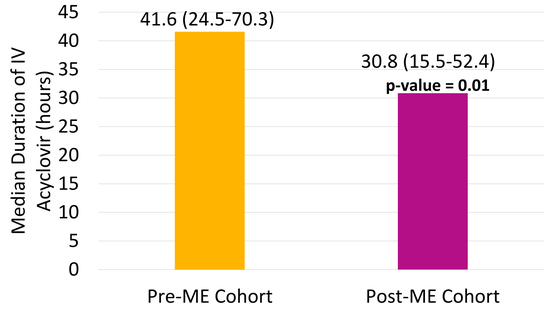
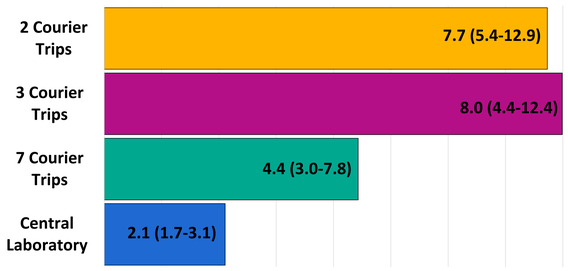


Table 3. Secondary Outcomes Data

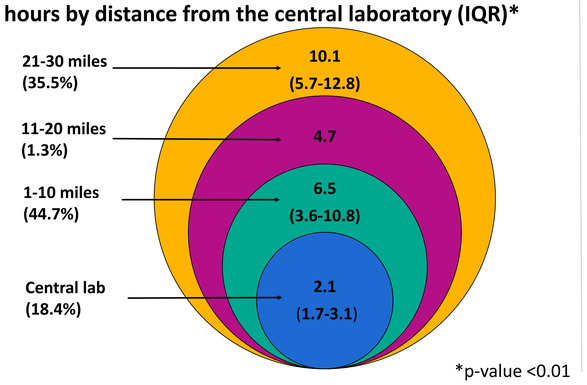
Characteristic	Pre-ME Cohort	Post-ME Cohort	P-value
Median duration of empiric ME antibacterials in hours (IQR)	37.3 (3.4-67.5)	45.3 (18.2-106.9)	0.28
In-hospital mortality, n (%)	2 (1.5)	4 (5.3)	0.19
Median hospital LOS in days (IQR)	6.1 (2.9-11.9)	5.2 (2.4-10.0)	0.59
Median ICU LOS in days (IQR)	4.8 (2.7-8.4)	4.0 (2.3-8.0)	0.49
Incidence of AKI, n (%)	7 (5.3)	3 (4.0)	0.47
Median TAT in hours (IQR)	37.9 (20.9-50.2)	6.2 (3.6-12.2)	**<0.01**
Median time from negative test result to acyclovir discontinuation in hours (IQR)	6.3 (1.5-24.8)	13.3 (7.4-22.8)	0.17

Figure 3. Subgroup Analysis of Post-ME Cohort: Median TAT in hours by number of daily courier trips to the central laboratory (IQR)*



*p-value <0.01

Figure 4. Subgroup Analysis of Post-ME Cohort: Median TAT in hours by distance from the central laboratory (IQR)*



*p-value <0.01

Strengths

- Adult and pediatric patients studied, including neonates
- Multicenter study, including both academic and community hospitals in urban and rural settings
- First to explore the clinical impact of the FilmArray ® BioFire® Meningitis/Encephalitis panel in a multicenter setting

Discussion

- Majority of cohort from non-central laboratory hospital site
- Difficult to assess clinical impact of primary outcome of decreased acyclovir duration
  - AKI due to IV acyclovir can occur anywhere from the first dose to 3 days after initiation of therapy[5-7]
- Limitations
  - Retrospective, chart review
  - Fewer patients included in the post-ME cohort, likely due to:
    - The unfamiliarity of the ME panel when first implemented
    - The enrollment period of the Post-ME cohort began immediately after ME panel go-live date in the health system

Conclusions

- Implementation of the rapid FilmArray® BioFire® ME panel significantly reduced the duration of IV acyclovir throughout the hospital system despite the presence of a central laboratory; however, TAT was significantly affected by both distance in miles and number of courier trips from distant sites to the central laboratory
- Further research should be conducted in a larger population to determine if the ME panel can improve clinical outcomes such as incidence of AKI and length of stay
- The results of this study could be applied to other multicenter health systems considering the implementation of rapid diagnostic tests such as the ME panel to support use
- Health systems implementing the ME panel may consider multiple on-site ME platforms if there are several hospital sites

Definitions

- **Acute Kidney Injury (AKI):** assessed via the RIFLE criteria and pediatric RIFLE criteria
  - Adults: SCr increased ≥1.5x baseline (defined as SCr prior to first dose acyclovir)
  - Pediatric: CrCl decreased by 25% (calculated with Schwartz equation: Length (cm) × K (constant)/SCr)
- **Test-turnaround time (TAT):** time elapsed (in hours) from CSF sample dispatched to laboratory to results updated in patient chart, defined as status change from "Collected" to "Complete"

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Disclosures

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation: All authors have nothing to disclose.

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