1033. Skin Surface Thermal Imaging to Differentiate Cellulitis and Pseudocellulitis in the Emergency Department

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Session: P-58. New Approaches to Diagnostics

Background. Cellulitis is misdiagnosed in up to 30% of cases, resulting in overuse of antibiotics. This represents a threat to patient safety and public health. Surface thermal imaging has been proposed as a tool to reduce errors in diagnosing cellulitis. The study objective was to compare skin surface temperature measurements between patients with cellulitis and pseudocellulitis.

Methods. We prospectively enrolled patients presenting to the emergency department (ED) with dermatologic lower extremity complaints that involved visible erythema. Using a thermal imaging camera, the maximum temperature value (Tmax) for the affected area of skin and corresponding area on an unaffected limb were captured. The Tmax gradient between the affected and unaffected limb was calculated. Gold standard diagnosis (cellulitis versus pseudocellulitis) was determined by consensus of a blinded, multidisciplinary physician review panel (two infectious disease, two dermatologists and two emergency medicine). Differences in temperature variables (Tmax and Tmax gradient) between cellulitis and pseudocellulitis were compared using t-tests.

Results. The sample included 204 participants, 59% male with an average age of 57 years. Based on expert panel consensus diagnosis, 92 (45%) of the participants had cellulitis. The cellulitis group had an average Tmax of 33.2°C and 30.2°C for affected and unaffected skin respectively, which was a significant difference of 2.9°C (CI: 2.5 to 3.6; p < 0.001). The difference in the Tmax gradients between patients with cellulitis and pseudocellulitis was 2.08°C (CI: 1.46-2.70; p < 0.001).

Conclusion. This represents the largest validation study of skin surface temperature differences between cellulitis and pseudocellulitis. Significant difference in temperature gradients between cases of cellulitis and pseudocellulitis suggests thermal imaging could be a useful diagnostic adjunct that can help differentiate these conditions. Such a modality could be particularly helpful in the ED setting where providers must balance diagnostic uncertainty with antimicrobial stewardship principles. Future work will identify the best performing temperature variables and determine optimal cutoff values for use in diagnostic algorithms.

Disclosures. All Authors: No reported disclosures

1034. FebriDx use in Immunocompromised Patients in a Real-World Hospital Setting during the second COVID-19 wave in Italy

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Session: P-58. New Approaches to Diagnostics

Background. The diagnosis of acute respiratory infection (ARI) in patients with immunosuppression secondary to disease or medications is often unclear. Symptoms may be absent or blunted, and acute phase reactants, like procalcitonin (PCT) and C-reactive protein (CRP) may not elevate. For these patients, minor signs or symptoms could lead to hospitalization and antibiotic prescriptions to prevent complications or death. FebriDx® is a rapid, qualitative immunoassay test designed to distinguish between viral or bacterial respiratory infection through simultaneous detection of both CRP and Myxovirus resistance protein A (MxA) from a fingerstick blood sample.

Methods. FebriDx was evaluated as part of a real-world prospective, observational study in hospitalized patients with symptoms of ARI and suspected COVID-19 in a single tertiary care center in Italy (August, 2020 - January, 2021). A sub analysis of patients with expected reduced host immune responses secondary to immunosuppression by disease or medication was performed. (Classified by treating clinician: patient on high dose steroids/ immunosuppressive therapy, or underlying condition like cancer or autoimmune disease). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratios were calculated for FebriDx with respect to the final diagnosis.

Results. We included 28 patients from 200 in the study, 16 patients had a final diagnosis of bacterial infection and 12 had viral infection. FebriDx showed a sensitivity of 91.7% to accurately diagnose viral infection and 93.8% for bacterial infection (see table). Serum CRP was not available for 4 of the patients included (14%) and elevated in the remaining patients. PCT was not available for one patient with viral infection and was elevated in 50.0%.

1035. Manufacturing Processes of SER-109, a Purified Investigational Microbiome Therapeutic, Reduce Risk of Transmission of Emerging and Undetected Infections in Donor Stool

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Session: P-59. New Drug Development

Background. Fecal microbiota transplantation (FMT) is vulnerable to emerging pathogens due to reliance on donor screening for risk mitigation. These concerns were highlighted by dual FDA safety alerts regarding FMT transmission of bacterial pathogens, which were recognized in hindsight only after hospitalizations and deaths. The FDA also warned of potential risk of SARS-CoV-2 transmission, leading to quarantine of FMT in March 2020, two months after COVID-19 was reported on US soil. Conversely, our development program for SER-109, an oral investigational microbiome therapeutic, was prospectively designed to inactive organisms of concern, while purifying the hardy Firmicutes spores. We evaluated whether the manufacturing processes for SER-109 inactivate model organisms, including a coronavirus with gastrointestinal tropism, and a representative Gram-negative bacterium.

Methods. Model organisms were selected based on biologic suitability, detectability, and laboratory safety. Porcine Epidemic Diarrhea Virus (PEDV, a coronavirus) was selected to model SARS-CoV-2. Quantitation used a Vero cell tissue culture infection dose (TCID₅₀) assay. For E. coli, a rifampicin-tolerant Salmonella enterica was selected and quantified with MacConkey lactose agar plus rifampicin. Spiking experiments into representative fecal suspensions were completed to measure inactivation of model organisms. Log-reduction factors (LRF) were calculated based on the drop in organism titer during inactivation. Hold controls in non-electrolyte test matrices were used to confirm specificity of the ethanol inactivation.

Results. In 70% v/v ethanol, PEDV was inactivated by more than 4.2 log₁₀ (to limit of detection, LOD) within 4 minutes (Fig1). In 50% v/v ethanol, S. enterica was inactivated by more than 6.5 log₁₀ (to LOD) within 30 seconds (Fig2).

Figure 1. Inactivation of Porcine Epidemic Diarrhea Virus (PEDV), log₁₀ reduction factor (LRF) versus time

Average of two experiments shown. Also shown is the maximum achievable inactivation based on the limit of detection (LOD).

Table 1: Results for Viral Infection

| FebriDx Result | Viral Infection |
|---------------|----------------|
| Present       | Absent         | Total |
| Positive      | 11             | 0     | 11   |
| Negative      | 1              | 16    | 17   |
| Total         | 12             | 16    | 28   |
| Sensitivity (95% CI) | 91.67% (61.52 - 99.79)% |
| Specificity (95% CI) | 100% (79.41-100.00)% |

Table 2: Results for Bacterial infection

| FebriDx Result | Bacterial Infection |
|---------------|---------------------|
| Present       | Absent              | Total |
| Positive      | 15                  | 1     | 16   |
| Negative      | 3                   | 12    | 15   |
| Total         | 18                  | 13    | 31   |
| Sensitivity (95% CI) | 93.75% (69.77 - 99.84%) |
| Specificity (95% CI) | 91.67% (61.52 - 99.79)% |
Average of three experiments with error bars represent 95% CI. Also shown is the maximum achievable inactivation based on the limit of detection (LOD).

Conclusion. These experiments demonstrate substantial inactivation of the model organisms and support the potential benefit of SER-109 manufacturing process to mitigate risks of undetected or emerging pathogens for which reliable screening is limited. Preclinical research to further characterize the antimicrobial activity of SER-109 is warranted.

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1036. In Vitro Analysis of AmpC β-lactamase Induction by Tebipenem in Enterobacterales and Pseudomonas aeruginosa

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Session: P-59. New Drug Development

Background. Tebipenem (TBP) is an orally bioavailable carbapenem in clinical development in the US for treating complicated urinary tract infections and acute pyelonephritis. TBP possesses broad-spectrum activity against isolates producing penicillinases, ß-lactamases, and AmpC ß-lactamases. Exposure to ß-lactams has been shown to increase AmpC production and impact susceptibility to ß-lactams. This study assessed the induction properties of TBP over AmpC production in Gram-negative organisms.

Methods. Eight Enterobacterales species and 1 P. aeruginosa isolate were selected for AmpC induction experiments for TBP, imipenem, ertapenem (ETP), and ceftazi dime. Induction experiments were performed at 0.25, 1, 4, and 16x MIC. AmpC induction was detected by measuring the intensity of nitrocefin hydrolysis compared to baseline. Isolates where a ≥4x induction of AmpC was detected were tested for susceptibility by the CLSI reference broth microdilution method. A second set of 36 Enterobacterales and 32 P. aeruginosa isolates with proven overexpression of AmpC by qRT-PCR were tested for susceptibility as well.

Results. In general, TBP and imipenem increased production of AmpC against all Enterobacterales, except for C. koseri and S. marcescens (Table). In contrast, ETP and ceftazidime did not seem to affect production of AmpC among the Enterobacterales species tested. All agents but ETP increased the production of AmpC in P. aeruginosa. Overall, an MIC increase (i.e., >4-fold) to various ß-lactam agents was not observed when tested against isolates that showed an increased production of AmpC after drug exposure. When tested against the second set of Enterobacterales that over-produced AmpC, TBP (MIC0.5–0.03/0.25 mg/L) inhibited all isolates at ≤1 mg/L. TBP showed MIC0.5 and MIC4 results of 4 and 4 mg/L, respectively, against P. aeruginosa isolates that over-produced AmpC.

Conclusion. Among Enterobacterales, exposure to either TBP or imipenem, but not ETP or ceftazidime, often resulted in increased measurement of AmpC production. However, increased production of AmpC did not translate into increased MIC values. Finally, TBP showed potent activity against Enterobacterales with confirmed overproduction of AmpC.