Integrating MALDI-TOF MS with Antimicrobial Stewardship for Bloodstream Infections

Katherine K. Perez, PharmD, BCPS
Infectious Diseases Clinical Specialist
Houston Methodist

Texas Medical Center
Houston, Texas, USA

- 5 hospitals, multiple offsite emergency departments, a research institute, and an education institute
- 1,633 operating beds
- 80,911 admissions/year
- 596,091 outpatient visits/year
- More than 15,000 employees and 4,000 affiliated physicians
- Largest lung and kidney transplant center in the USA
Our Microbiology Laboratory

- Reference lab for the system
- Operates 24 hours/7 days per week
- 37 employees
  - Include 4 lab technologists (processors), 7 MLTs and 26 MTs
  - Perform approximately 5,800 sets of blood cultures/month
**Significant Morbidity & Mortality**

**Gram-negative Bloodstream Infections**

- Account for 24% of nosocomial bloodstream infections in intensive care units
- Survival is directly associated with timely and appropriate initiation of antibiotic therapy
  - For every hour that appropriate antibiotics are delayed, survival decreases by 7.6%
- Treatment is increasingly becoming complicated by the emergence of antimicrobial resistance

The Ideal Treatment Scenario

- **Must be prompt**: delays in initiating effective antibiotics lethal
- **Appropriate**: must cover the offending pathogen(s)
- Administered at **adequate** dose and intervals consistent with pharmacokinetic/pharmacodynamic parameters
- Timely **streamlining** based on clinical response and microbiological data
- Prompt **discontinuation** when therapy complete

Moving Forward

• Conventional microbiology
  – Time consuming culture and biochemical phenotype

• New strategy: MALDI-TOF mass spectrometry
  – Direct pathogen identification and antibiotic susceptibility testing
  – Potential to:
    • Identify pathogens faster
    • Administer appropriate antibiotics sooner
MALDI-TOF Mass Spectrometry

• Rapid identification of bacteria, yeast & fungi
  – Minimum of 24-96 h reduced turnaround time compared to conventional culture-based methods
  – Even more dramatic results for certain organisms
    • (i.e. Legionella and Mycobacterium species)

• Test directly from positive blood cultures
  – Bypasses time-consuming subculture steps

Identify Gram-negative bacteria directly from positive blood culture media

- Transfer positive blood culture media to a serum separator tube
- Centrifuge to isolate the bacteria
- Transfer an aliquot of the bacteria from the pellet to the spotting plate
- Immediately perform organism identification using the MALDI-TOF
- Concurrently perform antimicrobial susceptibility testing using the pellet
Organism identification and antibiotic susceptibility testing directly from positive blood culture media.

- 110 positive blood cultures that recovered a Gram-positive organism were tested.
- Organism identification using the MALDI-TOF.
- Antibiotic susceptibility using the BD Phoenix.
Organism identification & antibiotic susceptibility testing directly from positive blood culture media

- Organism identification using the MALDI-TOF
  - 98% concordance with the reference method
  - Identification in approximately 2 h

- Antibiotic susceptibility using the BD Phoenix
  - 98% concordance with the reference method
  - Reduced turnaround time by >24 h

Training and Implementation

- All technical employees on all shifts in our microbiology laboratory are trained to use the MALDI-TOF instrument.
- At least one MALDI-TOF run is performed on each shift, with additional runs performed as needed for positive blood cultures.
  - One technologist per shift is dedicated to performing MALDI-TOF runs.
  - Approximately 8-10 runs/day
Operational Changes Implemented

• 2 new staff members were hired to support our rapid MALDI-TOF microbiology service.

• Reorganized workflow to optimize patient care.

• One technologist per shift is dedicated to performing MALDI-TOF runs.

• Validated the Sepsityper system to identify Gram positive organisms directly from blood culture media.
Antimicrobial Stewardship

• Key component of a multifaceted approach to prevent and reduce antimicrobial resistance

• Involves the optimal selection, dose, and duration of an antibiotic agent
  – Results in the cure or prevention of infection with minimal unintended consequences to the patient
  – Reduces conditions for selection of resistant bacterial strains

• Significant impact on antibiotic utilization rates, length of stay, survival, and costs

Integrating MALDI-TOF with Antimicrobial Stewardship

Houston Methodist Hospital
Rapid Pathogen Identification & Antimicrobial Stewardship for Gram-negative Bacteremia

Objective: Determine the clinical and economic impact of MALDI-TOF MS and infectious diseases pharmacists’ interventions on patients with Gram-negative bacteremia

Method: A comparative study of hospitalized patients before and after implementation of MALDI-TOF MS and real-time ASP notifications

ASP, Antimicrobial Stewardship Program
Innovation Plan

- Rapid identification (MALDI-TOF) and antibiotic susceptibility testing directly from blood cultures that recover a Gram-negative organism

- Microbiology laboratory results are immediately reported to the infectious diseases pharmacist who is on-call 24/7

- Pharmacist interprets clinical applicability of the MALDI-TOF data and contacts treating physician to recommend optimal antibiotic therapy
Patient Eligibility and Inclusion:
Bacteremia due to a Gram negative organism

Pre-intervention Arm
160 patients screened
Aug 15 - Nov 30, 2011
Excluded: 48 patients
- Anaerobic Gram negative (4)
- Previously enrolled (4)
- Expired before TTP (5)
- Not admitted (2)
- Transferred (2)
- Other BSI (9)
- Polymicrobial Index (10)
- Discharge subject to institutional policy (unable to leave)
  - ECMO (10)
  - VAD (1)
  - BMT (1)

Intervention Arm
157 patients screened
Feb 1 - May 25, 2012
Excluded: 50 patients
- Anaerobic Gram negative (11)
- Previously enrolled (5)
- Expired before TTP (7)
- Not admitted (2)
- Transferred (1)
- Other BSI (6)
- Polymicrobial Index (6)
- Discharge subject to institutional policy (unable to leave)
  - ECMO (6)
  - VAD/artificial heart (2)
  - BMT (4)

112 patients in final analysis
12 patients deceased
100 survivors included in LOS analysis

107 patients in final analysis
6 patients deceased
101 survivors included in LOS analysis

Perez, KK. Arch Pathol Lab Med. 2013.
Timeline (hrs) comparison of pre-intervention (PI) and intervention (Int) study periods

**Pre-Intervention (PI)**
- Blood culture drawn
- Culture positivity
- Growth on solid media
- Identification (Conventional)
- Susceptibility (Conventional)
- Passive notification via EMR
- Adjust therapy

**Intervention (Int)**
- Blood culture drawn
- Culture positivity
- Identification (MALDI-TOF)
- Susceptibility (BD Phoenix)
- Adjust therapy

### Average hours post-time to positivity

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Perez, KK. Arch Pathol Lab Med. 2012.
Clinical Outcomes

Antimicrobial Utilization

- De-escalation rates increased
- Time to de-escalation improved
- Decreased time on broad-spectrum therapy
- Faster time to active therapy
- Enhanced dosing and optimized regimens

Decreased Length of Stay
Kaplan-Meier curves compare time to hospital discharge between pre-intervention and intervention study periods.
Clinical Outcomes

MALDI-TOF and Antimicrobial Stewardship Significantly Reduces Hospital Length of Stay

\[ p = 0.01 \]

Perez, K. Arch Pathol Lab Med. 2012.
Economic Outcomes

MALDI-TOF and Antimicrobial Stewardship Significantly Reduces Health Care Costs

- The MALDI-TOF Antimicrobial Stewardship Program saved our hospital 1.97 million dollars (USD) during the study period.
- The program is estimated to save our hospital approximately $18 million dollars (USD) annually.

$0
$10,000
$20,000
$30,000
$40,000
$50,000

Total Hospital Costs per patient

Pre- Intervention (n = 100)
Intervention (n = 101)

p = 0.009

Perez, KK. Arch Pathol Lab Med. 2012.
First investigation to evaluate the impact of MALDI-TOF paired with antimicrobial stewardship on clinical and economic outcomes.

- Earlier initiation of targeted therapy informed by rapid identification and susceptibility testing significantly improved patient care and decreased LOS and expenditures.

Collaboration is key!

- An innovative microbiology laboratory with highly motivated technologists paired with an active pharmacy department was crucial to the success of our program.
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Current State

- All Gram-positive and Gram-negative bacteria from positive blood cultures are identified from positive blood culture bottles & followed up by PharmD
  - 3 ID-trained pharmacists & one resident trainee, notifications now automated
- Validating yeast identifications
- Pharmacy interventions implemented at one community hospital, working with second hospital
- All 5 hospitals in the system will have pharmacy interventions by mid-2014