Journal of Microbiology, Immunology and Infection (2017) 50, 662–668

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jmii.com

ORIGINAL ARTICLE

Routine identification of microorganisms by matrix-assisted laser desorption ionization time-of-flight mass spectrometry: Success rate, economic analysis, and clinical outcome

Mao-Cheng Ge [a,d], An-Jing Kuo [a,b,d], Kuei-Lan Liu [a], Ying-Hao Wen [a,b], Ju-Hsin Chia [a,b], Pi-Yueh Chang [a,b], Ming-Hsun Lee [c], Tsu-Lan Wu [a,b], Shih-Cheng Chang [a,b,*], Jang-Jih Lu [a,b,*]

[a] *Department of Laboratory Medicine, Chang Gung Memorial Hospital at Linkou, Taoyuan, Taiwan*
[b] *Department of Medical Biotechnology and Laboratory Science, College of Medicine, Chang Gung University, Taoyuan, Taiwan*
[c] *Division of Infectious Diseases, Department of Internal Medicine, Chang Gung Memorial Hospital at Linkou, Chang Gung University College of Medicine, Taoyuan, Taiwan*

Received 10 March 2016; received in revised form 26 May 2016; accepted 13 June 2016
Available online 24 June 2016

KEYWORDS
antibiotic treatment;
cost;
matrix-assisted laser desorption/ ionization time-of-flight mass spectrometry;
processing time;
success rate;
waste

Abstract *Background:* Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) has been widely used in microbial identification. This study evaluated the performance of MALDI-TOF MS and investigated the economic and medical impact of MALDI-TOF MS implementation.
Methods: A total of 12,202 clinical isolates collected from April to September 2013 were identified using MALDI-TOF MS, and the success rates in identifying isolates were analyzed. The differences in the processing time, cost of consumables, weight of waste, and clinical impact between MALDI-TOF MS and biochemical reaction were compared.
Results: MALDI-TOF MS successfully identified 96% of 12,202 isolates, including 96.8% of 10,502 aerobes, 90.5% of 1481 anaerobes, 93.8% of 81 yeasts, and 90.6% of 138 nontuberculous mycobacteria at the genus level. By using MALDI-TOF MS, the processing time for aerobes decreased from 32.5 hours to 4.1 hours, and that for anaerobes decreased from 71.5 hours to 46 hours.

* Corresponding authors. Department of Laboratory Medicine, Chang Gung Memorial Hospital at Linkou, 5, Fu-Hsing Street, Kueishan 333, Taoyuan, Taiwan.
E-mail addresses: changsc137@cgmh.org.tw (S.-C. Chang), janglu45@gmail.com (J.-J. Lu).
[d] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.jmii.2016.06.002

For detection of aerobes and anaerobes, the cost of consumables was estimated to decrease by US$0.9 per isolate, thus saving US$94,500 in total annual isolation. Furthermore, the weight of waste decreased six-fold, resulting in a reduction of 350 kg/month or 4.2 tons/year. MALDI-TOF MS also increased the percentage of correct antibiotics treatment for *Escherichia coli* and *Klebsiella pneumonia* from 56.1% to 75% and shortened the initiation time of the correct antibiotic action from 3.3 hours to 2.5 hours.
Conclusions: MALDI-TOF MS is a rapid, reliable, economical, and environmentally friendly method for routine microbial identification and may contribute to early appropriate antibiotic treatment in clinical settings.

Introduction

The conventional methods for identifying microorganisms in clinical microbiology laboratories are based on biochemical methods and gene sequencing identification techniques. However, these procedures take considerable time, and the results may be difficult to interpret occasionally because of indistinct reactions or outdated databases.[1,2] Recently, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) has been effectively used as a rapid method for identifying a wide array of microbial species.[3,4] In MALDI-TOF MS analysis, abundant structural proteins such as ribosomal proteins are extracted from an intact bacterial colony. The ionizing laser vaporizes the abundant structural proteins of microorganisms, and unique mass spectra are generated, having mass-to-charge ratio (m/z) peaks with varying intensities. The mass spectra of test isolates are sequentially compared with those in a reference database for identification. Unknown organisms can be identified by matching the organism's spectrum to the most similar spectrum in the database. Depending on the MALDI-TOF MS score, the genus and species identification for an organism may be accurate.

MALDI-TOF MS can provide advantages for a universal procedure of microbial identification. Only a small amount of an organism, typically a fraction of a single colony from primary culture plates, is required for analysis. Comparatively, a larger inoculum and subculture is often required for conventional biochemical methods or other automated systems. The differences in procedure time and cost per isolate between MALDI-TOF MS and biochemical identification have been shown in previous studies.[1,5] However, cost assessment related to the subcultures required for the biochemical method, secondary biochemical testing such as coagulase for staphylococci, and the annual maintenance cost of MALDI-TOF MS should be considered when implementing MALDI-TOF MS in clinical settings. Furthermore, biohazard waste generated daily from microbial cultures and laboratory analysis may affect human health, waste management costs, and the environment. Because of its relative simplicity and speed, MALDI-TOF MS enables reducing the time spent on microbial identification. Rapid identification of microorganisms may contribute to the early treatment of patients by using an appropriate antimicrobial therapy, thereby improving patient outcomes, reducing the potential for microorganisms to develop antimicrobial resistance, and lowering mortality among bacteremic patients with sepsis.[6–8]

Although the use of MALDI-TOF MS for microbial identification has been well established,[9,10] its performance in identifying success rates and scores among different microbial species has yet to be extensively evaluated in clinical practice by using numerous clinical isolates. In addition, evidence of the impact of MALDI-TOF MS on costs, waste reduction, and the clinical outcomes of patients remains limited. In April 2013, the laboratory at Linkou Chang Gung Memorial Hospital switched from the conventional biochemical method to MALDI-TOF MS for microbial identification. Over a 6-month period, we evaluated the success rate of MALDI-TOF MS in identifying clinically relevant microorganisms, including aerobic and anaerobic bacteria, yeasts, and nontuberculous mycobacteria (NTM), at a 4000-bed tertiary teaching hospital (Linkou Chang Gung Memorial Hospital). In addition, we compared the processing time, cost of consumables, weight of waste, and clinical outcome of microbial identification between MALDI-TOF MS and biochemical methods.

Materials and methods

Microorganism isolates

A total of 12,202 clinical isolates, comprising aerobes (n = 10,502), anaerobes (n = 1481), yeasts (n = 81), and NTM (n = 138), were included in this study. The clinical isolates were obtained from fresh clinical specimens at Linkou Chang Gung Memorial Hospital in Taiwan from April to September 2013.

Sample preparation and MALDI-TOF MS analysis

The microorganism identifications and data analyses were performed using the Bruker LT microflex MALDI-TOF mass spectrometer (Bruker Daltonics, Bremen, Germany). Sample preparation methods for MALDI-TOF MS analysis were performed as recommended by the manufacturer's protocol. A direct smear method with a 70% formic acid overlay was used for preparing aerobic and anaerobic bacteria samples, and ethanol–formic acid extraction and silica bead-based extraction methods were performed for