

Field Study of a New Surveillance Method for Rapid Detection of MRSA

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Abstract

Background: Compulsory MRSA screening of hospitalized patient results in a decrease of infections, a better patient outcome and a shorter length of stay. Detection of colonised patients is also crucial for initiation of infection control procedures and proper therapy in case of infection.

Objective: Performance of a new system for detection of MRSA in real life.

Methods: We compared the real-time PCR system GeneXpert MRSA, culture on chromogenic agar and the new developed HB&L MRSA kit for their diagnostic performance in MRSA admission screening in a 450 beds hospital in northwest Germany.

Results: A total of 523 clinical swabs (nose, throat) of successive patients were analysed (02-04/2016). The HB&L MRSA kit performed superior to culture and GeneXpert MRSA with sensitivities of 90.9%, 76.9% and 83.3%; the specificities were 99.8%, 99.9% and 98.8%; positive predictive values were 90.9%, 90.9% and 62.5% respectively.

Conclusion: In comparison to chromogenic medium and GeneXpert MRSA, the HB&L MRSA test showed either a higher sensitivity and/or a better PPV, avoiding unnecessary isolation of false positive tested patients. The HB&L MRSA test offers a fast and reliable tool for the rapid identification of MRSA negative and positive patients in a low prevalence MRSA area.

Keywords: MRSA; Detection; HB&L; GeneXpert; Chromogenic Agar; Field Study

Abbreviations

HA-MRSA: Health Care Associated Methicillin Resistant *Staphylococcus aureus*; CA-MRSA: Community Acquired Methicillin Resistant *Staphylococcus aureus*; LA-MRSA: Livestock Associated Methicillin Resistant *Staphylococcus aureus*; *mecA*, *mecC*: Gene Encoding Penicillin Binding Protein 2A Resulting in Methicillin Resistance; NPV: Negative Predictive Value; PPV: Positive Predictive Value; TAT: Turn Around Time; PCR: Polymerase Chain Reaction

Introduction

Despite the decline of HA-MRSA e.g. in Germany and England [1,2], colonization, transmission and infection are still an issue in patient care and prevention. Besides HA-MRSA other MRSA sources are now in the focus of interest. CA-MRSA are widespread in USA [3], whereas in Europe, e.g. in the Dutch-German border region called EUREGIO, LA-MRSA are posing a problem, rising from 9.6% of all MRSA strains in 2004 up to 35% in 2013, contributing substantially to the total burden of MRSA colonization and infection at an University hospital [4]. In addition, besides MRSA strains with *mecA* a second gene called *mecC* was detected in strains found in cattle as well as in humans [5,6].

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These strains were primarily not detected by methods based on PCR, because this method only can detect what is already known. In our opinion, methods based on culture and phenotypic detection of resistance should be preferred in the daily routine [7]. Compulsory MRSA screening of hospitalized patient results in a decrease of infections, a better patient outcome and a shorter length of stay [8]. Detection of colonised patients is also crucial for initiation of infection control procedures and proper initial antibiotic therapy. However, screening by traditional culture needs 24 to 72h and screening by amplification of bacterial DNA may result in high costs. The HB&L kit is a rapid culture based semi-automated method, able to detect HA-, CA- and LA-MRSA strains as well as *S. aureus* strains carrying *mecC* (D. Knaak and K. Becker, personal communication, University of Münster). These properties were the reasons why we investigated the performance of the HB&L method in a setting of a mid-sized Hospital.

Materials and Methods

The study has been performed from February 2016 to April 2016 at the Laboratory of Microbiology of Hospital "Ludmillenstift" in Meppen, situated in the northwest of Germany (EUREGIO), where HA-MRSA as well as LA-MRSA strains are distributed in the human population. Samples (nose, throat) were taken from consecutive patients within 24h after hospitalisation by a liquid swab (Σ -Transwab, MWE Medical Wire & Equipment, England). The analysis was done by means of the HB&L instrument (Alifax S.r.l., Italy), using the HB&L MRSA kit. The kit consists of two components: vial with 1.8 mL of a saline culture-medium suppressing growth of *Enterococcus* spp. by Lithium Chloride and a lyophilized supplement containing cefoxitin to be added in the saline culture-medium after inoculation of the sample (200 μ L). Resistance to cefoxitin is a sensitive and specific marker of *mecA/mecC*-mediated methicillin resistance [9]. The HB&L device monitors automatically bacterial growth phases using light scattering technology during 7h (modifiable). An internal algorithm of the software interpreted data, and positive vials were confirmed as MRSA by the application of two tests: latex agglutination (Pastorex, Bio-Rad, Germany) and PBP2a test (Alere, Germany). All positive HB&L vials were subcultured for regrowth of MRSA. In parallel to inoculation of the HB&L, aliquots of the liquid sample (100 μ L) were tested by means of a rapid fully automated PCR instrument (GeneXpert MRSA, CEPHEID, USA), samples with positive signals were subcultured and confirmed by the tests mentioned above. The third method was a direct culture of an aliquot (10 μ L) on chromogenic agar (MRSA select II, Bio-Rad, Germany) with overnight incubation. Red coloured colonies were also tested by latex- and PBP2a-agglutination.

Results and Discussion

During February and March 2016 a total of 523 clinical swabs (nose, throat) of successive patients admitted to the hospital were analysed. Combining the results of all three methods, a total of 10 true positive MRSA were detected, accounting for 1.91% of the hospitalized population. According to previous studies carried out in the same region (EUREGIO), the figures were between 0.5 and 2.4%, which is in the same range as our finding [10].

There were nine strains detected by the HB&L system, seven by chromogenic agar and eight strains by GeneXpert. HB&L was rated false positive in one case with no growth of MRSA in subculture after positive confirmatory tests. The same was true for the chromogenic agar, growth of red colony signalling MRSA but negative in confirmatory tests. Contrary to the low figure of false positives by these methods, a total of six false positive results were reported by GeneXpert, but no growth of MRSA after subculture was detected. Sensitivity, specificity, PPV and NPV of all three methods are depicted in the table.

Method / TAT (h)	Sensitivity	Specificity	NPV	PPV
HB&L MRSA / 7	90.9%	99.8%	99.8%	90.9%
MRSA select II / 18-24	76.9%	99.8%	99.4%	90.9%
GeneXpert MRSA / 3,5	83.3%	98.8%	99.6%	62.5%

Culture on MRSA select II chromogenic agar was the least sensitive method, probably why we included no enrichment broth. However, using an enrichment broth, the incubation period extends up to 72h [11], too long for clinicians and hospital hygiene to make decisions for patient care (treatment and/or isolation). Not unexpectedly, specificity and NPV were > 99%. GeneXpert MRSA had the shortest turnaround time with 3.5h, specificity and NPV were comparable to MRSA select II and HB&L MRSA. However, sensitivity was lower than HB&L MRSA and PPV only reached 62.5%. This finding is in agreement with other data published before, Trevino, *et al.* [12] reported a sensitivity of 83.3%, specificity of 94.7%, PPV of 45.6%, and NPV of 98.9%. Continued vigilance is needed to monitor for *Staphylococcus aureus* leading to inaccurate results in genotype based screening assays like GeneXpert MRSA or BD MAX MRSA [13].

The problem is that a low PPV results in additional costs for isolation procedures, in some patients to unnecessary antibiotic therapy and also to profound unsettlement. The HB&L MRSA kit showed the highest sensitivity of all tests, specificity, NPV and PPV were equivalent to the chromogenic medium. The TAT was 7h, fitting within a work shift of the laboratory, resulting in same day results.

Conclusion

In comparison to chromogenic medium and GeneXpert MRSA, the HB&L MRSA test showed either a higher sensitivity and/or a better PPV, avoiding unnecessary isolation of false positive tested patients. The HB&L MRSA test offers a fast and reliable tool for the rapid identification of MRSA negative and positive patients in a low prevalence MRSA area.

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Conflict of Interest

W.R.H. received study and presentation honorarium by Alifax S.r.l., Italy.

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