Utilisation of Staphylococcal Interspersed Repeat Unit (SIRU) typing in neonatal infection control management.

Public Health England

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INTRODUCTION

Transmission of nosocomial pathogens in critical care settings results in significant morbidity and mortality. *Staphylococcus aureus*, especially methicillin resistant *Staphylococcus aureus* (MRSA), are seen as indicator organisms of infection prevention and control failure if the same strain is identified as part of a cluster investigation. Efforts to reduce MRSA infection involve the coupling of screening, decolonisation and outbreak management. These strategies should not, however, be restricted to MRSA, as methicilin sensitive *Staphylococcus aureus* (MSSA) has been found to be equally invasive and pathogenic. This becomes even more relevant as the rates of MSSA bacteraemias in the UK are increasing at the expense of MRSA bacteraemias.

Neonates admitted to the neonatal intensive care unit (NICU) are immunosuppressed as a result of immaturity and sepsis. Additional risk factors for nosocomial infection include the presence of vascular and urinary catheters as well as endotracheal tubes. All of our neonates are screened for pathogens on admission, as well as weekly screens for MRSA. It is through these screens and positive blood cultures that the clusters were identified.

Seven variable-number tandem repeats (VNTRs) novel to Staphylococcus aureus, termed staphylococcal interspersed repeat units (SIRUs) are distributed around the genome occurring in both unique and multiple sites, and varying in length from 48 to 159 bp. SIRUs provide a greater degree of discrimination than multi-locus sequence typing, thus resulting in an appropriate tool for studying transmission events.

We employed rapid Staphylococcal Interspersed Repeat Unit (SIRU) typing methodology to investigate clusters of *Staphylococcus aureus* infections in our neonatal intensive care unit (NICU) and thus prevent transmission.

METHODS

Epidemiological Typing

Overnight bacterial cultures were used to extract DNA for each isolate[1].
All isolates were typed staphylococcal interspersed repeat unit (SIRU) typing. Seven VNTR regions located around the genome were amplified by PCR[2].
The products of PCR were sized using the QIAxcel capillary based gel electrophoresis platform (Qiagen), and number of repeats for each locus determined to generate a seven digit digital profile.

Infection Prevention and Control Measures

Results of SIRU typing were used to influence patient care and determine whether transmission of MRSA between patients on NICU had occurred.

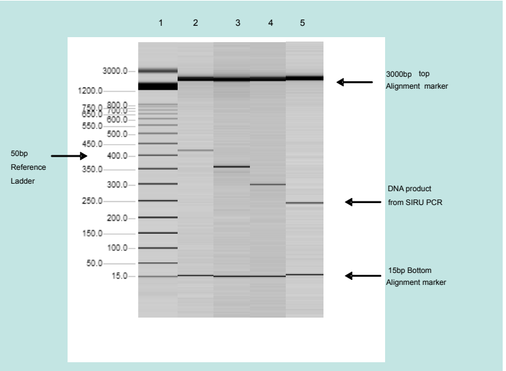

Figure1. Electropherogam of QIAxcel pseudo-gel image used to size amplified DNA products from SIRU typing PCR

RESULTS

A total of 8 clinical samples were analysed as part of an investigation into a period of increasing incidence of *Staphylococcus aureus* infection.

In cohort 1, isolation of MRSA from neonatal secretions from patient 1 and an MRSA positive screening swab from patient 2 were typed and found not to be related. Patient 3 was a staff member with a positive screen and a different SIRU type, thus transmission was not demonstrated.

In cohort 2, three patients were confirmed the same SIRU type on screening, indicating a transmission event. All patients in the unit were decolonised with mupirocin and Octenisan or chlorhexidine, no further transmission occurring. In cohort 3, two SAB blood culture isolates were related by SIRU typing. Subsequent investigation into the root cause identified a breakdown in line insertion practices.

- SIRU typing, performed in real time demonstrated that a transmission event had occurred in the second cohort.
- SIRU typing when applied to sterile site isolates demonstrated that transmission events can occur during device insertion.

Patient #	Cohort	Source	Date	Organism	SIRU
1	1	Secretion	06/05/2012	MRSA	1 6 2 2 15 5 2
2		Nose	25/05/2012	MRSA	3 3 5 - 12 4 2
3		Skin	08/06/2012	MRSA	1 4 0 3 17 - 2
4	2	Nose	19/06/2012	MRSA	3 3 7 3 12 4 2
5		Nose	19/06/2012	MRSA	3 3 7 3 12 4 2
6		Nose	19/06/2012	MRSA	3 3 7 3 12 4 2
7	3	Blood	22/03/2014	MSSA	X 3 3 3 11 - 3
8		Blood	26/03/2014	MSSA	X 3 3 3 11 - 3

Figure 2. Isolate and SIRU typing data.

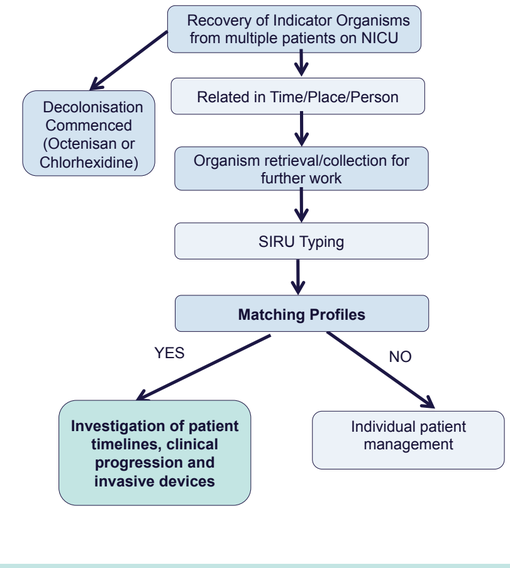

Figure 3. Implementation of SIRU typing

DISCUSSION

SIRU typing is an established methodology for discriminating between isolates of *Staphylococcus aureus*[3,4] as part of the investigations of defined outbreaks. Molecular typing can be used to determine person-to-person strain transmission in clinical settings, which is important to develop strategies to prevent further spread.

We would recommend a program of surveillance of indicator organisms (those that are responsible for healthcare associated infections) in augmented care units. Isolation of organisms from screening and clinical isolates that form part of a period of increased incidence should be stored by the laboratory. A preliminary review of these by the infection control team should trigger a request for typing. If isolated are found to be related, then a formal outbreak may be declared. Root cause analyses should be performed as part of a multidisciplinary team in order to identify failures in practice to prevent further transmissions.

SIRU typing is inexpensive, highly reproducible, easy to perform, interpret and can be done around the suspected incident to confirm an outbreak and immediately inform control measures. Whole genome sequencing[5] can provide clinically relevant data but is not yet in routine use.

CONCLUSIONS

- Augmented care units should have regular screening of indicator organisms.
- Periods of increased incidence should be assessed as a possible emerging outbreak.
- Organisms from both clinical samples and screens should be saved by the routine laboratory and then sent for the appropriate typing methodology.
- Outbreak teams should review the clinical, microbiological and typing data.
- Transmission of certain organisms in sterile site specimens can direct the outbreak teams investigations in the root cause analysis.

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