Methicillin Sensitive Staphylococcus Aureus bacteraemia: Does Management Matter?

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- *Methicillin Sensitive Staphylococcus Aureus (MSSA)* is a bacterium that lives commonly on the surface of the skin. When it penetrates the body's natural defences, it can cause serious infections including bacteraemia (blood), cellulitis (soft tissue), endocarditis (heart valves), osteomyelitis (bone marrow) and septic arthritis (joints).
- Timely diagnosis, appropriate empirical therapy, identification and sanitation of the suspected source followed by focused antibiotic therapy is critical in achieving good patient outcomes.
- Expert opinion guides the management of MSSA infections with no universal consensus on what is best practice. Tong et al published a review of MSSA infection management in 2015[1] and Healthcare Improvement Scotland gave guidance on the initial and therapeutic management of staphylococcus bacteraemia in adults in 2017[2].
- These documents were used to identify key diagnostic activity and treatment regimes. Retrospectively, patient records were used to identify if these were carried out and the impact on patient outcomes was assessed.

1. Is the literature guidance for management of MSSA bacteremia being followed within NUTH?
2. Is the literature specified course of IV antibiotics associated with a better outcome?

Population

- The initial sample included all those who had a positive MSSA blood sample recorded at the Newcastle Trust Hospitals in the calendar years 2016 – 2017 (n=374). A number of patients were excluded (n=46) due to:
  - Sample taken was not a blood sample e.g. pleuritic fluid in a blood culture bottle.
  - Insufficient information in patient notes e.g patients who were transferred in/out of the trust during treatment.

Population Statistics	Frequency (%)		Frequency (%)
Total	328 (100)	**Known to have…**	
Gender		Intracardiac device or prosthetic valve	44 (13.4)
Male	202 (61.6)	Joint/bone prosthetic	53 (16.2)
Age (Years)		Soft tissue infection	111 (33.8)
< 16	35 (10.6)	Urinary tract infection	30 (9.1)
16 to 65	166 (50.6)	Admitted for surgery	101 (30.8)
> 65	127 (38.7)	On imunosupressive therapy or chemotherapy	76 (23.2)
Mean	52.2	On dialysis	47 (14.3)
SD	25.2	Any IV device, central or peripheral	160 (48.8)
Hospital or Community Aquired Infection			
Hosptial	164 (50.0)		

Outcomes

Poor:

- Recurrence, positive MSSA blood cultures recorded on e-record after 2 weeks and within 90 days of the first positive blood culture. **(n=18, 6%)**
- 30 day all cause mortality, date of death recorded in patient notes or on e-record within 30 days of the first positive blood culture. **(n=47, 14%)**
- 90 day all cause mortality, date of death recorded in patient notes or on e-record within 90 days of the first positive blood culture. **(n=17, 5%)**

Good:

- No positive MSSA blood cultures recorded on e-record within 90 days of first positive blood culture. **(n=246, 75.0%).**
  - If the patient met this criteria it was deemed that the patient was cured as a further episode of MSSA bacteremia would necessitate re admission to hospital. No other biochemical markers or cessation of symptoms were used.

Is the literature guidance for management of MSSA bacteremia being followed within NUTH?

Diagnostics

- Surveillance blood cultures should be carried out 24 – 48hrs after the first positive blood culture, to identify persistent sources of infection.
  - **70% (n = 230) received a surveillance blood culture.**
- Transthoracic (TTE) / Transesophageal (TOE) Echocardiograms should be conducted to investigate infective endocarditis.
  - **66% (n = 216) received either TOE, TTE or both.**
- Imaging studies should be carried out to identify the source of infection.
  - **86% (n = 281) received ≥1 imaging study. Of the 14.3% (n = 47) who had no imaging studies, a likely source of infection had been identified.**

Imaging		
Number of modalities		**Modality**
0	47 (14.3)	Ultrasound
1	124 (37.8)	Xray
2	99 (30.2)	CT
3	48 (14.6)	MRI
4	10 (3.4)	

- 151 patients (46%) received surveillance blood cultures + TTE or TOE + at least one other imaging study. These patients were more likely to have a good outcome (p = 0.006).

Treatment

- The infective source should be removed including but not limited to, removal of IV devices, drainage of abscesses, removal of infective prostheses and washing out of infected wounds.
  - **75% (84/112) patients that had documented removal their IV device had a good outcome.**
  - **82% (41/50) patients that had documented drainage or surgical wash out had a good outcome.**
  - **100% (6/6) patients that had documented removal of infected prostheses had a good outcome**.
- Treatment should be with appropriate anti-staphylococcal IV antibiotics (Abx) for at least 14 days or longer dependent on the location of infection. **In all cases the mean length of IV antibiotic treatment was less than the literature suggests.**

IV Antibiotic treatment	Frequency (%)	Mean IV Abx Course/days (Recommended/days)	Good Outcomes (% of identified source)
Total	328 (100)		
Identified Source			
IV Device	92 (28.0)	8.9 (14)	67 (72.8)
Bone/Joint	50 (15.2)	26.1 (28)	44 (88.0)
Skin & Soft Tissue	48 (14.6)	12.9 (14)	36 (75.0)
Respiratory Tract	22 (6.7)	11 (14)	12 (54.5)
Urinary Tract	21 (6.4)	11.9 (14)	16 (76.1)
Cardiac	15 (4.6)	24.4 (40)	12 (80)
Surgical Site Infection	14 (4.3)	12.4 (14)	9 (64.3)
Hepatobillary	8 (2.4)	7.9 (14)	4 (0.5)
Gastrointestinal tract	5 (1.5)	9.2 (14)	4 (0.8)
CNS	1 (0.3)	9 (14)	0 (0)
Unknown	19 (5.8)	11.8 (14)	14 (73.7)
Other	33 (10.1)	8.6 (14)	21 (63.6)

Is the literature specified course of IV antibiotics associated with a better outcome?

- For IV Devices, skin and soft tissue, bone and joint and cardiac infections. The outcome means were compared in a two sample t test to identify if the recommended length of antibiotic therapy was significantly better.

Treatment length				
Source	**Recommended length of IV Abx (days)**	**Mean Outcome (1=Good, 0=Poor) ≥ recommended duration**	**< recommended duration**	**Significance level (p)**
IV Device	14	0.77	0.71	0.28
Skin/Soft tissue infection	14	0.83	0.70	0.16
Bone and Joint	28	0.87	0.86	0.45
Cardiac	40	1.00	0.64	0.09

- In all cases the longer therapy had a higher outcome mean but only in cardiac infections did the longer duration of antibiotic therapy approach a significantly better outcome for the recommended duration.
- It is thought a a shorter course of IV antibiotics may be appropriate in IV device related infections. Using a proposed 'recommended length' of ≥/< 7 days IV therapy showed a trend towards a significantly better outcomes for at least 7 days of IV therapy.

7 Day comparison for IV related infections			
	Mean Outcome (1=Good, 0=Poor)		
Source	**≥ recommended duration**	**< recommended duration**	**Significance level (p)**
IV Device	0.79	0.66	0.09

Conclusions and Future Work

- Good patient outcome was associated significantly with surveillance blood cultures + echocardiography + at least one other imaging study. This is most likely related to identification of the source of the infection to allow focused management. The removal of the infective source, if accessible and indicated, is also important for good patient outcomes.
- In our cohort, across all sources the mean duration of IV antibiotics was lower than the literature recommendations. This may be related to generic IV to PO antibiotic switching guidelines.
- The literature recommend duration guidelines where not significantly associated with a better outcomes in IV, SSTI and bone infections. In cardiac infections the recommended duration was trending towards significantly better outcomes. 7 day treatment may be suitable for IV device related infections.
- The marker for cure in this study was the absence of recurrence or mortality. Other biochemical and symptomatic markers may give a better indication of suitability for length of IV antibiotics and should be investigated e.g. CRP, pyrexia.
- The utility and length of course of oral antibiotics is not mentioned in any detail across the literature and its effect could also be studied.

References
1. Tong SYC et al . Staphylococcus aureus Infections: Epidemiology, Pathophysiology, Clinical Manifestations, and Management. *Clinical Microbiology Reviews*. 2015;28(3):603-661. doi:10.1128/CMR.00134-14.
2. Healthcare Improvement Scotland. Guidance on management of proven or suspected Staphylococcus aureus bacteremia in adults. 2017.