Time for a new CoNSensus?

Species specificity of coagulase negative staphylococci (CoNS) antibiograms in neonatal bloodstream isolates across Europe

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BACKGROUND

Coagulase negative staphylococci (CoNS) are the leading cause of neonatal late onset sepsis (LOS) in high income settings and increasingly implicated as significant pathogens in low- and middle-income settings. There has been an emergence of multi-drug resistant CoNS clones with differing susceptibility profiles, including vancomycin heteroresistance, such as *Staphylococcus capitis* NRCS-A.

Hypothesis → In terms of antibiotic resistance patterns, grouping CoNS together is now outdated

METHODS

Population: Infants were recruited from neonatal intensive care units (NICUs) to the NeoVanc randomised controlled trial (RCT). NeoVanc was a FP7-funded, multi-centre RCT comparing an optimised and standard course of vancomycin (NCT02790996).

neoVanc

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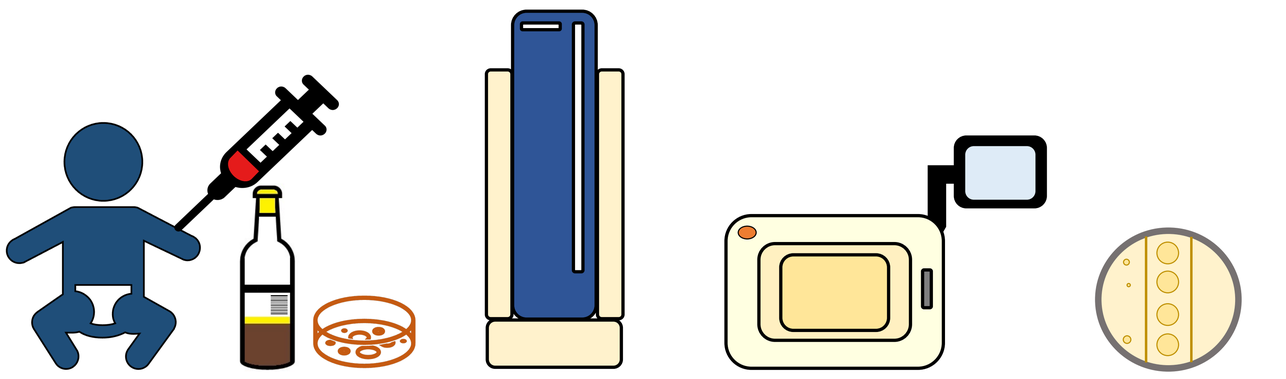

*Brain heart infusion agar method validated against PAP-AUC with control organisms

Resistance was defined as per EUCAST. The Chi-squared test was performed to assess if antibiotic resistance rates differed between CoNS species.

RESULTS

116 CoNS bloodstream isolates from 67 NeoVanc participants were available for analysis.

Antibiotic susceptibility patterns by species are show in Table 1. Almost all isolates were methicillin resistant (92%) with overall gentamicin resistance rates being 93%. All *S. haemolyticus* isolates were resistant to ceftaroline. Teicoplanin resistance was seen in *S. capitis*, *S. haemolyticus* and *S. epidermidis*. All CoNS were susceptible to linezolid and daptomycin. No organisms were resistant to vancomycin although heteroresistance was detected in 87% of isolates including all *S. capitis*, *S. haemolyticus* and *S. warneri* (Figure 1); a significant difference in vancomycin heteroresistance was seen between species (p = 0.002) .

There were significant differences in antibiotic susceptibility profiles between CoNS species with patterns of resistance by species being antibiotic dependent. In general, *S. haemolyticus* isolates were more resistant and *S. hominis* and *S. warneri* were more susceptible.

References
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Table 1: Rates of antibiotic resistance in coagulase negative staphylococci bloodstream isolates from infants recruited to the NeoVanc randomised controlled trial

	COAGULASE NEGATIVE STAPHYLOCOCCAL SPECIES						
	S. epidermidis N = 83	*S. haemolyticus* N = 18	*S. hominis* N = 6	*S. capitis* N = 5	*S. warneri* N = 4	TOTAL N = 116	
ANTIBIOTIC	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	p-value
Methicillin	75/83 (90)	18/18 (100)	5/6 (83)	5/5 (100)	4/4 (100)	107/116 (92)	0.26
Gentamicin	79/83 (95)	18/18 (100)	4/6 (67)	5/5 (100)	2/4 (50)	108/116 (93)	**0.01***
Ciprofloxacin	54/82 (66)	18/18 (100)	3/6 (50)	0/5 (0)	0/4 (0)	75/115 (65)	**<0.001***
Ceftaroline	4/83 (5)	18/18 (100)	1/6 (17)	0/5 (0)	0/4 (0)	23/116 (20)	**<0.001***
Fosfomycin	9/83 (11)	0/18 (0)	0/6 (0)	3/5 (60)†	4/4 (100)	16/116 (14)	**<0.001***
Teicoplanin	3/80 (4)	1/18 (6)	0/6 (0)	2/5 (40)	0/4 (0)	6/113 (5)	0.14
Rifampicin	2/83 (2)	1/18 (6)	0/6 (0)	2/5 (40)	0/4 (0)	5/116 (4)	0.09
Vancomycin‡	0/83 (0)	0/18 (0)	0/6 (0)	0/5 (0)	0/4 (0)	0/116 (0)	1
Linezolid	0/83 (0)	0/18 (0)	0/6 (0)	0/5 (0)	0/4 (0)	0/116 (0)	1
Daptomycin	0/83 (0)	0/18 (0)	0/6 (0)	0/5 (0)	0/4 (0)	0/116 (0)	1

† *S. capitis* intrinsically resistant to fosfomycin; ‡ Vancomycin broth microdilution yielded the same results
*p-values ≤0.05 were considered statistically significant

0% of CoNS species resistant | 1 – 30% of CoNS species resistant | 31 – 70% of CoNS species resistant | >70% of CoNS species resistant

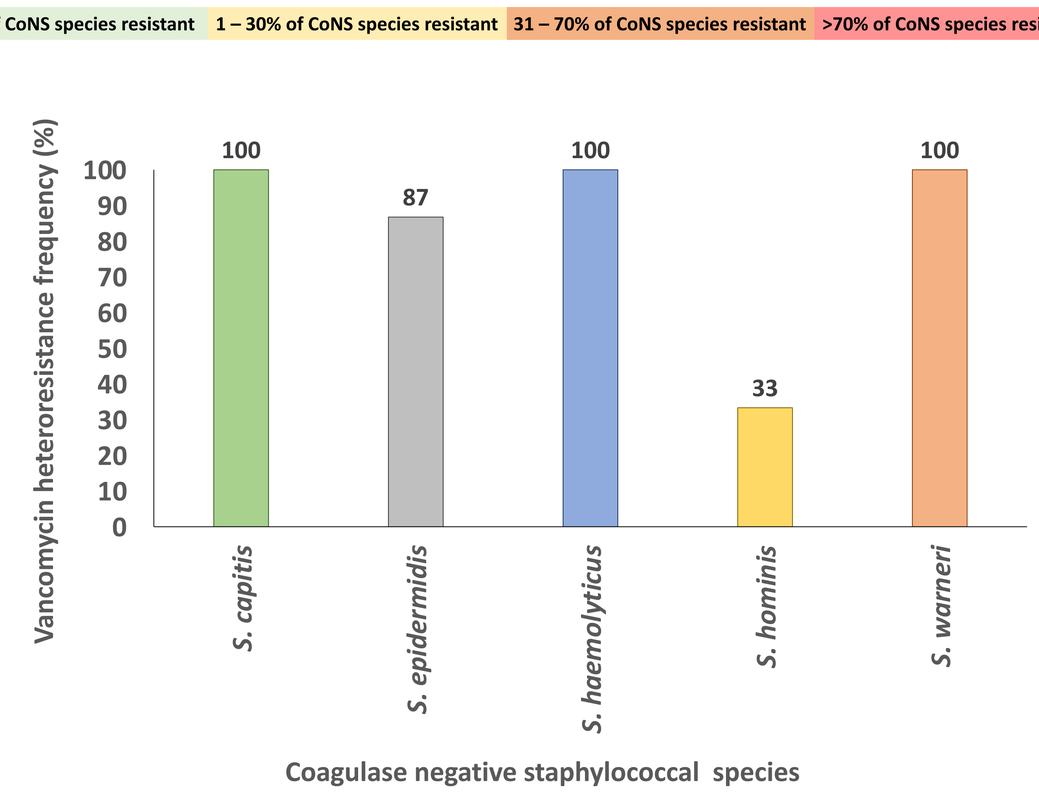

Figure 1: Rates of vancomycin heteroresistance seen in NeoVanc coagulase negative staphylococcal bloodstream isolates by species

DISCUSSION & CONCLUSIONS

High rates of methicillin and aminoglycoside resistance, vancomycin heteroresistance, and low rates of teicoplanin resistance likely reflect the antibiotics prescribed in this high antibiotic-use environment. The high rates of vancomycin heteroresistance are of concern given the importance of this antibiotic in the treatment of Gram-positive sepsis.

Less resistant profiles were seen in the *S. hominis* and *S. warneri* isolates. This study supports previous reports of *S. haemolyticus* being more often multi-drug resistant.

Although some species numbers were small, species could be considered in clinical management decisions of infants with CoNS LOS. Early species identification could guide empiric antibiotic treatment, whilst waiting for susceptibilities, allowing preservation of vancomycin for CoNS species not susceptible to other antibiotics.

Scan here for information about the NeoVanc trial

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