High rate of ceftaroline-resistance in *Staphylococcus haemolyticus* causing late-onset sepsis and colonizing preterm neonates and their mothers

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Background & Aim

- Ceftaroline is a new cephalosporin active against MRSA
- Susceptibility of *S. epidermidis* and *S. haemolyticus* causing late-onset sepsis (LOS) in preterm neonates warrants characterization before use of ceftaroline in treatment of LOS
- We aimed to determine susceptibility to ceftaroline in *mecA*-positive *S. epidermidis* and *S. haemolyticus* causing LOS and colonizing potential reservoirs of invasive strains (gut/skin of preterm neonates, mother's own milk (MOM))

Materials and Methods

- A total of 97 previously characterized *mecA*-positive strains of diverse multilocus sequence types (Table1)

Table 1. Number of isolates included in the study according to time, source and species

		Colonizing		Causing
		Gut/skin (n=41)	MOM (n=39)	LOS (n=17)
2007-2008	*S. epidermidis*	11	0	2
	S. haemolyticus	0	0	4
2014-2015	*S. epidermidis*	3	31	3
	S. haemolyticus	27	8	8

- Oxacillin and ceftaroline MICs were determined by MIC Test Strips (Liofilchem)
- Results interpreted according to EUCAST 2018 (Table 2)

Table 2.MIC breakpoints for determination of resistance (according to EUCAST 2018)

	Susceptible	Intermediate	Resistant
Ceftaroline*	≤1 mg/L	1<…≤2 mg/L	>2 mg/L
Oxacillin	≤0.25 mg/L	-	>0.25 mg/L

*Ceftaroline breakpoint for *S. aureus* (indications other than pneumonia).

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Results

- *S. epidermidis* compared with *S. haemolyticus* had lower ceftaroline MICs ($p<0.001$) and lower resistance-rate to ceftaroline ($p<0.001$) (Table 3)

Table 3. The results of susceptibility testing to oxacillin and ceftaroline

		MIC_{50}	MIC_{90}	Susceptible (%)	Intermediate (%)	Resistant (%)
Oxacillin	*S. epidermidis*	2	16	4	0	96
	S. haemolyticus	≥256	≥256	0	0	100
Ceftaroline	*S. epidermidis*	0.25	0.5	98	0	2
	S. haemolyticus	3	4	6.4	23.4	70.2

- *S. epidermidis* from MOM had lower ceftaroline MICs compared with *S. epidermidis* colonizing gut/skin of neonates or causing LOS (MIC_{50}/MIC_{90} 0.25/0.5 vs 0.38/0.5 mg/L; $p=0.012$ and $p=0.02$, respectively), but colonizing and LOS-causing *S. haemolyticus* had similar MICs (Figure 1)
- Ceftaroline-resistant *S. haemolyticus* isolates belonged to various sequence types (ST1, 3, 25, 42) and were detected in both time periods (2007-2008 and 2014-2015)

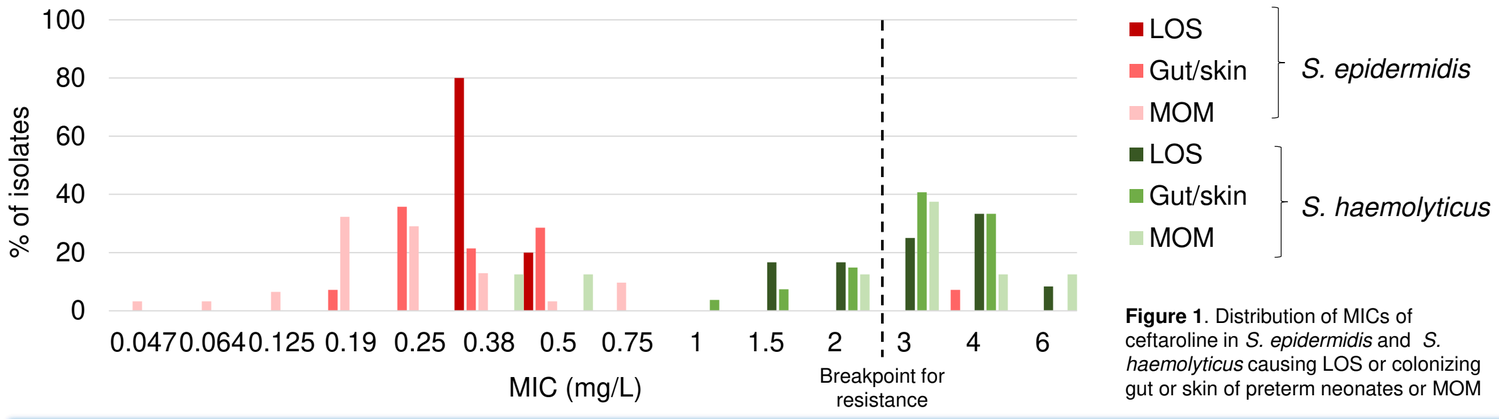

Figure 1. Distribution of MICs of ceftaroline in *S. epidermidis* and *S. haemolyticus* causing LOS or colonizing gut or skin of preterm neonates or MOM

Conclusion

- ***S. epidermidis* colonizing gut/skin and MOM or causing LOS in preterm neonates is mostly susceptible to ceftaroline.**
- **Widespread ceftaroline-resistance in *S. haemolyticus* may limit its potential use in treatment of LOS in preterm neonates.**