Minimum inhibitory concentration and minimum bactericidal concentration results for Brachyspira species– What is the difference?

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Introduction

- Terms used to describe the antimicrobial resistance breakpoint value for *Brachyspira* species can be confusing and ill-defined. Is it the epidemiological cut off value (ECOFF), an inhibitory breakpoint (IBP) or a clinical (therapeutic) breakpoint (CBP)?
- Minimum inhibitory concentration (MIC) can indicate the lowest concentration at which clear inhibition of bacterial growth has occurred or the lowest concentration at which no bacterial growth occurs. The latter circumstance describes the minimum bactericidal concentration (MBC).
- Attributing the correct term and cut-off/breakpoint in the test is particularly important for assessing the efficacy of agents that work by inhibiting the target organism.
- Comparative MIC and MBC results for *Brachyspira hyodysenteriae* are presented and compared with antimicrobial concentrations achieved in the colon contents, to estimate inhibitory breakpoints.

Methods

- The MIC and MBC were determined using the agar dilution method with the specified antibiotic incorporated in serial two-fold dilutions from 0.031µg/ml to 128µg/ml.
- The *B. hyodysenteriae* isolates were cultured from clinical samples submitted to SAC Veterinary Services, Edinburgh between the years 2004 - 2013. Samples were from pigs with a history of diarrhoea, mostly from herds in the UK.
- The ECOFF was determined by the MIC susceptibility pattern, the IBP by the maximum drug concentration in the colon contents (MCCC) and the CBP by dividing the MCCC by 4, approximately equivalent to the area under the curve (AUC) 24h divided by the MBC =100h[5].

Results

- The results of the MIC and MBC determinations are summarised in Table 1. Published data for antibiotic colon contents concentrations (CCCs) are in Table 2.

Table 1. Summary of MIC and MBC results (µg/ml)

Antibiotic	No of isolates	MIC 50	MIC 90	MIC range
Tiamulin	86	0.125	4.0	<0.031-32
Lincomycin	66	16	64	<0.031->128
Tylvalosin	45	8.0	32	0.5-64
Valnemulin	47	0.031	1.0	<0.031-16
Tylosin	18	>128	>128	>128
Antibiotic	**No of isolates**	**MBC 50**	**MBC 90**	**MBC range**
Tiamulin	86	0.25	4.0	<0.031-32
Lincomycin	66	32	128	<0.031->128
Tylvalosin	45	16	32	0.5->128
Valnemulin	47	<0.031	2.0	<0.031-16
Tylosin	18	>128	>128	>128

Table 2. Published data for colon contents concentration (CCC) for various antibiotics (E = estimated value)

Antibiotic	In feed (ppm)	CCC (µg/g)	Antibiotic	In feed (ppm)	CCC (µg/g)
Tiamulin	220(2)	8.05	Lincomycin	220(3)	101
	110	2.84		110	34.5
	40E	1.03		44E	13.8
			Valnemulin	200(1)	5.6
Tylosin	100E(4)	38		75	1.6
	40E	15.3		25E	0.53

- The susceptibility patterns for both MICs and MBCs and CCC relationships for tiamulin, lincomycin and valnemulin are highlighted in Figures 1-4.

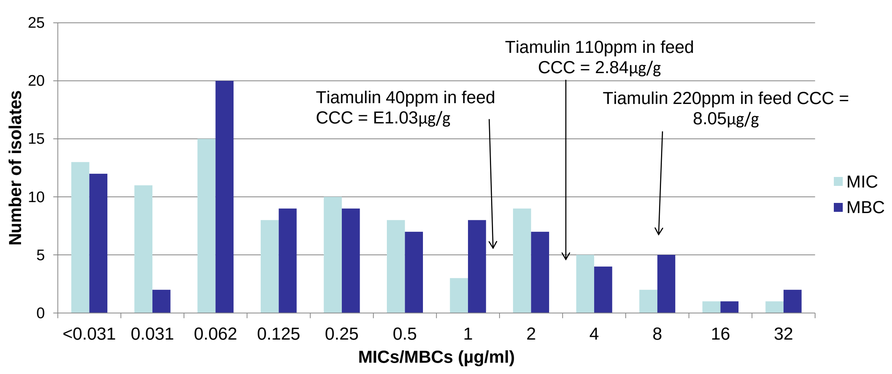

Figure 1. Susceptibility patterns for both MICs and MBCs and CCC relationships for tiamulin

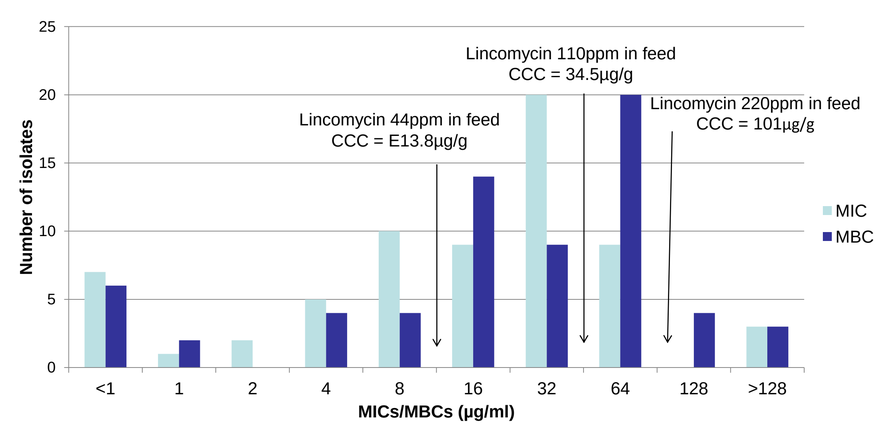

Figure 2. Susceptibility patterns for both MICs and MBCs and CCC relationships for lincomycin

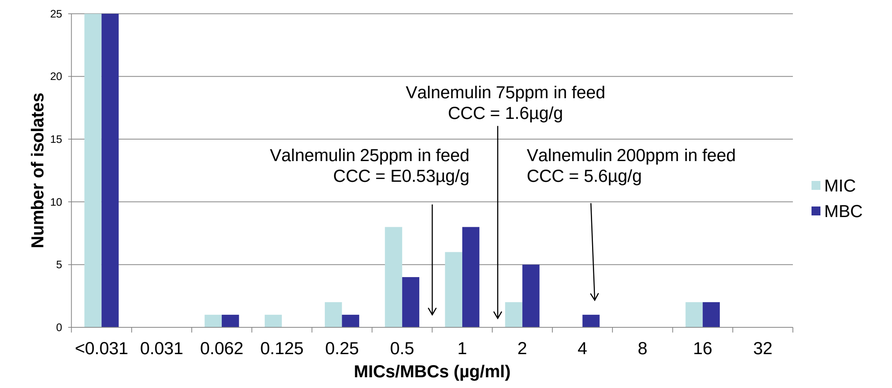

Figure 3. Susceptibility patterns for both MICs and MBCs and CCC relationships for valnemulin

Table 3. ECOFFs, IBPs and CBPs for various antibiotics against *B. hyodysenteriae*

Antibiotic	In feed conc (ppm)	ECOFF (µg/ml)	IBP (µg/ml)	CBP (µg/ml)
Tiamulin	220	1.0	8.05	>2.0
Lincomycin	220	2.0	101	>25
Tylosin	100	ND (all resistant)	38	>9.5
Valnemulin	200	0.062	5.6	>1.4

Discussion and Conclusions

- Most MIC:MBC 50 ratios are 1: 2 suggesting that these bacteriostatic antibiotics have bactericidal properties approximately double the MIC value.
- The establishment and differentiation of ECOFFs, IBPs for prevention and CBPs, where the drug may be used for treatment or even eradication purposes, is helpful not only for gauging the level of resistance in the field but also for the veterinarian making decisions on therapeutic choices.

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