

Antibiotic Susceptibility of *Stenotrophomonas maltophilia* in the Presence of Lactoferrin

Stenotrophomonas maltophilia is resistant to most antibiotics and infects the respiratory tract of cystic fibrosis (CF) patients (5). CF sputum contains a high concentration of lactoferrin (0.9 mg/ml) (9). Lactoferrin damages outer membranes of gram-negative bacteria (6), which might explain why MICs for *Pseudomonas aeruginosa* of rifampin and chloramphenicol were reduced in the presence of 0.9 mg/ml of human lactoferrin (7). Colistin (8) and other agents (4) that increase outer membrane permeability of gram-negative bacteria have enhanced the susceptibility of *S. maltophilia* to rifampin. As potentiation of antibiotic activity by lactoferrin may influence treatment of CF infections, we investigated the effect of lactoferrin (0.9 mg/ml) on susceptibilities of CF *S. maltophilia* isolates to drugs used to treat *S. maltophilia* infections (ceftazidime, gentamicin, trimethoprim, and rifampin). Lactoferrin enhanced the sensitivity of *P. aeruginosa* (7) to chloramphenicol, so we looked for similar effects with *S. maltophilia*.

Clinical isolates of *S. maltophilia* were from Booth Hall Hospital, Manchester, United Kingdom. Human recombinant lactoferrin was from Agennix Inc., Houston, Tex.; rifampin and chloramphenicol were from Mast Laboratories, United Kingdom; gentamicin sulfate from Sigma; ceftazidime pentahydrate was from GlaxoSmithKline; and trimethoprim was from APS-Berk, Sussex, United Kingdom.

Determination of MICs with and without 0.9 mg/ml lactoferrin was by broth microdilution (7) including antibiotic-free controls with and without lactoferrin. Bacterial suspensions were diluted to a final concentration of 10⁵ CFU/ml. The minimum bactericidal concentration (MBC) was the concentration that led to 99.9% killing.

For each MIC and MBC, eight replicate tests were per-

formed, and results are presented as medians. Analysis was by Mann-Whitney U test.

Rifampin MICs (Table 1) for all isolates were lower (2- to 16-fold) with lactoferrin than without, while the rifampin MBCs were lowered 2- to 4-fold in the presence of lactoferrin ($P < 0.001$ for all isolates). For two out of the three isolates tested for gentamicin sensitivity, median MICs and MBCs were significantly lower with lactoferrin. All MICs and MBCs of chloramphenicol and trimethoprim (four isolates tested) and MICs of ceftazidime (three isolates tested) were within the tested ranges and were not lower with lactoferrin (data not shown). MBCs of ceftazidime for two of the isolates were above the tested range (>256 µg/ml), and those for the remaining strains were unchanged on addition of lactoferrin. All isolates were resistant to trimethoprim (MICs, 64 to 256 µg/ml).

Rifampin MBCs for *S. maltophilia* were lower with lactoferrin, as were MICs which fell from levels that are not clinically obtainable to 12 µg/ml or below (levels that have been recorded in the sputum of some rifampin-treated patients) (1). This finding supports use of rifampin in treatment of *S. maltophilia* infections of CF patients. Our findings with rifampin concur with reports of similar effects with other gram-negative bacteria, such as *Burkholderia cepacia* (2) and mucoid *P. aeruginosa* isolates from CF patients (2, 7), *Escherichia coli* (3, 6), and *Salmonella enterica* serovar Typhimurium (10). In contrast to *S. enterica* serovar Typhimurium (10) and *P. aeruginosa* (7), susceptibility of *S. maltophilia* to chloramphenicol was not enhanced by lactoferrin. These and previous findings (2, 7) suggest that for CF respiratory infections, it may be more appropriate to test antibiotic sensitivities in the presence of lactoferrin.

TABLE 1. Median MICs and MBCs (µg/ml) of rifampin and gentamicin for clinical isolates (eight replicates per isolate) of *S. maltophilia* with (+LF) and without (–LF) lactoferrin (0.9 mg/ml)

<i>S. maltophilia</i> isolate	Rifampin						Gentamicin					
	MIC			MBC			MIC			MBC		
	–LF	+LF	<i>P</i>	–LF	+LF	<i>P</i>	–LF	+LF	<i>P</i>	–LF	+LF	<i>P</i>
I020	64	8	<0.001	128	48	<0.001	1,024	1,024		>2,048	>2,048	
I021	32	2	<0.001	128	32	<0.001	2	1	0.026	16	8	0.004
I221	32	12	0.003	64	32	<0.001	2	1	0.007	16	8	0.006
I384	64	8	0.003	128	64	<0.001						

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Ahmed O. Qamruddin
Department of Microbiology
2nd Floor Clinical Sciences Building
Manchester Royal Infirmary
Oxford Road
Manchester, M13 9WL, United Kingdom

Mustafa A. Alkawash
James S. Soothill*
Infectious Diseases and Microbiology Unit
Institute of Child Health
30 Guilford Street
University College
London, WC1N 1EP, United Kingdom

*Phone: 44 207 405 9200, ext. 5237
Fax: 44 207 813 8268
E-mail: soothj@gosh.nhs.uk