Anaerobe 54 (2018) 61–64

Contents lists available at ScienceDirect

Anaerobe

journal homepage: www.elsevier.com/locate/anaerobe

Short communication

Antimicrobial susceptibility of anaerobic bacteria

In vitro activity of lascufloxacin, a novel fluoroquinolone antibacterial agent, against various clinical isolates of anaerobes and *Streptococcus anginosus* group

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ARTICLE INFO

Article history:
Received 12 June 2018
Received in revised form
10 August 2018
Accepted 11 August 2018
Available online 13 August 2018

Handling Editor: Diane Citron

Keywords:
Lascufloxacin
Fluoroquinolone
Anaerobe

ABSTRACT

The *in vitro* activities of lascufloxacin were evaluated by comparison with seven reference compounds using 412 clinical isolates of anaerobes and *Streptococcus anginosus* group. Lascufloxacin showed potent and broad antibacterial activities greater than those of existing quinolones against the clinical isolates used in this study.

Anaerobes are associated with a variety of human infections [1–4]. In respiratory tract infections, for example, anaerobes are involved in the development of aspiration pneumonia, lung abscess, empyema, etc. [5,6], and recent reports indicated that anaerobes also play important roles even in the onset of community-acquired pneumonia [7].

Lascufloxacin (AM-1977; LSX) is a novel fluoroquinolone antibacterial agent developed for treatment of respiratory tract infections with both oral and parenteral formulations in Japan. Data from microbiological studies indicated that LSX has potent antibacterial activity against various aerobic respiratory pathogens, such as *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Mycoplasma pneumoniae*, including drug-resistant strains [8]. On the other hand, anti-anaerobic activity of LSX was not clearly identified. We conducted a comprehensive study to investigate the *in vitro* activity of LSX against various clinical isolates of anaerobes covering *Streptococcus anginosus* group, facultative anaerobes, and major pathogens involved in respiratory tract infections, such as aspiration pneumonia, and evaluated its potency by comparison with several classes of existing therapeutic agents. These data were presented in part at the Interscience Conference on Antimicrobial Agents and Chemotherapy/International Congress of Chemotherapy and Infection, San Diego, CA, 2015 [9].

A total of 412 clinical strains consisting of 15 bacterial species isolated from patients treated at Aichi Medical University Hospital and others in Japan between 2008 and 2014 were tested. All strains were isolated from blood, abscesses, genital secretions, urine, drain, and in case of *Clostridioides difficile*, from feces, taken from patients treated at these hospitals, surgery, otolaryngology, gynecology, urology, and so on. To investigate the potential of LSX, we compared *in vitro* activities against these clinical isolates of LSX, existing quinolones, levofloxacin (LVX), garenoxacin (GAR), moxifloxacin (MFX), and representative drugs from different chemical classes meropenem (MEM), piperacillin/tazobactam (TZP), clindamycin (CLI), metronidazole (MNZ), which are widely used for treating anaerobic infections in clinical settings. LSX was provided by Kyorin Pharmaceutical Co., Ltd. (Tokyo, Japan) and other drugs were manufactured by Toyama Chemical Co., Ltd. (Tokyo, Japan), Bayer Yakuhin, Ltd (Osaka, Japan), Sumitomo Dainippon Pharma (Osaka, Japan), Chem-Impex International, Inc (Illinois, USA), Pfizer Japan Inc. (Osaka, Japan), Sigma-Aldrich (Missouri, USA), Kyowa Pharma

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https://doi.org/10.1016/j.anaerobe.2018.08.002
1075-9964/

Table 1
In vitro activities of lascufloxacin and other agents against clinical isolates.

Organism (no. of isolates)	Drug	MIC range (μg/mL)	MIC_{50} (μg/mL)	MIC_{90} (μg/mL)
Gram-positive anaerobes and *S. anginosus* group				
Clostridium difficile (49)	Lascufloxacin	0.06 to 16	1	2
	Levofloxacin	0.5 to >64	16	>64
	Garenoxacin	0.25 to 32	1	32
	Moxifloxacin	0.25 to 64	4	16
	Meropenem	0.06 to 2	1	2
	Piperacillin/tazobactam	0.12/4 to 16/4	4/4	16/4
	Clindamycin	0.06 to >64	64	>64
	Metronidazole	≤0.03 to >64	0.25	1
Streptococcus anginosus (20)	Lascufloxacin	≤0.03 to 1	0.06	0.25
	Levofloxacin	0.5 to 4	2	2
	Garenoxacin	≤0.03 to 1	0.25	1
	Moxifloxacin	0.12 to 2	0.5	1
	Meropenem	≤0.03 to 0.25	0.06	0.12
	Piperacillin/tazobactam	≤0.03/4 to 0.5/4	0.12/4	0.25/4
	Clindamycin	≤0.03 to >64	0.12	>64
	Metronidazole	32 to >64	>64	>64
Streptococcus constellatus (20)	Lascufloxacin	≤0.03 to 0.25	0.06	0.06
	Levofloxacin	1 to 64	1	2
	Garenoxacin	0.06 to 1	0.12	0.25
	Moxifloxacin	0.25 to 8	0.5	0.5
	Meropenem	0.06 to 2	0.12	0.25
	Piperacillin/tazobactam	0.12/4 to 1/4	0.5/4	0.5/4
	Clindamycin	0.12 to >64	0.25	16
	Metronidazole	64 to >64	>64	>64
Streptococcus intermedius (20)	Lascufloxacin	≤0.03 to 0.5	0.06	0.12
	Levofloxacin	0.5 to 2	1	2
	Garenoxacin	≤0.03 to 0.5	0.06	0.25
	Moxifloxacin	0.12 to 0.5	0.25	0.5
	Meropenem	≤0.03 to 0.12	0.06	0.12
	Piperacillin/tazobactam	≤0.03/4 to 0.5/4	0.12/4	0.25/4
	Clindamycin	0.06 to 0.5	0.12	0.25
	Metronidazole	64 to >64	>64	>64
Finegoldia magna (23)	Lascufloxacin	≤0.03 to 8	1	4
	Levofloxacin	0.25 to 64	32	64
	Garenoxacin	≤0.03 to >64	32	>64
	Moxifloxacin	0.06 to 64	8	32
	Meropenem	≤0.03 to 0.12	0.06	0.12
	Piperacillin/tazobactam	≤0.03/4 to 0.25/4	0.06/4	0.12/4
	Clindamycin	0.06 to >64	0.25	>64
	Metronidazole	0.25 to 2	0.5	2
Peptoniphilus asaccharolyticus (19)	Lascufloxacin	0.06 to 4	0.25	2
	Levofloxacin	2 to 64	4	64
	Garenoxacin	≤0.03 to 16	0.12	16
	Moxifloxacin	0/12 to 16	0.25	16
	Meropenem	≤0.03 to ≤0.03	≤0.03	≤0.03
	Piperacillin/tazobactam	≤0.03/4 to ≤0.03/4	≤0.03/4	≤0.03/4
	Clindamycin	≤0.03 to >64	0.25	>64
	Metronidazole	0.25 to 2	0.5	2
Parvimonas micra (23)	Lascufloxacin	0.25 to 16	0.25	2
	Levofloxacin	0.12 to 8	0.25	2
	Garenoxacin	≤0.03 to 1	0.12	0.5
	Moxifloxacin	0.25 to 8	0.25	1
	Meropenem	≤0.03 to 0.5	≤0.03	0.06
	Piperacillin/tazobactam	≤0.03/4 to 0.5/4	≤0.03/4	0.25/4
	Clindamycin	≤0.03 to 0.5	0.06	0.25
	Metronidazole	≤0.03 to >64	0.25	>64
Gram-negative anaerobes				
Bacteroides fragilis (50)	Lascufloxacin	0.12 to 8	1	4
	Levofloxacin	1 to 64	2	32
	Garenoxacin	0.12 to 16	0.5	4
	Moxifloxacin	0.25 to 8	1	8
	Meropenem	0.06 to >64	0.25	4
	Piperacillin/tazobactam	≤0.03/4 to 64/4	0.25/4	1/4
	Clindamycin	≤0.03 to >64	>64	>64
	Metronidazole	0.25 to 8	1	2