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Comparison of Fluoroquinolone Resistance Genes of *Salmonella enterica* Serovar Choleraesuis Isolates in Japan and Taiwan

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In Japan's neighbor Taiwan, the occurrence and spread of fluoroquinolone-resistant *Salmonella enterica* serovar Choleraesuis infection in human and pigs was reported in 2002, pointing out the genetic relevance between human and porcine isolates during 2000 and 2001 (1). In 2001, we isolated the fluoroquinolone-resistant *S*. Choleraesuis from swine in Japan (3). At that time, no published was available on fluoroquinolone-resistant isolates of human origin in Japan. A considerable amount of pork meats each year (40% of all imported pork meats) were imported from Taiwan before an outbreak of foot-and-mouth disease there in 1997. In addition, business and sightseeing trips to Taiwan by Japanese travelers have seen large increases. To clarify the relevance of the fluoroquinolone-resistant *S*. Choleraesuis isolates between Japan and Taiwan, we examined the antimicrobial susceptibility and the sequence of the regions encoding the target enzymes of fluoroquinolones.

Seven isolates of *S*. Choleraesuis in Japan and Taiwan, including two fluoroquinolone-resistant isolates (13-PLS-6, Japan; CGSC18, Taiwan), were used in this study. The Japanese isolates were originated from swine and the Taiwanese isolates from patients. Antimicrobial susceptibility of *S*. Choleraesuis isolates against ampicillin (AMP), cefazolin, cefuroxime, ceftiofur, dihydrostreptomycin (DSM), kanamycin (KM), gentamicin, destomycin A (DMA), apramycin (APM), colistin, oxytetracycline (OTC), chloramphenicol (CHL), bicozamycin, nalidixic acid (NA), oxolinic acid (OA), enrofloxacin, ofloxacin, ciprofloxacin, sulphadimethoxine (SDMX), trimethoprim (TMP), and olaquindox were tested by an agar dilution methods in accordance with NCCLS guidelines (4). The 13-PLS-6 strain was resistant to seven antimicrobials (AMP-CHL-DSM-KM-OTC-SDMX-TMP) in addition to showing quinolone resistance. With regard to antimicrobial resistance type, the three NA-resistant isolates in Taiwan were resistant to DMA and APM together with the seven antimicrobial resistances of 13-PLS-6. The *Salmonella* isolates resistant to the two antimicrobials (DMA and APM) were rarely prevalent in Japan (2).

Mutations in quinolone resistance-determining region (QRDR) of the *gyrA* and *parC* gene were detected by direct DNA sequencing. In both fluoroquinolone-resistant isolates, two point mutations in the *gyrA* gene and a mutation in the *parC* gene were detected, as shown in Table 1. All of the fluoroquinolone-resistant isolates described in the previous report (1) had the same type of mutation in the *gyrA* gene (83Phe and 87Asn as CGSC18), differing from the *gyrA* mutation of 13-PLS-6.

We suspected the relevance of fluoroquinolone isolates in both countries, but these isolates did not seem relevant genetically. In recent years, the worldwide spread of antimicrobial-

Table 1. Susceptibility to quinolones and *gyrA* mutation of *Salmonella* Choleraesuis isolates in Japan and Taiwan

S. Choleraesuis isolates	MIC (mg/ml)			Mutation	
	NAL	CIP	enrofloxacin	*gyrA*	*parC*
Japan					
13-PLS-6	512	2	4	^{83}Ser→Tyr (TCC→TAC), ^{87}Asp→Gly (GAC→GGC)	^{80}Ser→Arg (AGC→AGA)
14-PLS-21	512	1	2	^{83}Ser→Phe (TCC→TTC)	none (wild type)
13-PLS-29	4	≤0.125	≤0.125	none (wild type)	none (wild type)
13-PLS-55	4	≤0.125	≤0.125	none (wild type)	none (wild type)
Taiwan					
CGSC18	>512	16	32	^{83}Ser→Phe (TCC→TTC), ^{87}Asp→Asn (GAC→AAC)	^{80}Ser→Ile (AGC→ATC)
CGSC1	>512	0.25	0.5	^{87}Asp→Asn (GAC→AAC)	none (wild type)
CGSC11	>512	0.25	0.5	^{87}Asp→Gly (GAC→GGC)	none (wild type)
CGSC42	4	≤0.125	≤0.125	none (wild type)	none (wild type)

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resistant *Salmonella* has become a global public and animal health concern. The multiresistant *S.* Typhimurium DT104 quickly spread throughout the world (5). After the first isolation of the fluoroquinolone-resistant *S.* Choleraesuis, the communicative surveillance on farms revealed the overuse and misuse of enrofloxacin for the treatment of various infectious diseases in pigs. By continuous surveys on the farms, the fluoroquinolone-resistant *S.* Choleraesuis was eradicated from the herd. It was reported in a recent study that the incidence of quinolone-resistant *Salmonella* is associated with 5-day enrofloxacin treatment to swine (2). The fluoroquinolone-resistance in *S.* Choleraesuis may arise rapidly due to inappropriate use of fluoroquinolone antimicrobials.

The Japanese Veterinary Antimicrobial Monitoring (JVARM) system will provide data verifying the significance of continuous monitoring and surveillance of antimicrobial resistance. Our report emphasizes the necessity of prudent usage of antimicrobials for animal use at food production.

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