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Antibiotic residues in meat, milk and aquatic products in Shanghai and human exposure assessment

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ABSTRACT

In this study, we screened 20 common antibiotic (three tetracyclines, four fluoroquinolones, three macrolides, three β-lactams, four sulfonamides, and three phenicols) residues in 125 samples from common types of livestock and poultry meat, milk and aquatic products in Shanghai by ultra-performance liquid chromatography coupled to high-resolution quadrupole time-of-flight mass spectrometry in 2016 and assessed their role in human exposure by Monte Carlo Simulation. Overall, 15 out of screened antibiotics were found in these samples and the overall detection frequency was 39.2%. Antibiotics were found in 28.6% of livestock and poultry meat (35.3% for pork and 22.2% for chicken), 10.6% of milk, and 52.1% of aquatic products. Of aquatic products, the overall detection frequency of antibiotics was 91.7% for snakeheads, 81.8% for loaches, 76.9% for carps, 40.0% for yellow-head catfishes, and 16.7% for shrimps, but none was detected in swamp eels. Four human antibiotics were detected: azithromycin was detected in 50.0% of snakeheads and 5.1% of loaches, roxithromycin in 5.9% of pork, and chloramphenicol and cefradine respectively in 5.3% of milk. Enrofloxacin and trimethoprim exceeded the maximum residue limits in 7.7% of carps and 8.3% of snakeheads, respectively. The estimated daily exposure dose by Monte Carlo Simulation was less than 1 μg/kg/day. Antibiotic residues in aquatic products and their consumption accounted for 74.71% and 70.35% of overall variance of estimated antibiotic exposure for men and women, respectively. These findings indicated a high level of antibiotic residues in meat, milk and aquatic products and aquatic products were an important source for exposure of human to antibiotics.

1. Introduction

Since penicillin was discovered in 1928, antibiotics have become one pillar of modern medicine (Kumar, Lee, & Cho, 2012). After it was found that they could be used not only to prevent and treat infectious diseases, but also to promote growth in animal in 1940s, antibiotics were extensively used in animal husbandry and aquaculture (Gustafson & Bowen, 1997), but hazards and benefits of this practice have been in controversy (Van Boeckel et al., 2015). In general, the extensive use of antibiotics in animal have two major adverse impacts on human health: bacterial resistance (Marshall & Levy, 2011) and toxicological effects resulting from their residues in food (Mund, Khan, Tahir, Mustafa, & Fayyaz, 2016). Bacterial resistance is putting the modern medicine to 'post-antibiotic era' and there is a possibility that the bacterial resistance genes deriving from animal microbiome can be horizontally transferred to human microbiota (Marshall & Levy, 2011). For toxicological effects, as it is becoming clear that human microbiome plays a key role in the physiological function, these effects have been extended from traditional side effects to immune and metabolic diseases (Shreiner, Kao, & Young, 2015).

Generally, the exposure of human to antibiotics primarily derives from their clinical use and residues in drinking water and food (Wang et al., 2015). The overall exposure of human to antibiotics from various sources is a better indication of exploring their toxicological effects. A few studies found that adult and children were

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extensively exposed to multiple human or veterinary antibiotics by biomonitoring antibiotics in urines (Ji, Kho et al., 2010; Ji, Lim, Park, & Choi, 2010; Wang et al., 2015, 2017) and that drinking water was not likely an important source to overall exposure of human to antibiotics (Ji, Kho et al., 2010; Ji, Lim et al 2010; Wang, Wang, Wang, Zhao et al., 2016). So far, however, there has been lack of comprehensive data concerning antibiotic residues in foods and their role in human exposure. For this, this study measured the residues of 20 common antibiotics from five categories in common types of meat, milk and aquatic products in Shanghai, and assessed their contribution to human exposure.

2. Materials and methods

2.1. Sample collection

A total of 125 samples, including 35 fresh livestock and poultry meat, 19 pure milk, and 71 fresh aquatic products, were collected in five administrative districts of Shanghai City in July 2016. Livestock and poultry meat samples were consisted of 17 pork samples and 18 chicken samples from thighs or wings, and 71 aquatic products were consisted of 18 shrimps and 53 fishes (12 snakeheads, 10 yellow-head catfishes, 11 loaches, 13 carps, and seven swamp eels). All samples were collected from 15 food markets and five supermarkets in 13 batches and of them, 74 samples were from food markets and 32 from supermarkets. About 200–500 g were collected for each of pock or aquatic product sample and 1–3 thighs or wings were collected for each chicken sample. Milk was all packed in paper cartons and collected from two supermarkets in two batches. Common domestic brands in market were included and their raw milk were all from domestic areas, including Shanghai City, Shandong Province, Jiangsu Province, Inner Mongolia Autonomous Region, Hebei Province, Anhui Province, Ningxia Autonomous Region, and Helongjiang Province.

2.2. Selection and analysis of antibiotics

To reflect both the residues of veterinary antibiotics and misuse of human antibiotics in animal, 20 common antibiotics from six categories (three tetracyclines, four fluoroquinolones, three macrolides, three β-lactams, four sulfonamides, and three phenicols) were selected, including three veterinary antibiotics (VAs) exclusively used in animal, four human antibiotics (HAs) exclusively used in human, and 13 veterinary/human antibiotics (V/HAs) used in both animal and human (Table 1) (Xiao, 2001; Zhang, 2015). Antibiotics in meat, milk and aquatic products were determined by the isotope-dilution ultra-performance liquid chromatography coupled to high-resolution quadrupole time-of-flight mass spectrometry following a modified method (Yamaguchi, Okihashi, Harada, Uchida et al., 2015). Briefly, after meat and aquatic products were minced and mixed completely, antibiotics were extracted by 80% acetonitrile water solution. After being added by isotope-labeled internal standards, the extraction solution was purified by the solid phase extraction and then analyzed by ultra-performance liquid chromatography coupled to high-resolution quadrupole time-of-flight mass spectrometry. For the analysis of antibiotics in milk, only sample pretreatment was modified. All analyses of samples were performed in July 2016 by the same analytical team in our lab. At least one solvent blank was prepared for each batch to monitor the background interferences. The limit of detection, defined as a signal-to-noise ratio of 3, ranged from 0.05 to 2.0 ng/g for meat and from 0.2 to 5.0 ng/ml for milk. No background interference was observed for antibiotics. The recoveries in the spiked meat and aquatic products at a concentration of 20 ng/g ranged from 66.7 to 130.5% with the elative standard deviations varying between 8.9 and 19.7% and the recoveries in spiked milk at a concentration of 40 ng/ml ranged from 76.2 to 113.7% with the relative standard deviations varying between 7.2 and 15.8%. Detailed parameters of analytical method were provided in Table S1 and analytical procedure was described in Supplementary Information.

2.3. Predication of antibiotic exposure

We estimated the daily exposure dose of antibiotics from livestock and poultry meat, milk and aquatic products for adults based on their average daily consumption. The calculation formula was as followed: $E_d = \frac{C_L \times M_L + C_A \times M_A + C_M \times M_M}{M_B \times 1000}$ (E_d: estimated daily exposure dose, μg/kg/day; C_L: antibiotic content in livestock and poultry meat, ng/g; M_L: daily adult consumption of livestock and poultry meat, g/day; C_A: antibiotic content in aquatic products, ng/g; M_A: daily adult consumption of aquatic products, g/day; C_M: antibiotic content in milk and its products, ng/g; M_M: daily adult consumption of milk and its products, g/day; M_B: average body weight, kg). After the probability distribution of each parameter in the formula was obtained, the probability distribution of daily exposure dose of antibiotics was predicted by 100,000 times of Monte Carlo Simulation (Claeys, De Voghel, Schmit, Vromman, & Pussemier, 2008). The probability distributions of antibiotic contents in livestock and poultry meat, milk and aquatic products and their contribution to overall variance of daily exposure dose were calculated by using the @Risk software (version 7.5.0, Palisade Corporation). According to a dietary survey conducted in Shanghai (Zhou, Xia, Zhou, Jiang, & Li, 2015), the daily consumption of livestock and poultry meat for adults aged 15 years or above was set as the normal distributions with a mean of 93.42 g (standard deviation (SD): 95.97 g) for men and 77.17 g (SD: 79.16 g) for women; the daily consumption of aquatic products was set as the normal distribution with a mean of 45.57 g (SD: 54.91 g) for men and 43.66 g (SD: 53.35 g) for women; the daily consumption of milk and its products was set as the normal distribution with a mean of 105.29 g (SD: 47.86 g) for men and 120.66 g (SD: 103.27 g) for women. The body weight of adults aged 20 years or above was set as the normal distribution with a mean of 63.8 kg (SD: 9.9 kg) for men and 56.5 kg (SD: 9.1 kg) for women according to the data provided by Group of China Obesity Task Force (Zhou, 2002).

2.4. Statistical analysis

Each antibiotic category was summed by the sum of residue contents of antibiotics, including tetracyclines, fluoroquinolones, macrolides, β-lactams, sulfonamides, and phenicols (Table 1). Because trimethoprim is usually used with sulfonamides in practice, it was analyzed with sulfonamides together. A positive detection of category in one sample was defined as a detection of any antibiotic(s) included in the category. The detection frequencies of combined residues in sample were determined according to the number of combined antibiotics. The maximum residue limits (MRLs) and regulations issued by the European Commission (EU, 2010), which were similar to those issued by the Ministry of Agriculture of the People's Republic of China (MOA, 2002), were used to check the health risk of antibiotic residues in livestock and poultry meat, milk and aquatic products. Detection frequency and selected percentile content of antibiotics in livestock and poultry meat, milk and aquatic products were provided in all samples and by sample types. Rank test and Chi-square test were respectively used to examine the differences in residue content distributions and detection frequencies of antibiotics among market types and so was done among sample types. All statistical analyses were performed by the statistical software packages SPSS (version 17; SPSS, Inc.,