Review of antibiotic resistance genes in urban water supply system

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Abstract. Antibiotics are a new type of pollutant, and antibiotic resistance has caused a crisis in global health. Urban water supply system plays an important role in purifying raw water and distributing drinking water. This review will cover two aspects: drinking water treatment system and water distribution system. It has been previously reported that not all water treatment processes can reduce antibiotic resistance. Furthermore, there is also a potential risk of secondary pollution in the water supply network. The research purpose of this paper is to summarize the existence and mechanism of antibiotic resistant bacteria (ARB) and antibiotic resistant genes (ARGs) in urban water supply system.

1. Introduction

Antibiotics were first discovered in 1928 and widely used in various fields since then [1]. However, due to the lack of sufficient understanding, people blindly believe in effectiveness of antibiotics which results in their excessive use. Data show that global antibiotic use increased by 35 % from 2000 to 2010 [2]. Studies reported that more Americans die from methicillin-resistant Staphylococcus aureus than from emphysema, AIDS, and other diseases combined [3]. In the United States, nearly three quarters of adults with acute bronchitis are being treated with unnecessary antibiotics [1]. Antibiotic resistance has been identified by the World Health Organization as the most serious threat to public health in this century [4].

The abuse of antibiotics can increase their residual amount in the water environment, and causes the enhancement of antibiotic resistance, which has been recognized as a new type of pollutant. At present, a variety of antibiotic resistance genes (ARGs) have been found in numerous environment media, for instance sewage plant [5], livestock wastewater [6], surface water [7], drinking water [8], and soil [9]. When the municipal sewage treatment plant discharges the wastewater containing faeces into the water, it also means that a large number of antibiotics are also discharged into aquatic environment [10]. As more and more ARGs are detected in aquatic environment, antibiotic resistance has become a global problem in face of mankind nowadays.

Moreover, it may be difficult to remove ARGs and antibiotic resistant bacteria (ARB) from the water thoroughly by conventional drinking water treatment process, and some treatment units even increase their abundance [11]. In addition, studies have shown that ARGs can be detected in tap water, indicating that drinking water distribution system is a source of pollution that cannot be neglected [12]. In this paper, the existence and transmission mechanism of antibiotic resistance in urban water supply system were discussed according to domestic and overseas literature.
2. Mechanisms for the bacterial resistance to antibiotics and transfer of ARGs

2.1. The origin and mechanisms of antibiotic resistance
ARB refer to the reduced sensitivity of the bacteria to the drug after repeated contact with the antibiotic drug, resulting in a decrease in the efficacy of the drug on the bacteria, or even ineffectiveness.

It is generally accepted that the drug resistance mechanism of ARB is mainly based on the following four aspects. 1) Some bacteria are inherently resistant to many antibiotics, because their cell membrane permeability is relatively low or lack genes to translate the target proteins that interact with antibiotics [13]. 2) Through the efflux pump on the cell membrane, the bacteria pump out the antibiotic molecules that spread into the cell, thus reducing the concentration of antibiotics in the cell [13]. 3) Bacteria produce enzymes that inactivate antibiotics [14]. 4) There is a mutation in the target protein that acts with antibiotics, which changes the affinity of antibiotics to the target protein, resulting in the resistance of bacteria [15].

2.2. Transfer of ARGs
The existence of internal drug resistance genes is the molecular biological basis of bacterial resistance to antibiotics. The resistance genes carried by bacteria mainly include their own inherent resistance and acquired resistance. The former is called vertical gene transfer, the method is applied to realize the transmission of ARGs between intermediate parents and offspring [16]. The last one is called horizontal gene transfer (HGT). The transfer of genetic materials between different species and main mode of HGT can occur due to several processes listed below. 1) Conjugation, which is the process that mainly depends on the mobile gene element (MGE) such as a plasmid, an integron, or a transposon [17]. 2) Transformation, a process when bacteria take up extracellular free DNA, make it their own genetic material, and integrate expression in vivo [18]. 3) Transduction, a method that allows horizontal transfer of resistance genes between viruses, mainly through bacteriophages [19].

3. Environmental risks of ARGs
The transmission of resistance genes in the environment is a cyclic process, which is easy to accumulate in the human body (Fig. 1) [20]. Animal faeces in farms contain a large number of resistant bacteria, which cause resistant pollution in the water environment due to surface runoff and rainwater scouring into soil, rivers, lakes, or groundwater. The resistance genes in these resistant bacteria can be transferred into environmental indigenous microorganisms by horizontal gene transfer. In addition, the resistance gene will enter the human body through the food chain in the carnivorous products provided by the livestock and poultry industry, and the resistance gene in the soil may also be transferred to the plant and eventually enter the human body through the food chain [21]. The resistance genes contained in human faeces have not been completely removed after entering the sewage treatment plant. The sewage is treated by the sewage treatment plant and discharged into the river, as a water source into the water treatment plant, and finally gets into the human body.

ARGs will be accumulated in the body of the human, enhance the drug resistance of human cells, and pose a serious threat to the public health and ecological security. When pathogenic bacteria acquire multiple resistance genes, they have both pathogenicity and multiple drug resistance. In 2010, superbugs containing NDM-1 gene were first found in humans in New Delhi, India, causing worldwide panic [22]. Superbugs can develop resistance to a variety of antibiotic drugs at the same time, resulting in human death due to no cure. In a word, we must find a reasonable and effective way to remove ARGs of the environment.
4. Occurrence and spread of ARGs in drinking water

4.1. Surface water
Although the treatment process of the sewage treatment plant can remove some resistance genes, there are still a large number of them discharged into the surface water with the effluent. Luo et al. have quantitatively studied the existence of ARGs in surface water by measuring the water and sediment samples of Haihe River in China. The results revealed that Sul1 and Sul2 concentrations in sediments were significantly greater than that in water [23]. Zhang et al. also got similar results. They detected and quantified class 1 integronase genes and tetracycline resistance genes tetA and tetC in various aquatic environment in Jiangsu Province in China. Their studies showed that the concentration of ARGs in lake sediments was much higher than that in water samples [24]. Moreover, the surface water contaminated by ARGs can lead to the emergence of ARGs in livestock, resulting in food chain pollution and a threat to human health [5].

4.2. Groundwater
Because of the infiltration of sewage tank and soil in livestock farm, ARGs began to exist in groundwater. Koike et al. detected tetracycline resistance gene in groundwater. Their studies showed that the exudation of animal waste had significant effect on the wide dissemination of ARGs in groundwater [25]. Another research in the US indicated that Enterococcus spp resistant to four kinds of antibiotics were isolated from groundwater samples near a pig farm. This agrees with previous studies proving that groundwater could be a reservoir of ARGs [26].

5. Removal of ARGs in drinking water treatment

5.1. Coagulation sedimentation and filtration
The main methods of handling in water treatment plants are coagulation, precipitation, filtering, and disinfection, which are designed to remove colloid, suspended solids, and pollutants from the water, and to decrease both chrominance and turbidity of the water [27].
In recent years, Li et al. have studied the removal of ARGs in the coagulation process. The results show that using FeCl₃ or perfluorinated compound (PFC) in municipal wastewater treatment plant can effectively remove ARGs, by about 0.5 to 3.1 log values, and conventional pollutants such as dissolved organic carbon (DOC) and dissolved ammonia nitrogen can also be effectively removed [28].

It is generally accepted that pH, temperature, and turbidity of raw water are obviously different from those of wastewater treatment plant, and the coagulants used in drinking water treatment plant are also different from those in sewage treatment plant. In the water treatment plant, the removal of resistance genes by coagulation and sedimentation will be slightly different. The related research mechanism in this area is still relatively rare, which can be used as a future trend [29].

The filtration process is a core unit in water treatment. The filter is the place with the highest amount of biological accumulation, and there is a great possibility of horizontal gene transfer. Xu et al. found that after being treated by the filtration unit in the water treatment plant, two types of resistance genes decreased. On the contrary, the relative abundance of most resistance genes increased after sand filtration [30]. Guo et al. also get a similar conclusion. Their team detected an increase in tetracycline resistance genes (tet A and tet O) after sand filtration [31]. Despite the fact that the filtration process can effectively remove suspended solids and part of organic matter in water, it is difficult to ensure biosafety. At present, the studies on mechanism of the increase in the absolute number of resistance genes in the effluent of filter may be a hot research topic.

5.2. Disinfection

The existing disinfection processes mainly include chlorination disinfection, chloramine disinfection, ozone disinfection, and ultraviolet disinfection. Among the many disinfection processes, chlorination disinfection and ultraviolet disinfection are the most widely used. Munir et al. discovered that the content of ARGs did not decrease significantly after chlorine disinfection [31]. Different from chlorination disinfection, ultraviolet disinfection is a physical process, and the specificity of ultraviolet light makes it possible to inactivate resistance genes effectively [32]. Some scholars have found that ultraviolet radiation can destroy the conversion ability of resistance genes in DNA, thus reducing the risk of horizontal transfer of resistance genes. McKinney et al. found that ultraviolet radiation could indeed reduce the content of resistance genes after UV disinfection, but the UV dose needed to inactivate resistance genes of 4 orders of magnitude was much higher than that in actual disinfection [33]. In recent years, different scholars have proposed that the combination of TiO₂ nanoparticles and near ultraviolet light can improve the efficiency of removing resistance genes, or the addition of Ag-TiO₂ composite nanomaterials can also greatly improve the efficacy of ultraviolet disinfection [32].

5.3. Spread of ARGs in water-supply pipeline

Although the ARG was significantly reduced in finished water after the treatment of source water, it still existed in the tap water and then entered the water supply network. It has been proved that the absolute abundance of ARGs in the effluent of the water supply network is significantly higher than that in the influent of the water supply network [12, 34]. For example, the research of Xu et al. shows that the absolute abundance of ARGs in the effluent of water supply network increases significantly, especially β-lactam ARGs [30], and there is a risk of ARGs contamination in water supply network.

The biofilm of the pipe wall in the water supply network can promote gene expression. Even if there is a small number of microbes in the pipe network, it will still attach to the pipe wall and form a biofilm [29]. The resistance gene in the water supply network may be absorbed by the bacteria attached to the biofilm, or the resistant bacteria in the drinking water transported by the pipe network may infect the indigenous bacteria attached to the biofilm through the horizontal transfer of the resistance gene. Therefore, the secondary pollution of microorganisms may be caused during pipe transfer of water.
The secondary pollution in the pipe network is a potential health risk, which has not received enough attention. The research on resistance genes in water supply network in China and abroad is still at a bare stage.

6. Conclusion

There has been a broad research in the literature about the existence of ARGs in urban water supply system. However, there has not been a clear explanation on ARGs removal through the conventional treatment process of water treatment plant. Besides, the drinking water distribution systems could serve as an incubator of ARGs. The biofilm and its effect on the enrichment of ARGs and ARB become a hotspot of research interests nowadays.

To guarantee the biosafety of drinking water, research and development of the most reliable, economical, and effective technology to remove ARGs are of great urgency. According to the above mentioned analysis, here we would like to propose several conceptions and suggestions about ARGs.

1) It is necessary to study the types and horizontal migration of multiple resistance genes in the environment as soon as possible, in order to evaluate their ecological health risks and provide a theoretical basis for the control of resistance gene pollution. 2) Drinking water treatment plant is not only an important repository of resistance genes, but also the key to remove resistance genes. In the future, we need to focus on the removal effect of resistance genes by a different combination of water treatment processes. 3) The secondary pollution of pipe network will be also the key content of future research. Necessary disinfection measures should be adopted at the end of the pipe network to control the content of ARGs entering the building pipeline system.

Overall, there is still little research on ARGs in urban water supply system, a detailed study is still necessary to examine their removal and spread with more quantitative results, which would help eliminating its threat to public security.

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