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ON QUANTITATIVE ASSESSMENT OF MICROBE RISK CAUSED BY EXPOSURE TO ENTERIC VIRUSES IN DRINKING WATER

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The authors assessed microbiological risks of acute intestinal infections (AII) with viral etiology caused by drinking water taken from centralized water supply systems among overall urban population in Arkhangelsk region over 2006-2017. The research was performed with Quantitative Microbial Risk Assessment (QMRA) procedure. It was revealed that acute intestinal viral infections prevailed among intestinal infections; the most widely spread ones were rotavirus infection (86.9%), norovirus infection (7.7%), and enterovirus infection (3.7%). The authors also performed comparative analysis of spatial distribution and long-term dynamics of incidence with AII which were possibly caused by infectious agents entering a body with water. The analysis revealed that rotavirus and norovirus infections frequently occurred in Arkhangelsk, Novodvinsk, Koryazhma, and Kotlas. Incidence with rotavirus infection among population in Koryazhma and Arkhangelsk grew 1.5-1.6 times faster than epidemiological processes on the reference territory. Coliphages contents were equal to P_{95}in drinking water taken from centralized water supply systems in Arkhangelsk and Koryazhma, and it was 1.4 and 2.2 times higher respectively than the hygienic standard. Rotavirus, norovirus, and enterovirus infections were highly likely to occur in Arkhangelsk (R=0.97-0.99), and rotavirus infection, in Koryazhma (R=0.95). Average probability of norovirus infection (R=0.58) and enterovirus infection (R=0.43) was detected in Koryazhma. The research results indicate that Quantitative Microbial Risk Assessment (QMRA) procedure is feasible and significant within the system of sanitary-epidemiologic surveillance over water treatment; it substantiates the necessity to create and implement virology monitoring over centralized drinking water supply.

Key words: *drinking water, water supply, acute intestinal infections, viral infections, coliphages contents, risk assessment, microbiological risk, QMRA.*

To ensure safety of drinking water supply is an efficient way to prevent diseases caused by drinking water consumption. In Russia, centralized water supply systems which are used to supply drinking water to consumers require urgent improvement [1]. Even if water purification is qualitative, there is still a possibility that infectious agents can penetrate water supply networks, for example, when water distribution systems are worn out, or in case of a damage done to water pipelines [2, 3]. Cases of acute enteric infections caused by infectious agents caught from water haven't been examined sufficiently due to epidemiologic analysis insensitivity and absence of research that allows to establish a direct correlation between drinking water contamination and a growth in sporadic incidence [4, 5].

Domestic techniques applied to assess microbe risks are based on factors which are directly related to contagion from water, for example, communal water supply and communal improvement of settlements, as well as quality of water taken from recreation water

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reservoirs and water sources[1]. Microbe risk assessment as a complex scientific approach based on quantitative assessment of influences exerted by microbe-related factors is widely used in foreign studies [6, 7]. Foreign techniques have some differences from domestic ones. In particular, Quantitative Microbial Risk Assessment, or QMRA, is a mathematical system for assessing infectious risks caused by pathogens which are hazardous for human health. The procedure can help to reveal and regulate risks related to microorganisms transferred with water, in particular, as regards sporadic diseases. It can be applied to analyze specific risk factors, for example, quality of water taken from a recreation zone or drinking water from centralized water supply systems; it can also become a part of complex research [8].

Virological monitoring over environmental objects involves exploring drinking water taken from centralized water supply systems aimed at detecting viruses in it; usually, a virological trap is used with subsequent application of polymerase chain reaction (PCR). However, this procedure doesn't allow to quantitatively assess infectious agent contents in water as it can only detect whether virus DNA or RNA are present in a sample without distinguishing between live or inactivated viruses in water [9]. Therefore, this procedure for detecting viruses in drinking water can't be applied to identify hazards; given that, data on microbe contamination indicators are the only available microbiological data that can be applied to characterize water quality.

In spite of some uncertainties in estimating pathogen concentrations quantified as per detected microbiological parameters of drinking water quality, literature contains some examples how to use a ratio of a pathogen to quality parameters in order to quantitatively determine pathogen concentrations in the environment for QMRA. If we take into account epidemiology (regularities in microbe prevalence and sources) and environmental context (relative resistance and transfer), than we can see that fecal indicators data are greatly significant for QMRA. For example, QMRA model utility was applied in research based on limited data, and a conclusion was reached that coliphages quantity can be considered equivalent to quantitative contents of a virus in water (notably, rotavirus)[2] [7, 14]. Results of examinations performed on a wide range of bacterial and virus parameters related to fecal water contamination indicate that coliphages contents in water are more closely related to gastrointestinal tract diseases than detection of any other indicators showing microbiological contamination of water, such as coliform bacteria [15]. It is shown that when unpurified sanitary sewage penetrate a city water supply network and beach zones aimed for swimming, it leads to a growth in incidence with norovirus infection detected via parallel epidemiologic research [16].

In Arkhangelsk region 82% population living in Arkhangelsk, Novodvinsk, Kotlas, Koryazhma, and Severodvinsk are provided with water from centralized water supply systems which is taken from surface sources. All water sources that provide drinking water for people living in Arkhangelsk, Novodvinsk, Kotlas, and Koryazhma, belong to Severnaya Dvina water basin. A river called Solza is used as a water source for Severodvinsk; the river doesn't belong to the above-mentioned water basin. In 2017 only 35% population living in Arkhangelsk region were provided with qualitative drinking water [17] and it proves that it is necessary to examine microbe risks caused by population consuming low-quality drinking water.

Our research goal was to assess microbiological risks of intestinal infections for Arkhangelsk region population caused by consuming water from centralized water supply systems.

Data and methods. According to the QMRA procedure, the examination included

[1] MG 2.1.10.0031-11. Risks of bacterial enteric infections caught from water: a complex assessment / approved by the RF Chief Sanitary Inspector on July 31, 2011) [web-source]. – URL: http://base.garant.ru/70105056/(date of visit October 20, 2018).

[2] On sanitary-epidemiologic welfare of the population in Arkhangelsk region in 2017: The State Report / edited by R.V. Buzinov. – Arkhangelsk, 2018. – 149 p.

four stages: 1) hazard identification, or selecting a specific microbe agent and possible outcomes caused by it; 2) exposure assessment depending on a type, scope, and duration of influence exerted on a human body by a microbe agent; 3) assessment of "dose - response" relationship; and 4) risk characteristics [18].

At the first stage, when hazards were identified, we selected focus territories, infectious diseases groups, and indicators related to environmental factors; then we performed a descriptive epidemiologic examination of sporadic incidence with acute intestinal infections (AII) among the total population as per three nosologic groups: rotavirus, norovirus, and enterovirus AII with the data taken from a statistical report No. 2 "Data on infectious and parasitic diseases" collected over 2009-2017 in 5 cities in Archangelsk region (Arkhangelsk, Novodvinsk, Kotlas, Koryazhma, and Severodvinsk). Spatial analysis of incidence was performed with average long-term incidence value, and average long-term incidence among the total population in Severodvinsk was taken as a reference level. Severodvinsk was chosen as a reference territory due to an alternative water supply source as it is provided with water taken from Solza River which doesn't belong to Severnaya Dvina water basin; as for four other cities, they are all provided with water which comes basically or even solely from Severnaya Dvina. We compared average incidence values on different territories with the reference level as per a fraction of differences in indicators and indicators ratio. Differences were considered to be epidemiologically apparent if a fraction of differences in indicators exceeded 20%, and indicators ratio was higher than 1.25.

When identifying hazards, we examined quantitative contents of infectious agents in drinking water taken from centralized water supply systems as per social-hygienic monitoring data collected in 2006–2017. To solve the task, we performed a sanitary-hygienic assessment of water quality as per coliphages contents for water taken from centralized water supply systems in 5 cities in Arkhangelsk region – Arkhangelsk, Novodvinsk, Kotlas, Koryazhma, and Severodvinsk. To describe an examined parameter, we applied a specific weight of samples which deviated from standards, a median (Me), 75-th and 95-th percentiles (P_{75} and P_{95}).

Microbe agent dose was calculated as per the following formula (1):

$$dose = C*V, \qquad (1)$$

where C is microbe agent concentration in 1 liter of consumed water, V is water consumption volume.

To calculate a dose, we applied coliphages contents at P_{95} level. Coliphages are more resistant to the environment than their host bacteria and it makes them able to indicate there is long-term fecal contamination. Researchers have proven there is a dependence between coliphages contents in water and contents of enteroviruses that are hazardous for human health [19, 20]. To calculate doses, we took water consumption as being equal to 0.743 l per day[3], which included tap water only and didn't take into account bottled water or other finished food products or drinks that contained water.

Exposure was assessed on the basis of openly published research results[4] [9, 10]. To assess probability of catching rotavirus and enterovirus infections, we applied "dose - response" exponential relationship model calculated as per the following formula (2):

$$P_{infection\ probability} = 1 - \exp(-dose * k), \quad (2)$$

where k quotient amounted to 0.00374 for enterovirus [22]; 0.173 [9], for rotavirus.

To assess probability of catching norovirus infection, we applied confluent hypergeometric function equation where α and β are Poisson beta-distribution parameters (3):

[3] Exposure Factors Handbook – Update (2009, External Review Draft) [web-source] // United States Environmental Protection Agency, Washington (DC), EPA/600/R-09/052A, 2009. – URL: https://cfpub.epa.gov/ (date of visit October 11, 2018).

[4] On sanitary-epidemiologic welfare of the RF population in 2017: the State Report. – M.: The Federal Service for Surveillance over Consumer Rights Protection and Human Well-being, 2018.– P. 105.

$$P_{\text{infection probability}} = 1 - {}_1F_1(\alpha, \alpha + \beta, -\text{dose}), \quad (3)$$

where α and β values for norovirus amount to 0.04 and 0.055 respectively [10]. To calculate equation values, we applied Wolfram Mathematic online, a software package used to calculate mathematical functions.

Probability of a diseases occurrence was calculated as per the following formula (4):

$$P = 1 - (1 - P_{\text{infection probability}})^n, \quad (4)$$

where n is a quantity of samples that deviate from the standard as per coliphages contents registered over the whole period under examination.

Results obtained for risk levels were assessed as per three ranges: R lower than 0.047 meant a risk of infectious disease occurrence among population was low (acceptable); R from 0.057 to 0.6095, average risk; R from 0.619 to 1 meant a risk was high [11].

Results and discussion. 48,931 AII cases with different etiology were registered in 5 cities in Arkhangelsk region in 2009-2017 among overall population living in them. Etiology remained unknown in 65.6% AII cases among all the registered ones and 34.4% had clear etiology. Ratio of AII with virus etiology to AII with bacterial etiology was 3:1.

Rotavirus infection took the first place among virus AII (86.9%); norovirus infection, the second one (7.7%); and enterovirus infection, the third one (3.7%). The lowest specific weight in virus intestinal infections structure belonged to hepatitis A (1.7%).

We analyzed AII incidence among population living in the examined cities and revealed that the highest incidence with rotavirus infection was registered in Kotlas ($299.4^0/_{0000}$) and Novodvinsk ($288.8^0/_{0000}$) as compared with other territories (Table 1). The highest frequency of norovirus infection and enterovirus infection was registered in Arkhangelsk and Novodvinsk, $19.4^0/_{0000}$ and $16.8^0/_{0000}$; as well as enterovirus infection, $11.0^0/_{0000}$ and $12.4^0/_{0000}$ respectively.

Rotavirus infection developed most rapidly in Novodvinsk and Kotlas where its advance ratios were 2.6-2.9 times higher than in Severodvinsk. Incidence with rotavirus infection developed among population in Koryazhma and Arkhangelsk 1.5-1.6 times faster than in Severodvinsk. As for incidence with norovirus infection, it developed in Novodvinsk and Arkhangelsk 10.3 and 9.1 times faster respectively than in Severodvinsk. No enterovirus infection cases were registered in Kotlas and Koryazhma; bearing in mind a persistent growing trend for this nosology in the country in general, we may assume that in these cities there is no epidemiologic suspicion as regards enterovirus infection. Thus, long-term incidence with enterovirus infection, including recent years (2015–2017) grew 1.5 times, and taken in comparison with long-term average level measured over previous ten years, it was 3.3 times higher [12].

Table 1

Spatial and time characteristics of incidence with virus AII among overall population living in the examined cities in Arkhangelsk region

Parameters	Territories (cities)				
	Arkhangelsk	Novodvinsk	Kotlas	Koryazhma	Severodvinsk
Rotavirus infection					
Average incidence, ($^0/_{0000}$)	161.8	288.8	299.4	159.2	104.0
Average advance ratio*, (times)	1.6	2.8	2.9	1.5	–
Norovirus infection					
Average incidence, ($^0/_{0000}$)	19.4	16.8	2.7	9.4	13.6
Average advance ratio*, (times)	1.4	1.1	0.1	0.7	–
Enterovirus infection					
Average incidence, ($^0/_{0000}$)	11.0	12.4	–	–	1.2
Average advance ratio*, (раз)	9.1	10.3	–	–	–

* means in comparison with Severodvinsk.

So, epidemiologic analysis of sporadic incidence with AII allowed to reveal the most widely spread infectious agents at the hazard identification stage. We performed a comparative analysis of spatial distribution and long-term dynamics of incidence with AII probably caught from water and revealed high frequency of rotavirus infection and norovirus infection in Arkhangelsk, Novodvinsk, Koryazhma, and Kotlas.

Specific weight of samples which deviated from hygienic standards as per coliphages contents in drinking water amounted to 6.2% and 7.0% after water treatment in Koryazhma and Kotlas respectively (Table 2). We didn't detect any microbiological abnormalities in drinking water at the median and 75-th percentile levels. Specific weight of samples taken from water pipelines in Arkhangelsk and Koryazhma that contained coliphages in quantities higher than fixed in hygienic standards amounted to 6.2% and 7.0% respectively. We detected samples deviating from hygienic standards as per coliphages contents at P_{95} in Arkhangelsk and Koryazhma; coliphages contents exceeded hygienic standards by 1.4 and 2.2 times respectively.

Quantitative risk of virus AII occurrence was assessed in the present research only for Arkhangelsk and Koryazhma as water samples taken from water supply systems with coliphages contents that exceeded hygienic standards were registered only in these two cities over the whole examined period.

We quantitatively assessed microbiological risks of AII occurrence related to centralized water supply systems and revealed that rotavirus, norovirus, and enterovirus infections were highly likely to occur in Arkhangelsk (R = 0.97–0.99); rotavirus infection, in Koryazhma (R = 0.95) (Table 3). Average probability of norovirus and enterovirus infection caused by consuming drinking water from centralized water supply systems was detected in Koryazhma (R = 0.58 and R = 0.43 respectively).

Conclusions. The performed research allowed to establish a structure of sporadic incidence with AII probably caught from water; it indicated that virus AII were the most widely spread with rotavirus, norovirus, and enterovirus infections prevailing among them.

Table 2

Quality of drinking water taken from centralized water supply systems assessed for a period 2006–2017 as per coliphages contents in pipelines

Territory	Number of samples			Me	P_{75}	P_{95}	X_{max}
	total	Higher than HS*	%**				
Arkhangelsk	1,382	86	6.2	0	0	1.4	16.1
Severodvinsk	337	0	0.0	0	0	0	0
Kotlas	153	0	0.0	0	0	0	0
Koryazhma	129	9	7.0	0	0	2.2	16.1
Novodvinsk	155	0	0.0	0	0	0	0

Table 3

Microbe risk related to occurrence of intestinal infections which are probably caught from water

Nosology	Infection probability	Disease probability	Probability characteristics
Arkhangelsk (dose = 10.4)			
Rotavirus infection	0.16	0.99	high
Norovirus infection	0.09	0.99	high
Enterovirus infection	0.04	0.97	high
Koryazhma (dose = 16.4)			
Rotavirus infection	0.24	0.95	high
Norovirus infection	0.11	0.58	average
Enterovirus infection	0.06	0.43	average

We assessed microbiological quality of drinking water taken from centralized water supply systems and detected there were deviations from hygienic standards in tap water as per coliphages contents in Arkhangelsk and Koryazhma.

Consumption of drinking water taken from city pipelines caused high risks of rotavirus, norovirus, and enterovirus infections for population in Arkhangelsk; average risks of norovirus and enterovirus infections and high risk of rotavirus infection for population in Koryazhma.

The performed research substantiates a practical feasibility of implementing Quantitative Microbial Risk Assessment, or QMRA, into sanitary-epidemiologic surveillance over water treatment and indicates the necessity to work out practical recommendations aimed at improving a system of virological monitoring over centralized water supply, raising quality of drinking water, and preventing incidence with acute intestinal infections caused by infectious agents caught from water.

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