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Correlation of excess salt intake identified by the survey with urine sodium level and blood pressure: data of ESSE-RF study

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Aim. To study the association of blood pressure (BP) and hypertension (HTN) with salt intake estimated by the survey and the urinary Na^+ concentration among men and women 25-64 years old, examined within the ESSE-RF and ESSE-RF-2 studies.

Material and methods. Representative samples of the Russian population aged 25-64 years were examined. At the first phase in 2012-2014, 21888 people (men — 38,2%) were included, and at the second phase in 2017 — 6714 people (men — 44,7%). The response rate was 80%. We used standard questionnaire. Adding more salt and the consumption of salted foods (sausages, deli meats, and pickled foods) in the criteria "daily or almost daily" was considered excess salt intake (ESI). BP measurement was carried out in a sitting position on the right hand. BP was measured twice with an interval of about 2-3 minutes. HTN was diagnosed at a systolic BP (SBP) ≥140 mm Hg and/or diastolic BP ≥90 mm Hg, or in case of antihypertensive therapy. In ESSE-RF-2, an analysis of the morning urine was additionally performed. Na^+ was determined using the EX-Ds ion-selective electrolyte analyzer. All participants were stratified by the quintiles of urine sodium level. Data analysis was performed using the software package R 3.6.1. The models of linear and logistic regression were used. The differences were considered at $p<0,05$.

Results. The average level of SBP significantly increases with an increase in Na^+ in urine: 1,04 (0,60-1,48) mm Hg for the quintile of sodium distribution ($p<0,001$), the odds of HTN increases by 1,11 (1,05-1,17) times for the quintile ($p<0,001$). Questionnaire components of ESI are also significantly related to urinary Na^+ levels. The consumption of sausages and deli meats has the greatest effect, causing an increase in the average Na^+ level by 11,59 (7,06-16,12) mmol/l ($p<0,001$). The applied point scale is significantly related to urine sodium level and predicts HTN no worse than Na^+ in the urine ($p=0,15$ for the difference hypothesis). One point on the scale increases the Na^+ level by an average of 7,51 (5,01-10,02) mmol/l, SBP by an average of 0,74 (0,41-1,07) mm Hg and the odds of HTN by 1,1 (1,06-1,15) times ($p<0,001$ for all).

Conclusion. In the pattern of ESI components, processed meat and sausage products take first place in terms of association strength with urine sodium. The questionnaire used to assess the proportion of people with ESI can be recommended for assessing this risk factor during screening. ESI detected by the questionnaire is associated with elevated BP and urinary Na^+ values.

Key words: hypertension, blood pressure, excess salt intake, urine sodium level, ESSE-RF, risk factors.

Relationships and Activities: none.

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Excess salt intake (ESI) refers to behavioral risk factors (RF) associated with the eating habits of modern humans. The contribution of this RF to cardiovascular mortality is 12% [1]. Despite the World Health Organization guidelines on the daily intake of salt <5 g (2 g/day of sodium), the average consumption in the world is about 10 g/day (3,95 g/day of sodium) [2]. An analysis conducted within the The Global Burden of Disease (GBD) study showed that in 13 studies included in the analysis, salt intake ranged from 6,75 to 10,66 g/day, i.e., exceeded the recommended values in all regions [3].

The relationship between ESI and blood pressure (BP) level has been was studied for many years. The history of research was analyzed in detail by N. Poteshkina (2011, 2013) in reviews [4, 5]. Mentioned relationship was confirmed in the American population within the Multiple Risk Factor Intervention Trial (MRFIT). An international study by the Intersalt Cooperative Research Group (INTERSALT), in addition to the relationship, revealed a dose-dependent effect of salt intake on BP, which increases with age. A similar relationship was noted within the Norfolk Cohort of the European Prospective Investigation into Cancer (EPIC-Norfolk) [6]. In the International Study of Micro- and Macro-Nutrients and Blood Pressure (INTERMAP), in addition to the above, the relationship between the amount of salt consumed and the mortality rate due to stroke was confirmed. An increase in salt intake was associated with an increase in the hypertension (HTN) prevalence in the population. Moreover, the Prospective Urban Rural Epidemiology study (PURE) showed that the relationship between BP and salt intake is manifested precisely in regions with higher level of salt intake (>5 g/day) [7].

Some studies focused on the role of reducing salt intake in lowering BP at the population level. So, He FJ and Macgregor GA (Cochrane Systematic Review, 2013) observed a moderate decrease in salt intake over 4 weeks, associated with a significant BP decrease both among people with HTN and without it [8]. The decrease in salt intake in the UK from 2003 to 2011 explain the blood pressure decrease at the population level in the country [9]. Thus, reducing the level of salt intake among population is one of the important components of a multidimensional approach to HTN control. However, this poses the question of estimating salt intake by the population.

There are no many population-based studies evaluating salt intake and the prevalence of ESI in Russia. One of these studies is INTERSALT, con-

ducted in the last quarter of 20th century. According to this trial, the average salt intake in Russia in those years was 9,46 g/day. There was also sample monitoring of the diet of the population conducted by the Federal State Statistics Service in 2013 and 2018 in all subjects of Russia [10]. Salt consumption in this study was studied by questioning. The interviewers in this study were not medical professionals, but previously they all had a special interview on the rules for collecting information. BP and urine were not assessed. According to the ESSE-RF study, this RF amounted to 49,9% according to first section of the study [11].

When studying eating habits, including ESI, at the population level, a researcher must solve the question of the significance of results obtained by questioning. In short-term studies with large sample, original validated questionnaires are used to evaluate the RF. At the same time, the amplification of screening techniques by laboratory tests significantly increases the total cost of the study. Among laboratory methods for assessing urinary Na^+, the first place is the 24-hour urinary sodium excretion. However, there are difficulties with the preparation of a subject and the cost, which is high on a scale of population study. From this point of view, despite some distortion of result due to unbalanced salt intake during the day [12], the determination of Na^+ in the morning urine seems technically more feasible. At the same time, the predictive value of this technique is discussed by many researchers [13].

The aim was to study the association of BP and HTN with salt intake estimated by the survey and the urinary Na^+ concentration among men and women 25-64 years old, examined within the ESSE-RF and ESSE-RF-2 studies.

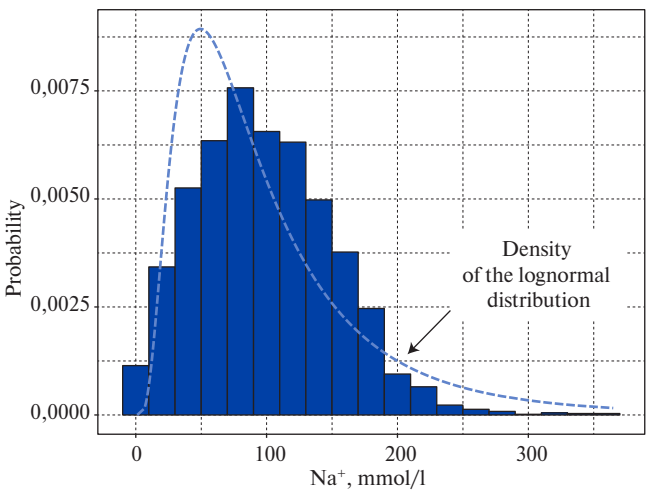

Figure 1. Histogram of urinary sodium distribution.

Material and methods

Representative samples of the Russian population aged 25-64 years were examined. At the first phase in 2012-2014, 21888 people (8354 men and 13534 women) from Volgograd, Vologda, Voronezh, Ivanovo, Kemerovo, Orenburg, Tomsk, Tyumen Oblasts, Krasnoyarsk Krai, Primorsky Krai, Republic of North Ossetia, St. Petersburg were included. At the second phase in 2017 — 6714 people (3000 men and 3714 women) from Krasnodar Krai, Omsk and Ryazan Oblasts, Republic of Karelia). A systematic stratified multistage random sample was used, created according to Kish selection grid, features of which were described in detail earlier [6, 14]. The response rate was about 80%. The study was approved by the Independent Ethics Committee of the National Medical Research Center for Therapy and Preventive Medicine. Each participant signed informed consent. For all participating regions, the same research tools were provided.

All subjects were interviewed according to a single standard questionnaire, created on the basis of adapted international methods. The analysis included the region and place of residence: (urban/rural area), age groups (25-34, 35-44, 45-54 and 55-64 years), level of education (below secondary, secondary and above secondary), income level, habits, anamnestic data. The module for assessing diet and eating habits included a standard questionnaire on the frequency of taking basic food groups with a partial semi-quantitative assessment of food intake, which was descripted in detail earlier [15]. Adding more salt in ready-to-eat meals and the consumption of salted products (sausages, deli meats or pickled products) in categories "daily" or "almost daily" was considered ESI. The components used in ESI were included in the score: the presence of one of them was equal to 1 point, two — 2 points, three — 3 points.

BP measurement was carried out in the sitting position with the right arm using Omron automatic BP monitor. The level of BP (systolic BP (SBP) and diastolic BP (DBP)) was measured twice with an interval of about 2-3 minutes. The analysis took into account the average of two measurements. HTN was considered at SBP ⩾140 mm Hg and/or DBP ⩾90 mm Hg, or when the subjects took antihypertensive drugs.

In two regions participating in ESSE-RF-2 (Krasnodar Krai and Ryazan Oblast), an analysis of urine was additionally performed. The collection of morning urine was carried out according to standard recommendations — on day before, vegetables and fruits that discolored urine (beets, carrots, etc.) and diuretics were excluded. Electrolytes (sodium (Na) and potassium (K)) in urine were determined by the ion selective electrode technique using an EX-Ds

Table 1

Characteristics of Na^+ levels in the morning urine in the age groups of men and women

Age groups	Men*			Women		
	N	Mean ± standard deviation	Median [Q25; Q75]	N	Mean ± standard deviation	Median [Q25; Q75]
25-34	449	103,17±53,67	97,2 [65,8; 136,7]	539	91,35±52,17	84 [51,2; 124,4]
35-44	388	105,02±56,68	100,9 [64,13; 139,8]	483	93,79±50,66	86,25 [58,63; 126,5]
45-54	399	108,54±54,13	107,2 [67,9; 149]	503	88,43±47,79	82,6 [51,8; 122,4]
55-64	384	110,05±53,80	107,4 [71,4; 145,6]	523	92,9±50,06	88,9 [54,6; 126,75]
25-64	1620	106,62±54,6	103,0 [66,85; 142,6]	2048	91,65±50,10	85,7 [54,10; 125,60]

Note: * — mean level increases with age (p=0,033).
Abbreviation: Q — quantile.

Table 2

Associations of excess salt intake according to the questionnaire with urinary sodium level. Results of a univariate regression analysis adjusted for sex and age

ESI and its components	Average increase in urinary Na^+ (CI 95%)	p
Adding more salt in ready-to-eat meals	7,44 (3,33-11,55)	<0,001
Daily/almost daily consumption of sausages and deli meats	11,59 (7,06-16,12)	<0,001
Daily/almost daily intake of pickled foods	6,77 (0,71-12,83)	0,0286
Score of ESI components*	7,51 (5,01-10,02)	<0,001
ESI in general	11,34 (5,75-16,94)	<0,001

Note: * — coefficient shows the average increase in urinary Na^+ (mmol/l) with an increase in score of 1.
Abbreviations: CI — confidence interval, ESI — excess salt intake.

electrolyte analyzer (JOKOH CO., LTD., Japan). All participants were stratified by the quintiles of urinary Na^+ (<50,76, <80,2, <109,18, <142,60, <364,90 mmol/l).

Statistical analysis was performed using the software package R 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria). To assess the association of questionnaire scores and levels of urinary Na^+ with SBP, DBP and HTN, linear and logistic regression were used, both with/without sex and age adjustment. The null hypothesis was verified by Wals test. The parameter effect in the linear regression model was estimated by its coefficient, in logistic regression model — the odds ratio (OR). The quality of linear regression predictions was estimated by coefficient of determination (R^2). The quality of logistic regression predictions was evaluated using the area under ROC curve (AUC). Comparison of linear regression models was carried out by the Wuong test [16]; AUC was compared using the bootstrap method for the pROC package [17]. The differences were considered significant at p<0,05.

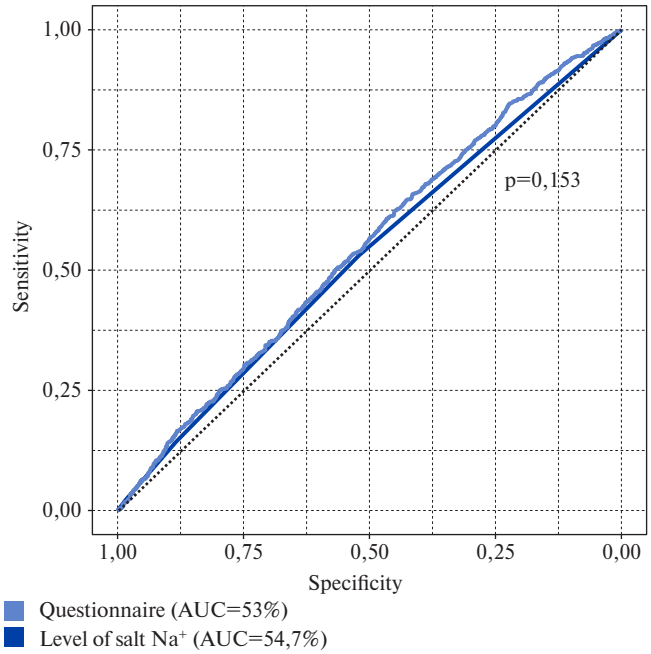

Figure 2. ROC analysis of the association of hypertension with urinary Na+ levels and questionnaire data.

Table 3

The relationship between the components of salt intake (according to the questionnaire) and SBP, DBP and HTN in ESSE-RF-1 and ESSE-RF-2 studies. Results of a univariate regression analysis adjusted for sex and age

	ESSE-RF-1						ESSE-RF-2					
	SBP		DBP		HTN		SBP		DBP		HTN	
	Coefficient	p	Coefficient	p	OR	p	Coefficient	p	Coefficient	p	OR	P
Adding more salt in ready-to-eat meals	0,01 (-0,5-0,52)	0,98	0,25 (-0,05-0,55)	0,10	1,09* (1,03-1,16)	0,0058	0,13 (-0,71-0,98)	0,76	-0,13 (-0,67-0,41)	0,64	1,09 (0,97-1,22)	0,15
Daily/almost daily consumption of sausages and deli meats	1,78* (1,17-2,39)	<0,001	1,16* (0,8-1,52)	<0,001	1,19* (1,11-1,28)	<0,001	1,0 (-0,002-2)	0,051	1,35* (0,71-1,99)	<0,001	1,24* (1,09-1,42)	0,0013
Daily/almost daily intake of pickled foods	0,61 (-0,21-1,44)	0,15	-0,16 (-0,65-0,33)	0,52	0,98 (0,89-1,09)	0,76	1,19 (-0,2-2,58)	0,092	1,11* (0,21-2)	0,015	1,08 (0,89-1,29)	0,44
Score of ESI components†	0,74* (0,41-1,07)	<0,001	0,48* (0,29-0,68)	<0,001	1,1* (1,06-1,15)	<0,001	0,65* (0,11-1,19)	0,019	0,64* (0,29-0,99)	<0,001	1,14* (1,06-1,22)	<0,001
ESI in general	1,38* (0,69-2,07)	<0,001	0,85* (0,44-1,26)	<0,001	1,18* (1,09-1,29)	<0,001	0,61 (-0,6-1,81)	0,32	0,98* (0,21-1,76)	0,013	1,2* (1,02-1,41)	0,027

Note: * — significant associations, † — coefficient shows the average salt increase with an increase in score of 1.
Abbreviations: HTN — hypertension, DBP — diastolic blood pressure, ESI — excess salt intake, SBP — systolic blood pressure, OR — odds ratio.

Results

ESSE-RF-2 study was performed later, however, in addition to the questionnaire, Na^+ in the morning urine was analyzed in 2 regions. The distribution of Na^+ is shown in Figure 1; the characteristics of Na^+ distribution depending on sex and age are shown in Table 1. Linear regression showed a significant increase in the average values of Na^+ with age in men (p=0,033), but not in women. In men, Na^+ levels are on average higher than in women (p<0,001).

Associations of SBP, DBP and HTN with the quintiles of urinary sodium distribution were statistically significant. The average level of SBP is incrementally increased by 1,04 (0,60-1,48) mm Hg for each quintile of Na^+, the average level of DBP — by 0,61 (0,33-0,88) mm Hg. The odds for HTN increases by 1,11 (1,05-1,17) times per quintile.

Further, according to ESSE-RF-2, an analysis was made on the relationship between the salt intake and urinary sodium (Table 2). The components of ESI were considered each separately: the adding more salt in ready-to-eat meals, daily/almost daily consumption of sausages and deli meats, and pickled products. Among these components, the most significant is the consumption of sausages and deli meats, which increased Na^+ by an average of 11,59 (7,06-16,12) mmol/l. Then the components of salt intake were included in the developed score. With a score increase of one point, Na^+ in urine increased on average by 7,51 (5,01-10,02) mmol/l. In general, ESI as RF increased the sodium level by an average of 11,34 (5,75-16,94) mmol/l. To find out how much predictive power is lost when using questionnaire data instead of urinary sodium, we compared their predictive performance in regression models. The level of urinary Na^+ explains 1,4% of the SBP variation, while the questionnaire accounts for 0,35%, which is significantly (p<0,001) worse. On the other hand, the level of urinary sodium predicts the HTN with AUC of 54,7%, while the questionnaire with AUC of 53% and the differences are not significant (p=0,15) (Figure 2).

An analysis of the relationship between BP values and HTN with salt intake components characterizing according to the questionnaire was carried out within ESSE-RF-2 and ESSE-RF studies with a large total sample size (Table 3). The most pronounced effect was shown by the consumption of processed meat, while adding more salt significantly affected only HTN in the ESSE-RF sample. Consumption of pickled products showed significant association only with DBP in the ESSE-RF-2 sample. The score of ESI components is reliable for all parameters in both studies — the OR for HTN — 1,18 (1,09-1,29) in ESSE-RF and 1,14 (1,06-1,22) in ESSE-RF-2.

Discussion

The main result of this analysis is the identification of associations of BP levels and hypertension with urinary Na^+ concentration, as well as the associations of urinary sodium and components of ESI obtained using the questionnaire. Each of the questionnaire components had a significant effect on BP and/or HTN. The closest relationship was observed with the consumption of meat and sausage products: their effect on the salt level was about 2 times stronger than the effect of the remaining two components. However, the introduction of a score taking into account the double effect of meat and sausage products did not lead to a significant increase in predictive performance. The salt intake variables obtained using the questionnaire were associated with HTN and BP. The predictive power of the questionnaire for HTN was 1,57 times lower than of a laboratory test, but this difference was not statistically significant. The close relationship between the consumption of meat and sausage products and urinary sodium level is of particular concern, because a study of the eating habits of Russians showed that about a quarter of men and a fifth of women consume it daily or almost daily [15]. The obtained relationships of eating habits, urinary sodium level, and parameters characterizing hypertension specifies the population-based prevention strategies. A previous analysis showed a significant increase in the HTN prevalence among men in recent years [15]. Among the RF associated with this growth, not only the increase in male obesity [18] is noteworthy, but also the dietary characteristics among men — high salt content in the food, adding more salt, higher consumption of sausages, pickled products, meat and sausage products, savory snacks [15]. It is noteworthy that among men included in the analysis, urinary sodium levels were higher compared to women.

American researchers also noted the negative role of processed meat products, noting that about 70% of Na^+ enters the body as part of processed and ultra-processed foods [19]. At the same time, salt remains an indispensable component of products made from processed meat, alternatives to which have not yet been developed [20].

The study of the population aspects of HTN control in Russia remains extremely relevant. Despite the known methods for diagnosing this disease, the availability of medications for its treatment, an increase in HTN is noted in Russia, and the proportion of people with high BP is 33,8% [21, 22]. In recent years, it has been noted that ESI has a negative effect not only on BP, but also independently affects target organs — heart, kidneys, brain, and bone mineral density [23].

There are few works evaluating salt intake using laboratory tests in Russia; such studies are more limited and are performed on certain categories of patients, but not on a population level. In the ESSE-RF study, the questioning was used, supplemented in ESSE-RF-2 by determining the level of Na^+ in morning urine. Although a positive relationship has been shown between age and average Na^+ levels in the morning urine only among men. The use of some drugs (nonsteroidal anti-inflammatory drugs, antitumor agents, diuretics, antibiotics, and a number of others) may affect its values — both increasing and decreasing Na^+ levels.

The question of using a morning urine to evaluate Na^+ remains debatable. This method was used as part of the PURE study in samples from 18 countries — a 24-hour urinary sodium excretion and further analysis using the Kawasaki formula were performed on the morning urine [7]. However, despite the fact that about 90% of the salt is excreted with urine, this process is unbalanced during the day [12]. Therefore, an assessment of morning urine may not provide true values and lead to underestimation. However, the researchers noted a correlation between one-time and 24-hour collection of urine, which allows the use of a regression coefficient of 0,375 to recalculate it [5]. The study on validation of data obtained in one-time urine collection in comparison with a 24-hour sample revealed the correlation of these parameters not at the individual level, but at the population level [24].

The International Consortium for Quality Research on Dietary Sodium/Salt (TRUE) [12] indicated the futility of using this method to calculate the 24-hour intake of Na^+. However, in population studies, an important problem is not only the predictive power of method, but also the complexity of collecting material and cost for analysis with a large number of respondents. Thus, the use 24-hour urinary sodium seems to be possible to use only on certain categories of individuals, but not on screening nationwide. Less expensive, but also less accurate is the analysis of a morning urine, but this method also increases the cost of the study with a large number of patients. In this case, the predictive value of survey is very important. Questionnaires studying salt intake by the semi-quantitative method or by evaluating the daily nutrition are most optimal in epidemiological studies and are widely used in the world. Thus, the survey method is used to assess the proportion of people with ESI in epidemiological monitoring using the STEPS method (WHO) [25]. The survey method allows identifying the proportion of people taking much salt and the individual dietary components that are present in excess. At the same time, the daily intake of Na^+ is not calculated.

Study limitations: the analysis was carried out within cross-sectional study, which does not allow us to assess the contribution of ESI to HTN. Analysis of Na^+ levels was performed on a morning urine.

Conclusion

In the pattern of ESI components, processed meat and sausage products take first place in terms of association strength with urine sodium. In population-based prevention programs aimed at reducing the BP levels, it is advisable to include measures reducing salt intake, paying particular attention to informing the population about the importance of reducing use of processed meat products.

The questionnaire used in population studies allows to estimate the proportion of people with ESI and its individual components. ESI detected by the questionnaire is associated with elevated BP and urinary Na^+ values, which justifies the use of this tool for epidemiological studies. High prevalence of ESI in the population may indirectly indicate the ineffectiveness of population-based preventive measures to reduce salt intake and its effect on BP in the population. However, it is not possible to use the questionnaire to calculate Na^+ consumption.

Relationships and Activities: none.

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