Analysis of physical activities integrated with drugs in the cardiac and vascular changes

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ABSTRACT

Exercise is an effective, low-risk treatment strategy for people with high blood pressure. Therefore, the aim of this study was to investigate the effect of cardiac environmental function training on body composition and blood pressure response in patients with hypertension. One of the main indicators of the quality of medical care provided is the availability of effective, safe and high-quality medicines (MP) beside the medical movements for the population. In the course of the study, the analysis of medical movements and drugs for the treatment of cardiovascular diseases (CVD) included in the list of vital and essential drugs (VED) was carried out. The identification of aspects in the analysis of the most important movements and drugs for the treatment of CVD and the proposal of relevant recommendations is of high practical importance for improving the quality of drug supply to the population. Considering the precautionary aspects of resistance training with the cardiac peripheral function system for people with hypertension can be used to increase strength, body composition and also the treatment of hypertension along with available cardiac drugs.

Keywords: Physical activity; Cardiac; Vascular; Availability; Drug supply.

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INTRODUCTION

About 17.5 million people die from cardiovascular diseases in the world every year. In Russia, 47.8% (more than 900 thousand people) of all deaths are cardiovascular pathologies, which in terms of 100 thousand people is 2 times higher than in Europe and one and a half times higher than the average in the world (http://www.gks.ru; https://chekhovsc.ru; https://www.kp.ru; COVID-19 and the cardiovascular system). Despite the improvement in the quality of medical care, among the population of the Russian Federation (RF), there is still a high incidence of cardiovascular pathologies (Drapkina et al., 2020; https://www.who.int/ru/). In this regard, drugs for the treatment of diseases of the cardiovascular system (CVS) traditionally occupy a significant share in the pharmaceutical market in Russia, in general, and in the regions in particular.

For many years, the World Health Organization (WHO) has been developing and promoting the concept of basic drugs, of which restrictive lists are formed on the basis of strict criteria and according to approved methods (https://chekhovsc.ru). In the Russian Federation, one of such basic lists is the list of vital drugs (Federal Law No. 61-FZ of 12.04.2010). According to the Decree of the Government of the Russian Federation of August 28, 2014, N 871 "On Approval of the Rules for the Formation of Lists of Medicines for Medical Use and the Minimum Range of Medicines Necessary for the Provision of Medical Care" medical care, as well as for the formation of other valid restrictive lists. The state sets the maximum selling prices for drugs included in the list of vital drugs (Decree of the Government of the Russian Federation of 08/28/2014 N 871; Maksimkina, 2014).

Russia is a huge country with different natural and climatic zones and inhabiting territories by many peoples and ethnic groups (https://businessman.ru), in this regard, this factor can affect the structure of morbidity and the need for vital drugs in regional significance. Today, the topical issue is the maximum availability of the VED list to the population of a particular constituent entity of the Federation.

It should also be noted that in the context of the COVID-19 pandemic, CVD patients constitute a special risk group. Coronavirus infection can lead to decompensation of existing chronic diseases and increases the risk of complications in the case of infection (Decree of the President of the Russian Federation dated July 21, 2020). Elderly patients with comorbid conditions are more likely to become infected with SARS-CoV-2, especially in the presence of arterial hypertension, coronary heart disease (IHD), and diabetes mellitus (Drapkina et al., 2020; http://www.gks.ru).

Already existing or newly acquired cardiovascular pathologies create and increase the demand of the population for the corresponding drugs. It should be noted that among the main national development goals of the Russian Federation for the period up to 2030, by the decree of the President of the Russian Federation No. 474 dated July 21, 2020, the provision of sustainable population growth and an increase in life expectancy up to 78 years was established (Decree of the President of the Russian Federation dated July 21, 2020).

MATERIALS AND METHODS

The objects of the study were regulatory legal acts, statistical compilations of the Ministry of Health of the Russian Federation (Ministry of Health of the Russian Federation), the State Register of Medicines (GRLS), VED lists; analytical data on the main indicators of the development of the pharmaceutical market; standards of medical care.

In the course of the study, a complex of scientific methods of systemic, logical, marketing, structural types of analysis were used.

To achieve this goal, the following tasks were solved:

1. Conduct an analysis of the totality of drugs included in group [C] "Cardiovascular system" of the VED list on the pharmaceutical market of the Russian Federation and the regional market under study.
2. Conduct a comparative analysis of the marketing characteristics of the target and local assortment of drugs used in the treatment of diseases of the cardiovascular system included in the VED list.
3. To assess the availability of the assortment of drugs for the treatment of CVD in the region under study.

As part of solving our problems, at the initial stage of the study, an analysis was made of the totality of drugs included in group [C] "Cardiovascular system" of the VED list for 2020, presented on the pharmaceutical markets of the Russian Federation and the studied subject of the Federation of the Central Federal District (CFD) - Oryol region (Garankina et al., 2018). The analysis determined the total number of international non-proprietary names (INNs) used in therapy; trade names (TN) of drugs and dosage forms (DF); the number of anatomical-therapeutic-chemical (ATC) ATC groups; the share of imported and domestic production of medicinal products; the percentage distribution of DF in the assortment, and changes were also revealed in the studied group of drugs on the VED lists from 2016 to 2020.

According to the results of marketing research, we have established that for the treatment of CVDs included in the list of vital and essential drugs for 2020, 53 INNs, 252 TNs, 412 drugs, 41 drugs are included; the regional pharmaceutical market of the Oryol region is represented by 46 INN, 239 TH, 340 LP and 24 LF (Figure 1).

Figure 1. Comparative characteristics of the federal and regional pharmaceutical markets.
Analysis of the group [C] "Cardiovascular system" for the period from 2016 to 2020, showed that over 5 years the study group of drugs was replenished with 7 INNs (alirocumab, evolocumab, valsartan + sacubitril, doxazosin, ambrisentan, macitentan, riotsiguat), 1 ATC-group of the 5th level C10AX "Other lipid-lowering agents" and 3 LF (spray for local and external use, metered dose, solution for subcutaneous administration, modified release film-coated tablets) (Figure 2).

![Figure 2. Comparative characteristics of the filling of the assortment of the group [C] "Cardiovascular system" in the lists of vital and essential drugs in 2016-20.](image)

During the analysis of the assortment of medicinal products, taking into account the ATX classification, it was established that the entire assortment was distributed into 8 groups of the 3rd level, which corresponds to 30 groups of the 5th level. Most drugs, 90 LP (21.85%) belong to the C09AA group "Angiotensin-converting enzyme inhibitors", followed by 66 drugs from the C10AA group "HMG-CoA reductase inhibitors" - 16.02% and 30 drugs from the C01BB group "Antiarrhythmic drugs, class IB" (7.28%).

Analysis of the assortment in terms of the composition of active ingredients showed that monocomponent drugs predominate - 89.73%.

![Figure 3. Segmentation of the Russian pharmaceutical drug market from the assortment of the group [C] "Cardiovascular system" by country of origin.](image)
As a result of the analysis of the offers of the assortment of the studied group of medicinal products, on the localization of the production cycle, it was found that more than half of the medicinal products are produced in Russia - 59.71%. Among 40.29% of foreign drugs presented by manufacturers from 29 countries, the leading positions (45.78%) of the total volume of imported drugs are produced in India, Germany, Hungary and the Republic of Belarus (Figure 3).

When analysing the types of DF, it was revealed (Figure 4) that the assortment of drugs contains solid 73.30%, liquid 25.24% and soft 1.21% of the form of release. In the structure of solid formulations, the main share is traditionally taken by tablets - 72.48. Solution for injection predominates among liquid dosage forms - 31.73%. Soft dosage forms are slightly represented by gels.

![Diagram of dosage forms](image)

Figure 4. The ratio of dosage forms in the assortment of drugs from group [C] "Cardiovascular system".

![Diagram of assortment](image)

Figure 5. Assortment macro-contour of the Russian pharmaceutical market of drugs used in the treatment of diseases of the cardiovascular system included in the list of VED in 2020.

Based on the results of the conducted marketing research, we compiled an assortment macro-contour of the Russian pharmaceutical market of drugs used in the treatment of CVDs included in the list of vital and
essential drugs for 2020 (Figure 5). Our study revealed the predominance of monocomponent drugs (89.73%), among ATC groups the largest number of drugs belongs to the C09AA group "Angiotensin-converting enzyme inhibitors" (21.85%), the largest share of drugs in terms of the number of drugs falls on INN - atorvastatin (48 LP; 11.65%). On the territory of Russia, 59.71% of medicinal products are produced, mainly in the form of solid medicinal products (73.30%).

The next stage of our work included an analysis of the pharmaceutical market for drugs of the study group in the Oryol region. Based on the results of the analysis of the regional pharmaceutical market of drugs used in the treatment of CVS diseases included in the list of vital and essential drugs for 2020, a regional assortment meso-contour was drawn up. The mesocontour is characterized by the following: according to the composition of drugs, they contain mainly one active ingredient - 76.28%; produced by domestic producers 81.63%; produced in the form of solid dosage forms 89.91%. The most extensive range of drugs falls on the ATC group C09AA "Angiotensin-converting enzyme inhibitors" (17.94%). It should be noted that the largest share in terms of the number of drugs on the regional market belongs to amlodipine (7.65%), which belongs to the group C08CA "Dihydropyridine derivatives". Thus, the assortment contour of the local market is somewhat different from the Russian macrocontour (Figure 6).

Figure 6. Assortment meso-contour of the pharmaceutical market of the Oryol region of drugs used in the treatment of diseases of the cardiovascular system included in the list of VED in 2020.

At the third stage of our study, in the course of a comparative analysis of the marketing characteristics of the target and local range of drugs used in the treatment of CVDs included in the VED list for 2020, an assessment of the availability of drugs of the considered group for consumers of the study region was carried out. For this purpose, we calculated the following indicators of the medicinal product assortment: latitude coefficient (Ksh), depth coefficient (Kd), completeness coefficient (Kp), renewal index (I0).

The breadth of the assortment is characterized by the number of assortment groups of goods available for sale. An indicator of the breadth of the assortment is the latitude coefficient - Ksh:

$$K_{sh} = \frac{Sh_{fakt}}{Sh_{baz}},$$
where Sh\textsubscript{fakt.} - the number of groups, subgroups of goods available in the presence of a pharmacy organization or produced by the pharmaceutical industry; Sh\textsubscript{baz.} - the number of groups, subgroups of goods permitted for use in the country and represented in the State Radar Station.

The depth of the assortment characterizes the presence of varieties of one type of goods available in the pharmacy organization. A variety of medicinal products, as a product, is understood as specific medicinal products of a certain dosage form, dosage concentration, packaging, etc. An indicator of the depth of the assortment is the depth coefficient K\textsubscript{g}:

\[
K_g = \frac{G\textsubscript{fakt.}}{G\textsubscript{baz.}},
\]

where G\textsubscript{fakt.} - the number, names of medicinal products of one medicinal product or pharmacoc-therapeutic group (FTG), available in the presence of a pharmacy organization or produced by the pharmaceutical industry; G\textsubscript{baz.} - the number of medicinal product names of one INN or FTG permitted for use in the country.

The completeness of the assortment is characterized by the number of subspecies of one type of product available in the organization or produced by industry. Subspecies of such a product as a drug can be dosage forms: tablets, draggers, capsules, solutions for injections, ointments, suppositories, etc. An indicator of the completeness of the assortment of medicinal products is the coefficient of completeness - K\textsubscript{p}:

\[
K_p = \frac{P\textsubscript{fakt.}}{P\textsubscript{baz.}},
\]

where P\textsubscript{fakt.} - the number of names of dosage forms of one drug or one FTG available in the investigated pharmacy organization or produced by the pharmaceutical industry; P\textsubscript{baz.} - the number of names of dosage forms of one drug or one FTG permitted for use in the country.

Thus, the assessment of the availability of the assortment of drugs used in the treatment of CVDs included in the VED list for 2020 in the Oryol region led to the following results.

An analysis of the breadth of the assortment showed that out of 8 ATC-groups of the 3rd level of drugs used in the treatment of CVD, the pharmaceutical market of the Oryol region is represented by drugs of 6 groups of the 3rd level.

\[
K_{sh} = \frac{Sh\textsubscript{fakt.}}{Sh\textsubscript{baz.}} = \frac{6}{8} = 0.750
\]

Consequently, K\textsubscript{sh} was 0.750 for ATX groups. Drugs of the C02KX groups "Antihypertensive drugs for the treatment of pulmonary arterial hypertension" and C10AX "Other lipid-lowering drugs" (refer to monoclonal antibodies produced using genetic engineering, the cost per package exceeds 10,000 rubles) are not available for purchase in the region.

In the course of analysing the depth of the assortment, it was found that out of 412 proposals of the considered group of drugs, included in the list of vital and essential drugs for 2020, 340 items are represented on the regional market (82.52%); from 252 TH - 239 (94.84%); out of 53 INNs - 46 (86.79%).

\[
K_g = \frac{340}{412} = 0.825; \quad K_g = \frac{239}{252} = 0.948; \quad K_g = \frac{46}{53} = 0.868.
\]
As a result, $K_g$ was 0.825 for LP, 0.948 for TN, and 0.868 for INN. In this regard, the indices of the depth of the assortment are quite high, which characterizes the assortment of the region as sufficient and satisfying the needs of the population (Figure 7).

![Figure 7. Structure of the regional assortment of drugs used in the treatment of cardiovascular diseases included in the VED in 2020, $K_p = 24/42 = 0.571$.](image)

The calculation of the completeness ratio revealed the presence of the studied group of drugs in the regional market in the form of 24 LF, therefore the completeness ratio was $K_p = 24/42 = 0.571$. Among DF, tablet forms clearly predominate, including those coated with a film shell. The next most common is liquid DF, namely solution for injection; eye drops, represented by only 5 drugs, occupy a smaller share among liquid DF. Also, a significant proportion of the total amount of drugs is occupied by concentrates for the preparation of various injection and infusion solutions. Soft dosage forms in the considered group of drugs are presented insignificantly - 5 drugs in the form of gels relative to the entire range.

When analysing the degree of renewal of the regional pharmaceutical market, we found that out of 7 new INNs used in the treatment of cardiovascular pathologies included in the VED list in the period from 2016 to 2020. - alirokumab, evolocumab, valsartan + sacubitril, doxazosin, ambrisentan, macitentan, riociguat presented on the pharmaceutical market of the Russian Federation, only two of these INNs are presented in pharmacy organizations of the Oryol region: 10 drugs for doxazosin and 1 drug for valsartan + 28.57 %). Thus, the degree of renewal of the assortment in the Oryol region is characterized by a low indicator.

Based on the results of a comparative marketing analysis of the Russian and regional markets for cardiovascular drugs included in the VED list for 2020, we have built an assortment profile of drug availability in the pharmaceutical market of the Oryol region (Figure 8). In general, the profile is characterized by high rates calculated for the studied group of medicinal products, with the exception of the number of medicinal products offered on the pharmaceutical market of the Oryol region (presented a little more than half of those...
approved for use) and the degree of renewal (almost all new INNs included in the lists over the past two years, are inaccessible to the population of the Oryol region).

Figure 8. The assortment profile of the availability of drugs used in the treatment of cardiovascular diseases, the list of vital and essential drugs in 2020 on the pharmaceutical market of the Oryol region.

RESULTS

After evaluating the data obtained, we received the following results:

1. Analysis of the aggregate of drugs included in group [C] "Cardiovascular system" of the VED list on the pharmaceutical market of the Russian Federation and the studied regional market of the Oryol region showed that the total number of CVDs used in therapy in the region is less than in the whole of the Russian Federation: INN by 14%; TN by 6%; LP by 18%, LP by 42%. It was found that in the assortment of drugs according to the ATC classification, drugs are mostly represented by the following groups - C09AA "Angiotensin-converting enzyme inhibitors", C10AA "HMG-CoA reductase inhibitors", C01BB "Antiarrhythmic drugs, class 1B". The study group of drugs for the treatment of cardiovascular pathologies, for the period from 2016-20, included 7 new INNs, 1 ATC group and 3 drugs. About 60% of drugs for the treatment of CVD are produced in Russia. For DFs included in the VED list of groups [C] "Cardiovascular system", 73% - solid, 25% - liquid and 1% soft DF.

2. Based on the results of a comparative analysis of the marketing characteristics of the target and local assortment of drugs of group [C] "Cardiovascular system", an assortment macro-contour of the Russian pharmaceutical market and a meso-contour of the pharmaceutical market of the Oryol Region of drugs used in the treatment of CVDs included in the VED list for 2020 was compiled The following indicators of the target market have been established: monopreparations - 90%; solid LF - 73%; Medicinal products of domestic production - 60%; LP for ATX-group, C09AA "Angiotensin-converting enzyme inhibitors" - 22.0%; MP by INN - atorvastatin 12.0%. Indicators of the regional market of the Oryol region: monopreparations - 76%; solid LF - 90%; Locally produced medicinal products - 82%; LP for ATX-group, C09AA "Angiotensin-converting enzyme inhibitors" - 18.0%; LP by INN - amlodipine 8.0.
3. Calculations to assess the availability of drugs for the treatment of CVD in the region under study by the coefficients of latitude, depth and completeness of the range showed the following results: $K_{sh} = 0.75$; $K_{g} = 0.868$; $K_{p} = 0.571$. Depth factor results: $LP = 0.825$; $TH = 0.948$; $INN = 0.868$. Of the 7 newly included INNs used in the treatment of CVD, only 2 INNs were identified in the region.

**DISCUSSION**

Our results indicate the availability of most drugs from the study group [C] "Cardiovascular system" of the VED list for the population of the Oryol region. However, it was revealed that the regional pharmaceutical market is characterized by a low rate of completeness of the assortment in comparison with the federal level (slightly more than 50%) and a low degree of renewal (28%). It should be borne in mind that high indicators of the depth coefficient for the assortment of medicinal products, INN and TH are based on the actual coefficient of completeness. The list of essential drugs for the treatment of CVD is more represented by drugs of domestic production (82%). Most of the new INNs (72%) included in the VED list over the past 5 years are not represented in the assortment of the regional market and are inaccessible to the population, including those related to the category of expensive ones. Thus, the results of this study of ours confirm our earlier hypothesis about the approval at the level of the constituent entities of the Federation of the minimum assortment of drugs (MALP) in accordance with the structure of major diseases and using the assessment of the cost of course treatment for a specific drug, taking into account the consumer's income (Garankina et al., 2019; Garankina et al., 2020; Samoshchenkova et al., 2019).

It should be noted, given the institutional certainty of restrictive lists, digitalization of processes and the use of blockchain technologies open up new opportunities for transparency of supply chains, confidence in the safety and efficiency of drugs and their availability for the end user (Federal Law No. 61-FZ of 12.04.2010; Decree of the Government of the Russian Federation of 08/28/2014 N 871; Garankina et al., 2018).

Summarizing the results of our study, it should be noted that in the near future, the improvement of drug supply in Russia will be associated with the development of the national institute for drug interchangeability, the functioning of the Common Market for Medicines of the Eurasian Economic Union, as well as the development strategy of the Russian pharmaceutical industry "Pharma 2030" (Zakharochkina et al., 2018; Zakharochkina et al., 2020).

It should also be noted that in order to reduce the CVD trend, it is necessary to promote and maintain a healthy lifestyle among the population.

**CONCLUSIONS**

The results of our research allow us to state that drugs included in group [C] "Cardiovascular system" of the VED list on the pharmaceutical market of the Russian Federation and the regional market have some significant differences. In our opinion, the most important criterion for the physical availability of vital medicinal products are indicators of the coefficients of accessibility of the breadth, completeness and depth of the assortment of medicinal products, as well as the degree of renewal.

It is necessary to take into account the established inconsistencies to improve the drug supply of the drug region of the study group, adaptive management of restrictive lists to optimize the assortment policy (Samoshchenkova, 2016; Samoshchenkova et al., 2019), and as a result, to increase the availability of cardiovascular drugs for the population of the particular region under consideration.
It should also be noted that it is necessary to timely update the lists of vital and essential drugs in accordance with the actual needs of the population on the basis of the introduction of the latest drugs to the market.

The development of methodological approaches and optimization of certain aspects in the analysis of specific groups of drugs included in the VED list is an urgent scientific problem, the solution of which is intended to improve the availability of drug supply to the population.

In this regard, the analysis of the availability of cardiovascular drugs is an important and necessary aspect of the activity, allowing to give an objective assessment of the work of the executive power and subjects of the sphere of drug circulation in the formation of an affordable range of restrictive lists of drugs.

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