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EXPERIENCE OF IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION PATIENTS MANAGEMENT IN URAL FEDERAL DISTRICT: FEATURES OF OUTPATIENT-HOSPITAL INTERACTIONS

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SUMMARY

Idiopathic pulmonary arterial hypertension (IPAH) is a severe chronic and rapidly progressive disease with increasing pulmonary vascular resistance (PVR) due to the ongoing pathogenic processes in the vascular wall that lead to obstruction of small pulmonary arteries and arterioles. IPAH takes a small part in the structure among all forms of pulmonary hypertension (PH), the median survival of patients with IPAH before any PAH-specific therapy became available were about 2,8 years, and the average time from the manifestation of the disease to its diagnosis took 2-3 years. This article is an attempt to present an unified data of adult patients with IPAH in Ural Federal district, and describe PH patients medical care service. The article presents the experience of PH Medical Centers across Ural Federal District.

Keywords: *pulmonary arterial hypertension (PAH), idiopathic pulmonary arterial hypertension (IPAH), registry, epidemiology, treatment.*

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Pulmonary hypertension (PH) represents group of the diseases that could be hemodynamically characterized as an increased mean pulmonary arterial pressure in pulmonary arteries and pulmonary vascular resistance, rapidly leading to right heart failure and death [1,2,5].

Idiopathic pulmonary arterial hypertension develops as a result of multiple complex pathogenic processes going on in vascular wall of pulmonary arteries including inflammation, vasoconstriction, proliferation, fibrosis, and thrombosis. These processes result in obstructive remodeling of pulmonary arteries of small and medium caliber. Increased pulmonary vascular resistance (PVR) is used to be a cause of right heart failure and premature death. It's been shown that median survival of IPAH patients without any PAH-specific therapy is about 2,8 years from diagnosis. Survival estimates of WHO FC IV patients even more modest and turn out to be nearly 6 month [2,13,23].

Epidemiologic data about PAH is very scarce that entangles exact prevalence and incidence figures unification. Most of the estimates derived from up-to-date PH registers [4-10]. In Europe, PAH prevalence and incidence vary in a wide range from 15 to 60 patients per million population and 5-10 patients per million population in a year, respectively. Idiopathic PAH, hereditable PAH, or drug-induced PAH constitutes about half of all PAH patients (group 1 of WHO clinical classification) [2,5]. According to recent epidemiologic data, in Europe (irrespective of country) true estimates of prevalence and incidence of PAH and IPAH could be 15 and 6 cases per million adult population, respectively [3].

Academician Irina E. Chazova et al. for the first time conducted open multicentral study [12] to evaluate demographic and clinical characteristics of PAH and CTEPH patients. It's been concluded that epidemiology estimates of PAH and CTEPH syndromes in Russia concede ones yielded from European registers and averages 60 cases per million adults. Bearing in mind overall Russian population and results from the above mentioned study (register), there should be at around 2 400 PAH patients in the country [15,17-19].

It looks like the main purpose of any register ultimately could be gathering information with regards to disease prevalence, clinical presentation, laboratory and instrumental methods of diagnosis and types of treatment [12].

Clinical registry participation is used to being mutually beneficial collaboration between HCP, patient, and government. A physician performs diagnosis procedures according to actual standards and guidelines having possibilities to conduct medical consultation (consilium) in an occasion of complicated clinical case. A patient included to the registry takes a chance to be treated according highly recommended modern standards. Theoretically speaking, all of it could shorten a time from symptoms onset to diagnosis verification and start of PAH-specific medication [12].

Lack of united Russian patient registry of all PAH subtypes and CTEPH poses some difficulties. Array of registries running in some provinces are being filled in very different ways. Annually, Heart and Vessels Center (part of Regional Clinical Hospital №1) gets new PH data from all across the Ural Federal District. Although the information receiving is quite valuable, its fragmented character complicates understanding of overall epidemiology landscape in the district.

All the data receiving is being analyzed by Chief Cardiologist of Ural Federal District on a regular basis. Processed results of such activity are usually delivered during Annual PH Specialists Conference. This article represents an attempt to reflect a real situation concerning IPAH patients in Ural Federal District

As of January 01, 2018, there are 12 356 229 habitants (Figure 1) living in Ural Federal District, including Sverdlovsk province- 4 325 256, Chelyabinsk province – 3 493 036, Khanty-Mansi Autonomous Area - 1 655 074, Tumen province - 1 498 779, Kurgan province – 845 537, Yamalo-Nenets Autonomous District – 538 547 habitants [24].

Taking into account rich experience of overseas colleagues, it would be quite brave to imply that PAH prevalence and incidence substantially higher than those we have seen from variety of fragmented registers. For the time being, patients registration suffering from IPAH is going

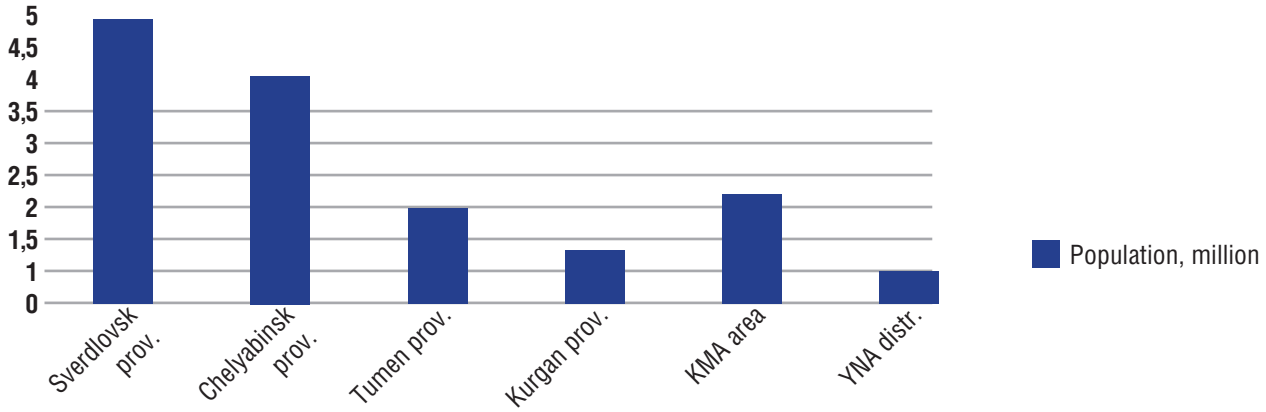

Figure 1. Ural Federal District population (in million habitants; as of January 01, 2018)

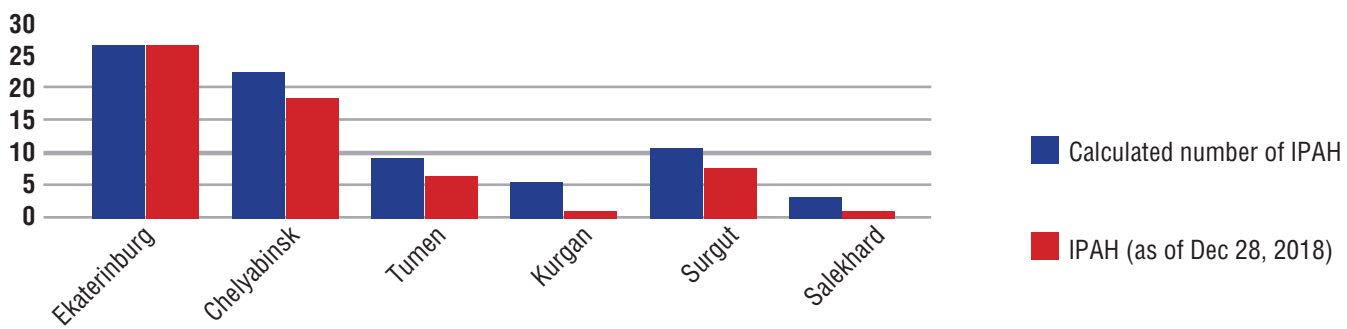

Figure 2. Calculated and factual number of patients with IPAH in Ural Federal District (2018)

on in PH Federal Registry. Some regions are reporting data on CTEPH and IPAH to the Registry, as well. Calculated estimates testify that true number of PAH and IPAH patients should be from 186 to 744 and 74 patients, respectively (Figure 2).

As depicted in a chart (Figure 2), IPAH prevalence in some provinces does not match epidemiologic data from European registers. At the time of population analysis (Table 2; as of December 28, 2018), 59 adult patients with IPAH have been registered; vast majority of them are young women WHO FC II-III. Median time from disease manifestation to diagnosis is 2,4 years. Mean age at the moment of patient inclusion to the Registry is 40,5±3,3 years; median of disease duration is 3,7 years (ranging from 2,6 to 4,2)

Usually, government receives statistics/epidemiological data on disease prevalence, incidence, mortality, medicinal therapy requirements. At the very end, PH Registry creation leads to bettering healthcare service to the nation, specifically to the ill persons with such a life-treating, devastating and orphan disease as pulmonary hypertension. PAH patients registry are running or going to be run in numerous countries across the globe [6,15-17].

IPAH has been included in 10 the most high-cost («stress») nosologies. Expenditures for IPAH constitutes 90% of the National budget for all orphan nosologies (2015) being at the 4th place (the proportion of the allocated budget 7,5%). The most prominent money deficit in covering needs of medicinal therapy to the patients included in Federal Registry amongst analyzing regions noted in different nosologies, including IPAH – 23,2% or 170,5 million RUR. [11]. An analysis of taking IPAH patient treatment in Ural Federal District showed that 93% of the patients are receiving

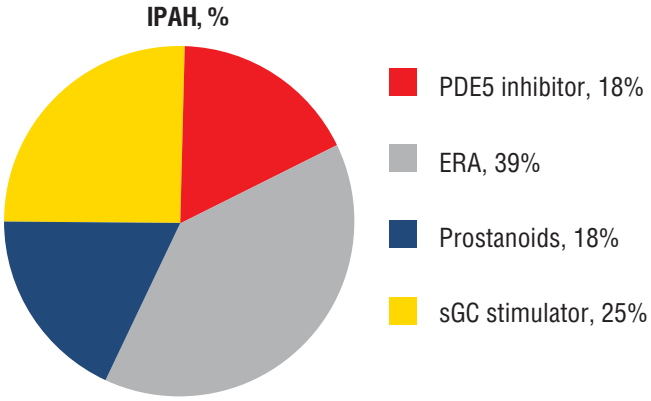

Figure 3. Percentage of PAH-specific drugs prescribed to IPAH patients.

PAH-specific therapy (Table 2). Most of them showed negative result in vasoreactivity testing (92%). A minor part of the patients (8%) turned out to be positively vasoreactive. In these 8% of patients high dosage calcium antagonists therapy did not appear to be effective, though.

Over the last decade, diagnosis and treatment pattern of PAH syndrome improved drastically [1]. Timely prescription of specific medications to the patients with RHC-verified PH is implicated in better outcomes, and could potentially improve overall therapy [22]. When scrutinizing drugs prescribing for PAH treatment purposes (Figure 3), it is worthwhile to note that quarter of all patients still

Table 1. Data on IPAH patients from Federal Registry 2012 – 2018.

IPAH patients registry management	Surgut 2012	Tumen 2012	Chelyabinsk 2012	Ekaterinburg 2012	Salekhard 2018	Kurgan 2018	Overall
Number of IPAH pts. in registry (as of December 28, 2018)	7	6	18	26	1	1	59
Calculated number of IPAH pts. with PAH/ IPAH (based on existing epidemiology)	26-102 10	23-90 9	53-210 21	65-258 26	8-30 3	14-54 5	186 – 744/ 74
Number of patients died from background disease at the moment of data analysis	4	7	8	8	0	0	27
Male/Female	2/5	1/5	4/14	1/25	0/1	0/1	8/51
Mean age, years	42,2	46,5	36,8	44,7	33	40	40,5
Mean time from symptoms onset to diagnosis, years	0,8	2	3,4	2	3	3,2	2,4
Median WHO FC at the moment of patient inclusion to the registry	II	III	III	III	III	III	III
Life duration of died patients on the established PAH-specific therapy, years	3,9	4,2	2,6	4	-	-	3,7
IPAH prevalence, cases per 1 million	4,1	4	5,1	6,1	2	1,2	4,7

Table 2. Patients receiving PAH-specific therapy

	Сургут	Тюмень	Челябинск	Екатеринбург	Салехард	Курган
IPAH patients (overall number 59)	7	6	18	26	1	1
Positive vasoreactive testing	2	1	0	2	0	0
Monotherapy	2	1	7	10	0	0
Double PAH-specific therapy	2	4	6	4	1	1
Triple PAH-specific therapy	1	1	5	10	0	0
Overall number of patients receiving PAH-specific therapy (55 pts.)	5	6	18	24	1	1

receives iPDE-5. It is allegedly circumstanced by low cost of the drugs from this class, in particular, sildenafil. For now, it has been demonstrated that up to 60% of PAH patients insufficiently response to iPDE5 [25-27]. The reason of such insufficient response may theoretically be explained by low level of endogenous nitric oxide in patients vascular wall of pulmonary arterial bed. Another reason is that cGMP could be degraded not only by PDE5, but also by numerous PDE isoforms. Inhibitory activity of sildenafil towards those isoforms is rather low or absent. [25,27,28]. In conjunction with it, it has been assumed that sGC stimulators, in particular, riociguat could serve a good alternative to iPDE5 in PAH patients do not responding (or insufficiently responding) to established iPDE5 therapy [25]. Riociguat is capable of stimulating cGMP synthesis in the condition of nitric oxide deficit, and this is going to be a potential advantage of sGC stimulators in comparison with iPDE5 [25]. At present, we see a tendency to iPDE5→sGCs replacing in PAH patients. Some favorable results of such replacing were demonstrated in recently completed clinical trials [23,29]. For now, 25% of patients from Ural Federal District receive riociguat.

Most of the patients, namely, 39% are taking medication from another drug class which is called endothelin receptors antagonists (ERA) (Table 3). Interestingly, that therapy with prostacyclin analogues, specifically, iloprost inhaled accessible to the wide range of patients in the district. This situation is quite unique and at the same time it is very important because iloprost inhaled represents an optimal treatment in moderate to severe patients (FC III-IV) with selected subtypes of PAH and inoperable CTEPH [30].

Rareness of the syndrome could also be explained by lack of knowledges and awareness about PH. Doctors do not follow current diagnostic algorithm (including invasive diagnostic procedure right heart catheterization) which appears to be complex. Many of those physicians who are trying to treat PH very often prescribe not appropriate/optimal specific therapy [20].

Apart of it, we have to keep in mind that PAH is rapidly progressive debilitating disease that requires constant patient following up and gradual treatment escalation. That is why all the patients discharged are best to be evaluated and followed up by experienced PH specialist [21].

Creating specific PH Expert Centers that deeply involved in such type of patients treatment across the Russia could potentially help to improve early diagnosis (without prolongation), timely start of optimal therapy and, at the very end, its correction/optimization if required [12]. All the above mentioned factors have served as prerequisites when creating PH Expert Centers network encompassing Ural Federal District, including Sverdlovsk province, Chelyabinsk province, Kurgan province, Khanty-Mansi Autonomous Area, Yamalo-Nenets Autonomous Area.

Within each province chief specialist, typically cardiologist, who is responsible for IPAH data reporting to Federal PH Registry was identified. A Registry management was established and optimized since after.

The Heads of budgetary governmental medical centers of Russian Federation provinces have appointed local HCP's who are supposed to be in charge for collecting and reporting data about all the patients suffering from IPAH. Completeness of entering data with respect to IPAH is being checked on a regular basis. The Heads of public administration and public health institutions of municipalities, medical organizations under the authority of medical universities organized PH Expert Centers on their bases. For instance, in Sverdlovsk province PH Expert Center was originally created on the base of Ural State Medical Academy (USMA), according to the law act issued by the rector of USMA. Since 2013, the same thing has been done on the base of Sverdlovsk Regional Clinical Hospital №1 (SRCH №1). Since October 22, 2013, on the base of SRCH №1 created very large PH Expert Center that embraced HCP's of different specialties forming so called multidisciplinary PH team.

Normally, PH Expert Center includes consultative and diagnostic outpatient department, cardiology department, cardiac surgery department, pediatric cardiac surgery department, X-ray surgical department, ICU, vascular surgery department, rheumatology department, gastroenterology, pulmonology, hematology. Organized in hospital and outpatient medical services help to suspect and diagnose the syndrome, identify further treatment tactics and follow-up. The calculation process of the need of financial resources to support persons suffering from IPAH within 15 working days after a patient inclusion into regional segment of the Federal PH Register has been organized as well.

For the time being, modern algorithms for diagnosis and treatment of PH were created. Right heart catheterization is a pillar and key aspect of diagnosis verification. During this invasive procedure array of hemodynamic parameters are measured and typically include mean pulmonary arterial pressure (mPAP), pulmonary arterial wedge pressure (PAWP), pulmonary vascular resistance (PVR), diastolic pressure gradient (DPG) etc. Acute vasoreactivity testing is also conducted in IPAH patient to check whether a particular patient could benefit from high-dosage calcium channel blockers therapy in a long run or not.

It worthwhile to note, that specific therapy favorable efficacy and safety profile have proven only for Group 1 and 4 of WHO clinical classification (ESC/ERS 2015). Due to low prevalence of PH, complexities in patient management and other reasons, epidemiological data is still rather raw.

According to the Federal PH Registry (Table 4), IPAH prevalence in Ural Federal District varies from province to province.

Outpatient medical care is well organized in Ural Federal District. Every citizen could be referred to PH Expert Center if their clinical presentation suggestive of possible pulmonary hypertension. For a particular patient visit regularity is usually defined on an individual basis depending on clinical condition and other factors. In case if patient is relatively stable, he is supposed to visit outpatient clinic every 6 month, as per European and Russian PH diagnosis and treatment guidelines. For patients changing therapy or initiating therapy, 3 month time lapse between visits is tought to be optimal. More frequent visits are indicated for the patients with inadequate clinical response to a therapy, or in case of severe pulmonary hypertension.

Table 3. PAH-specific therapy

Drug class	Surgut	Tumen	Chelyabinsk	Ekaterinburg	Salekhard	Kurgan	Overall
iPDE5	4	1	6	7	1	-	19
ERA	4	3	16	17	-	1	41
Prostanoids	1	4	4	10	-	-	19
sGC stimulator	2	4	6	14	-	1	27

During regular patient visit in outpatient clinic following parameters are being measured, including WHO FC, 6-minute walking distance (6MWD), laboratory parameters. Other methods of patient evaluation could also be applied, such as, cardiopulmonary exercise testing (CPET), echocardiography assessment (EchoCG), electrocardiography (ECG), CT or MR pulmonary angiography. Since PH diagnosis is established, right heart catheterization as an invasive diagnostic procedure is being performed annually or in case of clinical deterioration/changing therapy. In some case, if PH patient presented with cardiac ischemia, coronary angiography could be indicated, because this symptom may suggest left main coronary arteries compression by dilated pulmonary artery trunk. Some cases has been described by local researchers.

Echocardiography in PH patients still remains best screening method and could help to evaluate right heart chambers size, cardiac output, systolic PAP, TAPSE etc. A PH patient is undergone EchoCG once in 6-12 month depending on clinical condition (when changing therapy – every 3 month).

Laboratory parameters monitoring is also of utmost importance and scheduled to be done 2 times in a year for general blood analysis and blood chemistry. If patient is recieving established ERA therapy, blood chemistry is going to be done every month. International normalized ration is also should be constantly monitored because IPAH patients require effective anticoagulation. In efforts to control right heart failure progression BNP/NT-proBNP are useful to be measured (once in a 6 month).

Since the PH Expert Centers have started their work in Ural Federal District, we noted marked (2 time) increase in consultative activity. As we know, PAH is chronic lifetreating disease. To diagnose a patient with this syndrome ample of diagnostic measures are required. PAH diagnosis verification is available in 63% out of 59 provinces of Russia Federation (in a subjects involved in Federal PH Registry). In 3% of these 59 provinces molecular diagnostic technics for the diagnosis of hereditable PAH are feasible [11,12,14].

In some regions of Ural Federal District due to limited diagnostic armamentarium and low HCP's diagnostic skills required for final diagnosis of PH, certain number of patients are sent to Federal PH Expert Centers. Vast margin of IPAH patients, one way or another, was consulted by Federal PH Expert Centers specialists (table 5). Most of the patient are referred (in descending order) to National Medical Research Center of Cardiology named after A.L. Myasnikov, National Medical Research Center named after E.N. Meshalkin, National Medical Research Center of Cardiovascular Surgery named after A.N. Bakulev, Scientific and Research Institute of Pulmonology. Some patients are in the list of waiting for heart-lung transplantation.

Over the last several years great advancements in the diagnosis and treatment of PAH patients were archived, mainly because well-organized work of PH Expert Centers and respective specialists. PH burden became understandable for the wide audience of Ural Federal District cardiologists, disease awareness have skyrocketed since then. It is also recognizable as a tremendous problem by HealthCare Authorities.

Cardiologists and pulmonologists in outpatient department were prone to follow PAH-specific medication prescribed to the patient upon hospital discharge. Low competency of treating physicians in outpatient clinics and limited PAH-specific drugs accessibility was resulting in ill-timed therapy correction, later diagnosis.

In order to improve effectiveness of PH patients diagnosis and treatment, Healthcare Authorities of Ural Federal District ordered to create specific PH Expert Centers in the following cities, e.g. Ekaterinburg, Chelyabinsk, Tumen, Surgut, Kurgan, Salekhard.

The main goals staying before the region is providing proper level of examination, treatment and diagnosis of patients with various forms of PH, educating and training medical institutions on complex issues of diagnosis and treatment of PH patients, arranging various scientific events, organizational and methodological work, and PAH patient following up.

The advantage of creating PH Expert Centers throughout Ural region based on cardiology centers and State clinical hospitals with its included polyclinic, 7/24 hospital service (including cardiac surgery, radiology department, interventional surgery) provide an integrated approach to properly treat patients with PAH at all stages within one institution. Well-educated specialists trained in PH field in the Federal PH Expert Centers (cardiologist and pediatric cardiologist, physician, interventional surgeon) are sought after.

Outpatient care is provided in outpatient clinic, where any resident of a city or a province can refer in case of revealing high systolic (estimated) pressure in the pulmonary artery during an EchoCG procedure.

As a result of organized wide range of educational events, particularly with prominent opinion leaders and PH experts, leaflets and letters, lectures and seminars, PH schools, etc. physicians have actively began to refer high risk group of PAH patients for consultation. This problem has become more recognizable among doctors of other specialties.

A consultation activity in organized PH Expert Centers has increased compared with previous years since the PH Centers was established. The most difficult part is to identify PH patients and to send them for consultation. A step-by-step diagnostic algorithm is used according to current guidelines to verify the diagnosis and clarify the etiology of pulmonary hypertension syndrome [1,5]. Amongst adult patients (≥18 y.o.) presented to PH Expert Centers, we've seen a huge number of patients with left heart and congenital heart disease. CTEPH diagnosis is still very prevalent.

In some cases, a patient is hospitalized for diagnosis clarification and in a medical center additional examination and treatment are carried out. Since 2014 some PH centers in Ural have been performing right heart catheterization (RHC) following by acute vasoreactivity testing. A RHC was conducted in more than half of PH cases. According to its results, 25 patients with IPAH were verified.

Due to the cardiac surgery service, early verification of congenital heart disease among children allows to correct the situation in advance before the far-reaching and inevitable consequences of PH came. Precise attention to the problem led to an improvement of detection of patients not only with IPAH, but also PH patients of other subtypes. There were about 1-2 new detected cases of IPAH in 2014. Since PH Centers are at work, this indicator has grown to 5-6 new cases per year. There are still quite large gap between the manifestation of the disease and its verification. This period takes

Table 4. IPAH prevalence in Ural Federal District (as of December 28, 2018)

IPAH Registers management	Surgut	Tumen	Chelyabinsk	Ekaterinburg	Salekhard	Kurgan	Overall
Number of IPAH patients included into registry.	7	6	18	26	1	1	59
IPAH prevalence, cases per 1 million population	4,1	4	5,1	6,1	2	1,2	4,7

as many as 2.4 years.

The governmental expenses for PAH patients medicainal treatment, hospitalization, diagnosis and other related expenditures are significant. According to the "List of life-threatening and chronic progressive rare (orphan) diseases ..." [11], only IPAH is included in the list of government commitment. In the event of a PAH diagnosis, a medical commission with the participation of the chief specialist of the region is arranged to include the patient in the "Register of citizens who need drug provision". The registry of Ural Federal District includes 59 patients with IPAH, the source of PAH-specific therapy is the regional budgets funds (Table 2.3).

CTEPH patients and associated forms of PAH are partly provided with a specific treatment by a regional ministry of health. However, many patients are forced to purchase drugs for their own savings. Mostly, these drugs are generics (abbreviated drugs) of sildenafil, due to a relatively low price [11].

A patient with a confirmed diagnosis of PAH also requires regular monitoring by doctors. At the same time, due to the small number of patients with the disease (usually not exceeding 1-2 patients per hospital), it is not advisable to create a follow-up groups in the outpatient clinic similar to those created for the patients with ischemic heart disease, and hypertension.

Mostly, in the regions of the Russian Federation it remains customary to keep a personalized record of patients with IPAH in accordance with the place of their residence.

Thus, it seems obvious that early diagnosis, timely prescribing PAH specific therapy, and its correction during careful observation of clinical and hemodynamic parameters are the key factors to increase at the very end survival of PAH patients.

Analysis of the PH register data contributes to the development and implementation into clinical practice of common approaches to the diagnosis and treatment of this type of patients. Establishing of Federal Register for PAH and CTEPH patients helps to take diagnosis process and treatment of this category of patients to a new level. At the same time, it helps in evaluating the effectiveness and quality of medical care, and provides invaluable assistance in studying the volume of medical care and the utilization of healthcare resources [12].

DISCUSSION

If the global data are roughly comparable, the results of the Russian registries differ depending on a region, medical institutions and other features [3]. However, for the period of 2013-2015 a significant increase among patients with PAH (+ 35%) was demonstrated, which is likely to be associated with improved patient detection in Russian Federation [11].

The prevalence of the disease is determined, among other things, by the activity of the PH Expert centers in searching for patients and does not reflect the entire epidemiological situation in Russian Federation. The creation of the new PH Expert centers will presumably improve the early diagnosis of PAH and CTEPH, and ensure the registration of new patients and their monitoring [12].

International clinical protocols (the randomized controlled trial (RCT)) SERAPHIN (NCT00660179) in 2008 and the RCT GRIPHON (NCT01106014) in 2009 turned out to be a starting point for PH problem development.

Despite the late beginning of the Federal Register in the Ural Federal District, the prevalence and incidence of IPAH in some regions are more or less similar to world data (Sverdlovsk, Chelyabinsk), but there are also regions with lower numbers.

However, despite the wide range of drug therapy, PAH is still an unresolved problem for public health, because lifelong vasodilators expensive therapy is needed.

The main purpose of outpatient monitoring for patients with PAH is to achieve the satisfying parameters of physical, laboratory and instrumental examinations in order to prevent aggravation of the pathological process and patients decompensation, to improve quality of life, to increase life expectancy, and to identify the disease at early stages [3].

The Federal PH Registry of patients with PAH and CTEPH allows to evaluate the effectiveness and provided quality of medical care and will help to assess the needs of medical care, as well as the expenditure of health resources [12].

Ural Federal District is a quite huge region with a population of over 12 million. The prevalence of IPAH in the region is 4.7 cases per 1 million.

Probably, the one of many other reasons for such a relatively low IPAH rate is low awareness of population. Gaps in diagnosis (there are regions where it is not possible to perform right heart catheterization, coronary angiography, balloon angioplasty, etc.), absence of a unified monitoring system for such patients, poor level of expertise and experience are also could be implicated in low IPAH prevalence.

There are some challenges the Ural Federal District will meet going forward. First of all, is it going to be hard to reduce time between the occurrence of the first symptoms to the final diagnosis. For now, it takes about 2.4 years. To improve survival is going to be another challenge. The median survival of patients with IPAH without specific therapy is 2.8 years, which is unacceptable [2,13,23].

Table 5. Patients consulted in PH Expert Centers of Federal level (as of December 28, 2018)

IPAH registers management	Surgut	Tumen	Chelyabinsk	Ekaterinburg	Salekhard	Kurgan	Overall
Number of IPAH patients in register	7	6	18	26	1	1	59
National Medical Research Center of Cardiovascular Surgery named after A.N. Bakulev	2	2	4	2	-	-	10
Scientific and Research Institute of Pulmonology	-	-	-	3	-	-	3
National Medical Research Center of Cardiology named after A.L. Myasnikov	3	3	5	13	1	1	26
National Medical Research Center named after E.N. Meshalkin	2	-	8	8	-	-	18
Scientific and Research Institute of Rheumatology named after V.A. Nasonova	-	-	-	-	-	-	-
National Medical Research Center named after V.A. Almazov	-	-	-	-	-	-	-

There are also some acts to be done to shorten the period between the identifying IPAH and supplying with PAH-specific therapy (nowadays it takes about 3-6 months). Patients with IPAH cannot stay long without vital specific therapy.

Federal Register of IPAH is undoubtedly important for vulnerable patients, however, making a register for patients suffering from secondary forms of PAH and CTEPH is also very important. Some PAH and CTEPH data are collected by only a few subjects of the UFD.

The cumulative data will demonstrate the whole scope of PH rate in the region, and also entail some question about drug supply of other forms of PAH. Despite the lack of opportunities in some regions to perform right heart catheterization, coronary angiography, balloon angioplasty, the organization and starting of these methods of examination and treatment, is also in the task list of PH Expert Centers in the UFD.

Definitely, the quality of medical care to the patients who suffer from IPAH depends on many things such as disease awareness, skills, and experience of doctors of a PH Expert Centers in cities and districts. That is why it is still important to arrange numerous of educational events across Ural Federal District.

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