Rare Diseases, Orphan Drugs and the Scenario in 2019

Doenças Raras, Drogas Órfãs e o Cenário em 2019

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The concept of rare disease (RD) includes 6,000 to 8,000 clinical conditions characterized by low prevalence in the population, chronic and very debilitating course and lack of specific therapies.[1] There is no universal definition of RD accepted worldwide so, in Brazil, these include diseases that affect less than 65:100,000 inhabitants.[2] In Argentina and European Union (EU) countries, this figure is ≤5:10,000 inhabitants and, in the United States of America (USA), diseases that affect less than 200,000 individuals.[3] Translating this into absolute figures, there are about 30 million patients with rare diseases in the US, another 30 million in the EU[4] and 13 to 15 million in Brazil.[5]

About 80% of RD are of genetic etiology[6] and determine clinical disorders since birth. Thus, 50% of rare patients in the world are currently children. Of these, 30% do not survive to the 5th year of age if not treated accurately, early and effectively. Data from developed countries show that the time spent on diagnosis is 8 years on average and patients have been evaluated by 10 or more health specialists. Reports of therapeutic regimens with no benefits and conflicting diagnoses of different professionals are common complaints in this group.[7]

Despite the undeniable technological progress of recent decades that have made it possible to establish the etiology of RD at the molecular level, as well as allowing a better understanding of its pathophysiological mechanisms, there are few effective specific therapies. The medicines used in the treatment of RD are known as orphan drugs (OD) and, once under this name, they receive different benefits and incentives for development and marketing. As of 2018, these consisted of 164 substances approved by the European Medicines Agency (EMA) to be marketed in the European Community[8] and 500 OD approved in the USA by the Food and Drug Administration (FDA).[9] The pharmaceutical industry has a central role in the development and marketing of these new molecules, since university centers and governments do not always have the funds or technological structure to fund research.

In a context of integrality and universality of health and free access to knowledge through the internet, demand for these medications grows exponentially worldwide. The financial impact of these medications on the budgets of governments and health insurers around the world is very significant and target of extensive discussion. In a scenario of economic recession and population aging, treatments costing millions of BRL per year are able to make the cost of so many other health demands unfeasible and challenge the budgetary planning of institutions.

The often-slow regional regulatory procedures and the lack of specific regional protocols incorporating new technologies end up encouraging the adoption of marginal ways of access to treatment, such as going to court. The budgetary impact of going to court to handle the purchase of medications not registered by local governments, especially in developing countries, can be exemplified by figures from Brazil. In 2017, the federal and state governments, together, allocated about BRL 7 billion to the purchase of medicines required by court judgments. Of this, 92% were spent on 11 drugs alone. And demand grows annually to the extent that 1010% more were spent from 2010 to 2017.[10]

However, a scenario with no ODs available is neither more favorable nor less expensive for the parties involved. Considering that most RD have a multisystemic character, are highly disabling and progress to terminal disease due to organ system failure, expenses with clinical support and palliative treatment may be even higher. In addition to individuals economically inactive and in severe psychosocial distress, more expensive treatments than those with ODs, such as organ transplants, dialysis, implantation of expensive devices such as pacemakers, cardiac defibrillators, neuromodulators and others, may be required. Added to this is the need for special care, leading family members to stop working to support their sick relatives.

In view of the above, we should then discuss this issue such that we can ensure the right to health in a broad, cost effective and no-waste manner. At the speed with which the development of new treatments is taking place and with the real possibility of correcting DNA defects for curing diseases, it is necessary to look for ways of funding, providing equal access as well as training health professionals for diagnosis and treatment early enough for reducing damage.

From a governmental and regulatory point of view, Brazil has been adopting the programs followed worldwide. Since 2014, we have adopted the National Policy for Integral Attention to People with Rare Diseases, which advises on the structuring of care and decision making within Brazil's public health system.[11] We also have the National Commission for the Incorporation of Technologies (CONITEC), which coordinates the drafting of Clinical Protocols and Therapeutic Guidelines (PCDT) that serve to support, within Brazil's public health system, diagnostic, therapeutic and healthcare procedures.[12]

In civil society, there are numerous groups and associations

Keywords

Rare Diseases; Orphan Drug; Cardiology.

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DOI: 10.5935/2318-8219.20190045

of people with RD, who promote meetings with patients, family members and specialists in the field, and provide legal assistance and search for reference centers and specialized professionals. These entities serve as an important reference point for patients who, in countries such as Brazil, have an epidemiological profile with low education, low income and partial demographic isolation because they come from small towns in the countryside that are far from large urban centers.

Brazilian medical societies are taking action and seeking to be at the forefront of decision-making on RD issues. This year, the Brazilian Society of Cardiology, in collaboration with the Department of Clinical Cardiology and the Department of Cardiovascular Imaging, has approved the creation of a study group on rare diseases. Apart from other work proposals, the group aims to foster discussions of the topic among cardiologists, with emphasis on diagnosis, create education and recycling channels, stimulate the exchange of information between specialists and scientific production on the subject.

We will have many challenges to overcome in Brazil and sparking off debate is the first step towards success. We lack epidemiological data and national registries compiling data on the profile of RD in Brazil. The use of cardiovascular imaging through new technologies, such as myocardial strain indexes, may suggest and differentiate poorly diagnosed diseases, stimulating the continuation of workup.[13] Echocardiography and cardiac magnetic resonance imaging using strain and T1 mapping may provide early diagnosis, select patients for treatment and monitor response to therapy.[14] It is necessary to explore and assess the problem precisely in order to think about public policies and health promotion actions. Besides, we need to rethink medical curricula focused on high-prevalence diseases at the expense of rare diseases and make it possible for professionals to be able to engage in retraining and refer patients to reference centers when needed. Mapping out existing centers of excellence, multiplying them throughout the national territory and establishing channels of communication, discussion and referral of patients are some of the objectives to be achieved. That the word orphan be used only for drugs rather than to refer to patients with RD or to the health professionals involved in their support.

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