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EDITORIAL

Writing a little about so-called rare diseases

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Rare diseases are defined by their frequency in the population. In the United States, rare diseases are considered when they have a frequency of 1:500 (less than 20,000 affected in the total population). In Japan, a disease of this type is legally one that occurs in less than 50,000 patients, that is, 1:2,500 individuals. Korea is the country that presents the lowest frequency to consider a rare disease (5 in every 100,000 habitants) and China defines it in almost 80 cases per 100,000 individuals. For the European Union, a rare disease, of any etiology, must present chronic disability with a presence of less than 1 in 2,000 individuals in the general population. They are not considered rare if they are not life-affecting or debilitating. In Mexico we have considered an occurrence of 1:2000 patients. However, it is worth mentioning that there are more than 100 definitions for a rare disease worldwide.

Currently, it is considered that there are around 8,000 rare diseases worldwide. Apparently, 80% of these are of genetic origin, affecting mostly the child population. In general, these types of diseases have a monogenic inheritance pattern, a systemic condition or with multiple affected organs and taken as a whole, there are more rare diseases than common ones. Around 400 million people in the world have some type of rare disease.

A large number of cases of rare diseases are difficult to diagnose and remain without a definitive diagnosis for many years and even for life. Currently, the development of molecular technology, especially in the analysis of genes, has made it possible to clarify a large number of cases that remained undiagnosed.

The neonatal screening is a test which is used to diagnose various rare diseases early and in a timely manner, mainly metabolism errors. This detection test allows, once the corresponding diagnostic test has been carried out, to implement an appropriate treatment and thus, avoid complications in newborns and promote better development and even a normal life in affected children.

In the General Hospital of Mexico Dr. Eduardo Liceaga, neonatal screening has been carried out since 2006; In the last decade, 11 tests have been determined, including: Neonatal thyroid-stimulating hormone, Neonatal levothyroxine, 17-alpha-hydroxyprogesterone, Neonatal immunoreactive trypsinogen, Neonatal glucose-6-phosphate dehydrogenase, Total galactose, Galactose 1 – uridyl transferase, Biotinidase, amino acids: phenylalanine, tyrosine, phenylalanine/tyrosine ratio, leucine + isoleucine + hydroxyproline, valine, methionine, citrulline, arginine, glycine, ornithine, alanine, proline, acylcarnitines: free carnitine, acetylcarnitine, propionylcarnitine, butyrylcarnitine, isovalerylcarnitine, methylmalonyl + 3-Hydroxy-isovalerylcarnitine, Glutarylcarnitine + 3-hydroxy-hexanoylcarnitine, Octanoylcarnitine, Tetradecenoylcarnitine, 3-hydroxy-tetradecanoylcarnitine, Hexadecanoylcarnitine (palmitoylcarnitine), 3-hydroxy-hexadecanoylcarnitine, Octadecanoylcarnitine (stearoylcarnitine), Octadecenoyl-octadenoylcarnitine (3-hydroxydecenoylcarnitine), and normal hemoglobin and its variants.

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On the other hand, the genotypic matrix can analyze from 100,000 to 500,000 single nucleotide polymorphisms (SNPs) in a hundred samples in one to three days. This technique is used to characterize associations between SNPs and a characteristic phenotype of a rare disease. Often called SNPs (pronounced “snips”), they represent a very frequent type of genetic variability present in the world population. Each SNP is characterized by a single nucleotide change in what we know as DNA. That is, a SNP consists of the change of any nucleotide for another in the DNA sequence. SNPs are present in all DNA that identifies us as individuals. It is estimated that these occur approximately every 1000 nucleotides on average, so we would be considering that each of us has between 4 and 5 million in our genome. These changes occur in all individuals and must be present in at least 1% of the population. The importance of these SNPs in rare diseases is because they allow the identification of genes associated with these conditions.

Exome sequencing is a very useful molecular tool for the diagnosis of these patients. This technology identifies, at the gene level, the protein-coding regions of the genome, non-translated regions, and the intron-exon junction, at relatively affordable prices. However, it has its limitations for certain regions. In these cases, genome sequencing can identify canonical variants, tandem repeats, intronic and coding variants that may not be identified by exome sequencing.

There are more studies that allow us to accurately diagnose a rare disease at a more affordable cost. Fortunately, despite the complexity of the disease, some of them already have treatment. However, in some cases the cost is in the millions of dollars such as spinal muscular atrophy. We hope that in the near future the accessibility of the treatment will be present for any individual, since the purpose is not only to establish the correct diagnosis, but also to offer our patient a better quality of life.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments were carried out on humans or animals for this research.

Data confidentiality. The authors declare that no patient data appears in this article.

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