CHALLENGES OF ACCESS TO TREATMENTS: THE CASE OF LARON SYNDROME AND THE FIGHT FOR SOCIAL INCLUSION

Gabriel Alejandro Vasco-Toapanta 1
Alisson Mayerly Guanoluisa-Vasco 2
Gabriela Alejandra Ochoa-Núñez 3
Cristhian Santiago Vasco-Toapanta 4

ABSTRACT

Objective: To identify and disseminate the challenges faced by patients with Laron syndrome in accessing Mecasermin treatment in Ecuador.

Theoretical Framework: Laron syndrome is a rare genetic disease characterised by metabolic disorders such as hypoglycemia and severe growth retardation. Treatment with Mecasermin improves growth and thus quality of life for those affected. Ecuador has the largest Laron syndrome population in the world, extensively studied contributing to the understanding of the peculiarities and needs of these patients.

Method: Official documents, letters, news articles from national and international press, and legal and medical databases were reviewed. Legal and medical advice was sought for this study.

Results and Discussion: Over approximately ten years, a group of parents pursued national and international legal action to provide their children with the only scientifically validated treatment for this syndrome. However, authorities denied these requests without justification. It was only after the Inter-American Commission on Human Rights report the admissibility of this case that Ecuador began administering medication to children with Laron syndrome.

Research Implications: Increase public awareness of this rare disease and barriers faced by those affected, fostering empathy, and understanding of patients' needs.

Originality/Value: Identification of specific barriers to accessing treatment, while the quality of life of patients and their families is affected.

Keywords: Laron Syndrome, Human Rights Abuses, Receptor, IGF Type 1, Growth, Rare Diseases, Disabled Persons.

RESUMO

Objetivo: Identificar e divulgar os desafios enfrentados pelos pacientes com síndrome de Laron para obter acesso ao tratamento com Mecasermina no Equador.

1 Colegio de Ciencias e Ingenierías, Universidad San Francisco de Quito, Quito, Ecuador. E-mail: gvasco@estud.usfq.edu.ec Orcid: https://orcid.org/0000-0003-4986-0020
2 Carrera de Fonouaïologia, Facultad de Ciencias de la Discapacidad, Atención Prehospitalaria y Desastres, Universidad Central del Ecuador, Quito, Ecuador. E-mail: amguanoluisav@uce.edu.ec Orcid: https://orcid.org/0009-0003-8987-7481
3 Colegio de Comunicación y Artes Contemporáneas, Universidad San Francisco de Quito, Quito, Ecuador. E-mail: gaochoa@estud.usfq.edu.ec Orcid: https://orcid.org/0009-0006-0078-2681
4 Colegio de Ciencias de la Salud, Universidad San Francisco de Quito, Quito, Ecuador. E-mail: csvasco@estud.usfq.edu.ec Orcid: https://orcid.org/0000-0002-2874-9836
Referencial Teórico: A síndrome de Laron é uma doença genética rara, caracterizada por distúrbios metabólicos como hipoglicemia e grave retardamento no crescimento. O tratamento com Mecasermina melhora o crescimento e, portanto, a qualidade de vida dos afetados. A população equatoriana com síndrome de Laron é a maior do mundo e tem sido amplamente estudada, contribuindo para compreender as particularidades e necessidades desses pacientes.

Método: Foram revisados documentos oficiais, cartas e artigos da imprensa nacional e internacional, além de bases de dados legais e médicas. Contou-se com assessoria legal e médica para este estudo.

Resultados e Discussão: Durante aproximadamente dez anos, um grupo de pais de pacientes apresentou ações legais nacionais e internacionais para fornecer aos seus filhos o único tratamento científicamente validado para esta síndrome. No entanto, tais pedidos foram negados sem justificativa pelas autoridades. Somente após a Comissão Interamericana de Direitos Humanos apresentar seu relatório de admisibilidad do caso; o governo equatoriano começou a administrar o medicamento às crianças com síndrome de Laron.

Implicações da Pesquisa: Aumentar a conscientização pública sobre essa doença rara e as barreiras enfrentadas pelos afetados, promovendo empatia e compreensão das necessidades desses pacientes.

Originalidade/Valor: Identificação de barreiras específicas para acessar o tratamento, enquanto a qualidade de vida dos pacientes e de suas famílias é afetada.

Palavras-chave: Síndrome de Laron, Violações dos Direitos Humanos, Receptor IGF Tipo 1, Crescimento, Doenças Raras, Pessoas com Deficiência.

DESAFÍOS DEL ACCESO A TRATAMIENTOS: EL CASO DEL SÍNDROME DE LARON Y LA LUCHA POR LA INCLUSIÓN SOCIAL

RESUMEN

Objetivo: Identificar y difundir la problemática que enfrentaron los pacientes con síndrome de Laron para obtener acceso al tratamiento con Mecasermina en Ecuador.

Marco Teórico: El síndrome de Laron, es una enfermedad genética rara, que se caracteriza por trastornos metabólicos como hipoglicemia y un severo retraso en el crecimiento. El tratamiento con Mecasermina mejora el crecimiento y por tanto la calidad de vida de los afectados. La cohorte ecuatoriana con síndrome de Laron es la más numerosa del mundo, y ha sido ampliamente estudiada, lo que ha contribuido a entender las particularidades y necesidades que tienen los pacientes.

Método: Se revisaron documentos oficiales, cartas y artículos de prensa nacional e internacional, además de bases de datos legales y médicas. Se contó con asesoramiento legal y médico para este estudio.

Resultados y Discusión: Durante un periodo de aproximadamente diez años un grupo de padres de los pacientes, presentaron acciones legales nacionales e internacionales a fin de proveer del único tratamiento validado científicamente para esta síndrome a sus hijos. No obstante, dichas peticiones fueron denegadas sin justificación alguna por parte de las autoridades. Solo después que la Comisión Interamericana de Derechos Humanos presentara su informe de admisibilidad del caso; el gobierno ecuatoriano inició la administración del medicamento a los niños con síndrome de Laron.

Implicaciones de la investigación: Aumentar la conciencia pública sobre esta enfermedad rara y las barreras que enfrentan quienes la padecen, generando empatía y comprensión de las necesidades de estos pacientes.

Originalidad/Valor: Identificación de las barreras específicas para acceder al tratamiento, mientras se ve afectada la calidad de vida de los pacientes y de sus familias.

Palabras clave: Síndrome de Laron, Violaciones de los derechos humanos, Receptor IGF Tipo 1, crecimiento, enfermedades raras, Personas con Discapacidad.

RGSA adota a Licença de Atribuição CC BY do Creative Commons (https://creativecommons.org/licenses/by/4.0/).
1 INTRODUCTION

Laron syndrome, described by the physician Zvi Laron in 1966 (Laron, 2015; Laron et al., 1966), is characterized by complete insensitivity to growth hormone, manifests with hypoglycemia, significant growth retardation, muscle and skeletal underdevelopment, as well as a particular facial distinction. (Laron, 2008)(Latrech & Polak, 2016) This genetic condition arises when the child inherits a mutated copy of a gene from each of his parents (J Guevara-Aguirre et al., 1993, 2018). Globally, Laron syndrome is classified as a rare disease, with only about 250 cases recorded as of 2009, according to Orphanet (Orphanet, 2009). Although, Dr. Laron (Laron & Werner, 2021), estimates there are about 500 cases. One third of the world’s population is affected by the disease in Ecuador.

In countries where the problem has been identified, most governments have provided treatment with Mecasermin. This drug has been shown to improve height and restore some metabolic parameters (Fintini et al., 2009; Kemp, 2009; Laron, 2008; Laron & Werner, 2021). However, in Ecuador, access to treatment has been a cause of prolonged struggle on the part of the parents of those affected for several years. This delay has resulted in many patients reaching bone maturity, without receiving the treatment they needed, which could have meant a radical improvement in their quality of life.

The objective of this case study is to analyze the challenges faced by patients with Laron syndrome and expose the problems that this group of patients still faces in Ecuador to access timely medical treatment. Through this analysis, the bureaucratic obstacles and unjustified delays encountered, as well as the refusal by the Ecuadorian state to provide access to the required treatment, are exposed.

2 THEORETICAL FRAMEWORK

In Ecuador, Dr. Jaime Guevara has studied in detail the characteristics of the Ecuadorian cohort with Laron syndrome; this study has contributed to understanding the particularities and needs of patients with this syndrome (Guevara-Aguirre et al., 1993, 2018).

Without treatment, patients present with severe short stature, in addition to the bone and muscle complications mentioned above (Laron, 2008). On the other hand, long-term follow-up studies have demonstrated excellent drug tolerance in all published trials, and side effects are rare with proper drug management (Bang et al., 2021; Kemp, 2012; Laron, 2008).
Mecasermin treatment is needed for children and adolescents with Laron syndrome, a condition that can also cause physical disability. In accordance with the provisions of the Ecuadorian Constitution, the rights of this group of patients prevail over those of other people due to their condition of double vulnerability (“Constitution of the Republic of Ecuador,” 2008)

3 METHODOLOGY

Letters and official documents addressed to various authorities were examined, an online search was carried out for both national and international press articles, and the public legal database of the Constitutional Court of Ecuador and the Inter-American Commission on Human Rights (IACHR) was consulted. In addition, the Medline medical database was used to collect and synthesize relevant data. To address the legal aspects, advice was obtained from a lawyer specializing in law, while a pediatrician provided guidance for the search and compilation of the medical literature included in this case study.

4 RESULTS

Patients with Laron, since their first months of age do not register an adequate growth, also present intense and recurrent symptoms of hypoglycemia that lead them to be hospitalized repeatedly.

Dr. Jaime Guevara is recognized for his extensive experience in the study of this condition for several decades in the country. In addition, Dr. Guevara was a pioneer in providing treatment for this disease globally. (Guevara-Aguirre et al., 1995, 1997; Guevara-Aguirre, Guevara, & Guevara, 2018).

Since 2007, a father has gone to different authorities and institutions in Ecuador to request that the Ministry of Public Health (MSP) provide the treatment that children with Laron syndrome needed. Mecasermin, in turn, is a drug that had no national health registry and is known internationally as an orphan drug, that is, it is only used to treat patients with growth hormone receptor deficiency (Laron syndrome) and therefore its sale is restricted. After years of not getting a positive response, a group of parents organized themselves and decided to file a Protection Action against the MSP. The judgment of this Protection Action filed was issued on December 1, 2010 by the Second Court of Criminal Guarantees of Pichincha, noting the acceptance of the protection action. The judgment had the following measures:
“a) That a bipartite commission be formed, composed on the one hand of the shareholders in which Dr. Jaime Guevara, a medical researcher of Laron Syndrome, will be included; and on the other hand, by representatives of the Ministry of Public Health.

b) The shareholders submit the protocol of technical guidelines through the Central University of Ecuador on Laron syndrome to the Ministry of Health within thirty (30) days.

c) The Ministry of Public Health, once it has received the technical guidelines protocol under the auspices of the Central University of Ecuador, shall in turn effectively and expeditiously manage and, within a reasonable period, provide medical support for the treatment of Laron syndrome for the benefit of the Ecuadorian population affected by this disease, before SENESCYT” (SECOND COURT OF CRIMINAL GUARANTEES OF PICHINCHA, 2010, pp. 282–283).

This sentence was agreed by the procedural parties during the hearing, however, it was not complied with by the MSP. As a result, parents were forced to appeal to the Second Criminal Court of Pichincha on three additional occasions: on December 23, 2010, March 15, and May 20, 2011. In addition, on March 4, 2011, they addressed the Ombudsman’s Office to file the corresponding complaint (CONSTITUTIONAL COURT OF ECUADOR, 2020). In the absence of a response from the relevant institutions and authorities, the parents decided to take their complaint to the Inter-American Commission on Human Rights (IACHR), an organ of the Organization of American States (OAS), on July 27, 2011 (IACHR, 2020).

Hearings and conversations continued, while those affected by this disease continued to receive no treatment, despite the fact that national and international media reported the situation (Loaiza Y, 2019; Mella, 2014, 2019; Valerio M, 2011b; Wade, 2011a), in addition, there were publications about patients being immune to cancer and diabetes, which attracted the attention of scientists, doctors and also of several national and international institutions (Bai, 2011; Naik, 2011; Park, 2011; Publimetro, 2011; Saber, 2011; Sturm, 2011; Valerio M, 2011a; Wade, 2011b; Winerman, 2011).

Multiple offices were sent to the highest authorities of the state as the then president of the republic, vice president, national assembly and others. However, none of the requests received a favorable response. The MSP was also sent letters that responded with technical justifications, including: denying the supply of the medication on the grounds of alleged risk, citing only its possible adverse effects, lack of health registration in the country, and supposedly its experimental nature. In addition, the MSP stated that patients do not experience any effect
on their quality of life. Instead, its legal department said it would not respond until the IACHR rules on the case (IACHR, 2020; CONSTITUTIONAL COURT OF ECUADOR, 2017).

Patients faced these conditions until 2014. With the support of the legal department of the non-profit San Francisco University of Quito, the parents of the patients filed an action for noncompliance with the Constitutional Court. It was in 2016 that the court finally convened the hearing and accepted the action for non-compliance (CONSTITUTIONAL COURT OF ECUADOR, 2016).

On December 12, 2016, they issued the ruling that provided for reparation measures, including the immediate purchase of the medicine needed for patients. This judgment corresponds to Judgment No. 074-16-SIS-CC, published in the Official Registry Constitutional Edition No. 12, on October 3, 2017 (CONSTITUTIONAL COURT OF ECUADOR, 2017). In this regard, the Constitutional Court recognized that the right to health of pediatric patients with Laron must be understood in a broad and comprehensive sense, so that it includes not only timely access of patients to medical services, but also the provision of Mecasermin, the dispensing of which was denied without any justification.

The constitutional court's subsequent ruling referred to:

a. That the representative of the Ministry of Public Health, in coordination with the representative of the Agency of Regulation, Control and Health Surveillance will analyze the protocol referred to in the protection action, adapt it and approve it within 30 days. It was determined that compliance with this measure should be notified to the Constitutional Court “within 5 days, from the approval of the aforementioned protocol”

b. “That the representative of the Ministry of Public Health, in coordination with the Health Regulation, Control and Surveillance Agency to initiate immediately the corresponding procedures for INCRELEX (commercial name of Mecasermina) to obtain the respective sanitary registry”, within the maximum term of 60 days. Once the procedure began, it was ordered that the Ministry of Public Health “proceed with the supply of this to the children have the informed consent of their legal representatives; and that, after certification by the Ministry of Public Health, prove the suffering of Laron syndrome”

c. “That the representative of the Ministry of Finance allocates the corresponding financial resources to the Ministry of Public Health, for the purpose of the continuous acquisition of the drug INCRELEX. It was pointed out that compliance with this measure should be reported quarterly to the Constitutional Court.”
d. “That the Ministry of Health Within 60 days, develop and implement a nationwide training program on Laron syndrome for children and adolescents affected by Laron syndrome and their close family members. It was pointed out that compliance with this measure should be reported quarterly to the Constitutional Court.”
(e) As a rehabilitation measure, the representative of the Ministry of Public Health formulates and implements a program of psychological care, at the national level, for girls, boys and adolescents affected by Laron syndrome and their close relatives. Compliance with this measure must be reported to this body quarterly (CONSTITUTIONAL COURT OF ECUADOR, 2017, p. 53).

Almost 10 years after the first ruling only after the IACHR issued REPORT No.75/29 PETITION 1011-11 ADMISSION REPORT:

1. Declare the present petition admissible with respect to Articles 4, 5, 8, 19, 24, 25 and 26 of the American Convention on Human Rights and Article XI of the American Declaration;
2. To declare this petition inadmissible in relation to Article VI of the American Declaration.
3. Notify the parties of this decision; continue with the analysis of the merits of the matter; and publish this decision and include it in its Annual Report to the General Assembly of the Organization of American States (IACHR, 2020, p. 7).

Only after issuing this report did the MSP finally begin to acquire and administer Mecasermin in October 2020.

At a working meeting between representatives of the Ministry of Public Health, the Constitutional Court, Dr. Jaime Guevara and parents of patients, it was revealed that the Ministry had developed a treatment protocol that unjustifiably excluded patients over the age of 12. Dr. Guevara stressed that chronological age should not be a restrictive criterion, since patients with Laron syndrome may have a delay in bone age, which implies that, although they are over 12 years old, they can still benefit from treatment if they have active growth cartilage (CONSTITUTIONAL COURT OF ECUADOR, 2020).

Due to the delay in the process for the provision of Mecasermin by the MSP, a considerable number of patients who claimed the medicine reached bone maturity without receiving the treatment they needed. On the other hand, patients who are being treated have been shown to have favorable results.
4.1 WITH REGARD TO MECASERMIN

The drug Mecasermin was approved for use by the Food and Drug Administration (FDA) in 2005 (FDA, 2005) and by the European Medicines Agency (EMEA) in 2007 (EMEA, 2007), these institutions control medicines and medical supplies for use in humans. This is the only treatment that currently exists and that has the capacity to increase the growth of a patient with Laron syndrome.

Scientific studies have shown the safety and efficacy of Mecasermin. However, it needs to be prescribed and monitored by highly qualified doctors to prevent possible adverse effects and ensure the greatest benefits in patients. In order to meet this objective, and as established in the previous judicial judgment of 2010, it was requested that Dr. Jaime Guevara, a renowned expert in this pathology, be in charge of the administration of the medication or share his knowledge about its correct use.

On the other hand, thanks to the communication with IPSEN (the company that produces the drug) (Fabre, 2012) and aware that some patients were close to bone maturity, the following offer was presented:

- A special price for each package of "INCRELEX".
- FREE treatment for a limited number of patients.
- Support and training for doctors who supply the medicine.

5 ANALYSIS AND DISCUSSION

The results of this case study demonstrate that Laron syndrome, despite being a disease considered rare, has a high prevalence in Ecuador and has been the subject of several clinical studies, scientific, social publications and even legal litigation in order to recognize the right of patients to access timely and adequate treatment (IACHR, 2020; CONSTITUTIONAL COURT OF ECUADOR, 2020; López Núñez, 2020). In the Constitution and the legal system of Ecuador, several constitutional guarantees are written to seek the rights. In the case of Laron's patients, the action for protection and the action for non-compliance were ineffective, since the sentences were not executed in full and immediately (López Núñez, 2020). Against this background, the IACHR issued its report on the admissibility of the case (IACHR, 2020).

If pharmacological treatment had been initiated in a timely manner, favorable results could have been obtained, especially in those patients who reached bone maturity while waiting for the start of treatment. Previous studies on this syndrome suggest that the earlier the therapeutic
intervention, the greater the chances of achieving adequate growth and development rates. In addition, it is a safe and effective medicine that allows patients to grow to a height that facilitates their independence for daily activities (Bang et al., 2021; Yakar et al., 2018).

6 CONCLUSION

Early detection of rare diseases needs to be improved through continuous and appropriate training for health teams and decision-makers. Countries should ensure universal access to scientifically validated medicines, including those targeted at treatments for rare diseases such as Laron syndrome, and the prevention of noncommunicable diseases. Proper and timely treatment of patients can prevent the disease from causing irreversible damage to their bodies.

The research carried out by Dr. Jaime Guevara on this pathology is relevant at an international level. However, their extensive clinical experience and contributions to understanding this syndrome are not exploited locally.

This study seeks to raise awareness among the population and especially among public servants who make decisions, to promote values of respect, equity and justice towards the most vulnerable groups.

REFERENCES


CORTE CONSTITUCIONAL DEL ECUADOR. (2016). Sentencia No. 074-16-SIS-CC Caso No.0010-14-IS.
Challenges of Access to Treatments: The Case Of Laron Syndrome and the Fight For Social Inclusion

CORTE CONSTITUCIONAL DEL ECUADOR. (2020). Auto No. 10-14-IS/20 Caso No. 10-14-IS.


Challenges of Access to Treatments: The Case Of Laron Syndrome and the Fight For Social Inclusion


