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Opinion

Clinical trials in Honduras: ethical considerations

Ensayos clínicos en Honduras: consideraciones éticas

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Clinical trials represent the penultimate step in the hierarchy of scientific evidence and are crucial in developing new therapies. Therefore, rigorous design and ethical considerations must be implicit in all scientific inquiry's construction and review process. During scientific research, the ethical component is crucial and must be prioritised over any other interest. When designing a study and in its subsequent evaluation, the ethics committee must independently assess the ethical justification of the study. In other words, the result of the ethical review must be framed using human rights standards, must be independent and complete, regardless of the country where the study is carried out.

Low-middle income countries (LMIC) represent a challenging scientific environment for developing and executing clinical trials, for which their implementation must be strictly monitored. The barriers include lack of funding and trained human resources, lack of a scientific research environment, operational barriers, and obstacles in the regulatory and ethical systems (Alemayehu et al., 2018). The absence of robust ethical systems has led some researchers in high-income countries (HIC) to develop clinical trials in LMIC, which has deep regulatory and ethical implications.

Scientific research and ethics

Throughout history, scientific research on humans has borne great accomplishments for the benefit of humanity. For example, vaccinology first arose in the late 18th century when most of the world population was afflicted with smallpox, except for those who tended cattle. These observations culminated in Edward Jenner inoculating an 8-year-old boy with cowpox, rendering him immune to smallpox. This represented an advance against viral diseases; however, Edward Jenner's approach would not be allowed in current times due to possible ethical and legal implications.

On the other hand, there are also studies with negative outcomes. This is due to the interest in acquiring scientific knowledge divorced from ethical principles or rooted in racist doctrines and knowledge acquired in the pursuit of economic profit. In 1946, 23 German doctors were charged with war crimes for scientific experimentation on concentration camp victims. Consequently, the Nuremberg Code was created, which stipulates that the voluntary consent of the human subject is absolutely necessary in any scientific study. Subsequently, the World Medical Association (WMA) published the Declaration of Helsinki stipulating that significant *in vitro* and *in vivo* findings must precede human research. In addition, an independent committee must review research protocols, informed consent of the participants must be safeguarded, and the benefit of the research must be greater than the risk of the research.

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Table 1
The Belmont Report is a guide about the various ethical issues that may be encountered during scientific research.

Principle	Application
Respect for people	**Informed consent**
-Individuals should be treated as autonomous agents. -People with reduced autonomy must be protected.	-To the degree of their capacity, the individuals should be given the opportunity to understand what is going to happen or not happen to them -Consent must have three elements: *Information *Understanding *Being volunteer
Beneficence	**Risk and benefit evaluation**
-Humans must not be harmed. -Research should maximise benefits and minimise harms.	-The nature and the scope of the risk and benefit must be evaluated systematically.
Justice	**Subject selection**
-The benefits and risks of research must be fairly distributed.	-There must be fair procedures and outcomes in selecting research individuals.

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1979).

The relevance of ethical considerations in any study lies in protecting the individuals under study, since the participants may be part of vulnerable populations (e.g., low-income, with physical or mental disabilities, children, incarcerated people, among others). Between 1932-1972 (Tuskegee, Alabama, United States), four hundred low-income African Americans, who were purposely infected with syphilis, were monitored to evaluate the natural course of the disease, without being offered any penicillin treatment. Likewise, in 1942 (Guatemala), the government of the United States of America (USA) conducted studies on 696 marginalised people by inoculating a quarter of them with syphilis without their knowledge. These experiments, together with those carried out by the Nazis and the Willowbrook Hepatitis Study (New York, USA), resulted in the creation of the Belmont Report (Table 1), which serves to help guide different ethical questions of the scientific process (Mandal et al., 2011).

Human rights standards and scientific research

Human rights standards and principles were created to safeguard people's dignity. These principles are closely related to ethical considerations when carrying out scientific research since both seek to protect all people involved, especially those who may be considered vulnerable. It is important to remember that states have the responsibility and obligation to safeguard the rights of people, making sure that neither the state nor third parties (i.e., individuals, companies, etc.) violate them.

The International Covenant on Economic, Social and Cultural Rights (ICESCR) of 1966 is a binding international human rights instrument that establishes that the States Parties recognise the right of everyone to "enjoy the benefits of scientific progress and its applications." This entails respect for ethical principles in scientific research. In its General Comment No. 25 (Alto Comisionado de las Naciones Unidas para los Derechos Humanos [ACNUDH], 2022), the five interrelated principles regarding the advancement of science were established (availability, accessibility, quality, acceptability, and protection of academic freedom). Additionally, it was noted that scientific research must "incorporate ethical standards to ensure its integrity and respect for human dignity, such as the standards proposed in the Universal Declaration on Bioethics and Human Rights" (ACNUDH, 2022). Therefore, although enjoying the benefits of a clinical trial is a right, this scientific progress cannot override the other rights that violate or could violate the dignity of people.

Honduras, scientific research, and ethics

In Honduras, clinical trials have been carried out that have contributed to scientific development during difficult times. During the COVID-19 pandemic, Honduras participated in a study aimed at identifying existing drugs that could be used to manage patients afflicted with COVID-19. The conclusion was that these drugs had little or no effect on patients hospitalised for COVID-19 (WHO Solidarity Trial Consortium, 2021).

Despite this, some of these drugs (e.g.,

hydroxychloroquine) were integrated into national protocols and continue to be used in managing COVID-19 patients in Honduras. Likewise, preliminary studies that motivated health personnel to prescribe treatments, such as ivermectin, have been retracted in the absence of significant evidence that its administration benefits patients with COVID-19. More than two years after the pandemic, no clinical or toxicological studies, among others, have been conducted to assess the impact on both tissues and organs caused by the intake of repurposed and new drugs.

Currently, there are 64 clinical trials of drugs or other interventions registered in Honduras, according to the US National Library. Additionally, other identified trials have not been registered. Some of these trials study treatments for diseases such as Human Immunodeficiency Virus (HIV). It is unknown if there is monitoring by Honduran regulatory institutions such as the Sanitary Regulatory Agency (ARSA), which is the state entity that regulates and controls clinical trials in humans and biological samples.

Given that the main objective of developing therapies focused on implementing clinical trials is to ensure the safety and protection of the subjects participating in the study, scientific rigor and research ethics must prevail throughout this process. The United States Food and Drug Administration (FDA) as a regulatory agency requires compliance with numerous regulations to maintain high ethical values in clinical trials, good clinical practices and, above all, protection of the individuals participating in them.

Honduras has socioeconomic characteristics that limit scientific development at all levels. One of them is the percentage of investment in research and development of the Gross Domestic Product (GDP), scientific production per million inhabitants, and the limited number of ethics committees (9) registered in the Portal of the Network of Ethics and Research Committees of Honduras with irregular coverage, directly influencing quality scientific production and evaluation times of research protocols. Undoubtedly, these conditions represent a challenge for researchers, ethics committees and regulatory agencies so that the development of clinical trials adheres to all ethical standards.

Conclusions

Ethical evaluation processes implicit in research are a fundamental part of the scientific development of any country. These offer safe environments for the subjects and facilitate the implementation of solutions that result from them, offering benefits to humanity. In Honduras, the limited scientific production affects most of the population when it is difficult to discern between misinformation, the need, and the hope of obtaining treatment for a certain disease and what science shows us with evidence.

It is essential to ensure that the scientific production carried out in Honduras is accompanied by regulations and rigorous ethical principles that respect the human rights of each person involved without taking advantage of their vulnerability conditions. To this end, it is imperative to create and promote independent ethics committees, invest in research, professionalisation, and training of researchers, and promote the regulation and constant monitoring of state and academic organisations.

Author Contributions

JS conceptualised the idea of the article. All authors carried out the literature review and wrote the manuscript, as well as read and approved the latest version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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