

Review about the Pre-embryo Concept: Diverse views and their Foundations

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Abstract:

Introduction and Purpose: Reproductive medicine has experienced exponential advances. However, these advances are not exempt from ethical responsibility. Thus arises the term "pre-embryo", which refers to the first 14 days of the embryonic process from fertilization, due to its variable meaning it is important to review the concept in greater detail. The following work pretends to analyze the concept of pre-embryo from a scientific, legal, ethical and religious point of view, and its different foundations.

Material and Method: Bibliographic review of quantitative and qualitative studies, special articles, communications, gray literature or any other document that had a maximum age of 10 years (2008 - 2018), with free access to the full article, in Spanish and that was relevant to the topic. It was carried out during May 2018, using MESH and DeCS keywords, plus extra words, since pre-embryo is not a descriptor.

Results: A total of 5 papers were reviewed from which 4 views were extracted; scientific; that sets arbitrary limits to define the pre-embryo and not be judged morally, legally; that grants rights to the pre-embryo, but ponderable for research, ethics; reaffirms that the concept is a linguistic trick so as not to judge the investigation and not to inquire into the utilitarian sense of the embryo, and the religious one; that defends human life from conception, attributing the quality of person, and therefore, considering the pre-embryo as a subject of rights.

Conclusions: The concept of pre-embryo is conflicting, since it confronts the usefulness of the use of the pre-embryo for research in reproductive medicine with the amoral of experimenting in humans, if the pre-embryo is considered a human being. Thus, the legal vision is the most pragmatic because it considers the concept, despite the arbitrary, and weighs its rights for research, since it would be the role of bioethics to guarantee that the use is for the correct purposes, while defining the true meaning of pre-embryo.

Keywords: Embryonic development; Bioethics; Bioethical Issues; Humans.

I. INTRODUCTION

Starting in the second half of the 20th century, the scientific and technological development of medicine has experienced exponential advances, such as assisted reproductive techniques or the implementation of intensive care units, improving the conditions of the human being today. However, these advances are not exempt from ethical responsibility in relation to scientific actions carried out on human life, other living beings and the environment. In this way, the incorporation of Bioethics as a discipline that helps in the discernment of the ethics of said actions is necessary. [1]

One of the scientific advances that has caused the most a stir in terms of bioethical aspects is that of reproductive medicine, raising the question: When does life begin? Or rather, When is it being human? It is necessary to answer these questions to determine the limits in which scientific action does not involve an ethical conflict, so that the values and moral norms that govern society are respected. [1]

In this way, the term "pre-embryo" arises, which is a concept recently coined to designate the first 14 days of the embryonic process after fertilization. It began to be used in the context of the bioethical debate around reproductive medicine, mainly in relation to the destruction of embryos in the in vitro fertilization process. [1]

Etymologically, the term pre-embryo derives from the word "embryo" from the Greek <Τὸ ἐμβρυο>, which is formed by the Greek words "in" (in the middle) and "bryo" (to be born, shoot, flourish), which is freely translated, refers to the unborn fetus, that is, the embryo is something that is about to bloom. By adding the prefix "pre" (which precedes a), a simple deduction leads to the conclusion that the etymological concept of pre-embryo refers to that which precedes what sprouts or flowers. [2]

It was used as such for the first time by the scientist Clifford Grobstein in 1979, however the concept of 14 days was previously proposed by the American

bioethics committee Ethics Advisory Board (EAB) in the context of addressing the ethical aspects of fertilization in vitro, and the possibility of investigating with embryos to improve the techniques used, thus suggesting that the human embryo in its early days is only an incipient form of human life and not an individual itself, its use in experimentation being considered ethically acceptable. [1]

Later, in Great Britain in 1984, the concept is used in the Warnock report, in the context of the study of a possible legal regulation of in vitro fertilization, accepting again the experimentation with embryos during the 14 days following fertilization. In this way, in 1985, the Medical Research Council (MRC) created the Voluntary Licensing Authority (VLA) to supervise research with embryos until the law in this regard is approved. The term pre-embryo was widely used by the body and began to be disseminated by scientists in favor of experimentation with embryos, insisting on the quality of "non-human individual", but rather a mass of undifferentiated cells from which a human individual could develop and alluding to the advantages against infertility and diseases of genetic origin that such investigations could have. [2]

At the same time, in the United States, the American Fertility Society (AFS) organized an ethical committee that in 1986 published a report that concluded the same as its European counterpart. However, despite the favorable evidence for embryo research proposed by the Committee, the US government was prolonging the discussion on the matter. [2]

In 1993, the United States Government signed the NIH Revitalization Act, constituting the Human Embryo Research Panel (HERP) commission, dependent on the NIH (National Institutes of Health), which in September 1994, despite maintaining the 14-day criterion for being able to experiment with human embryos, it does not accept the term "pre-embryo" for the early human embryo. This due to the confusion it caused. [1]

From that moment on, the use of the term "pre-embryo" began to decline, using the term "zygote" for the organism that develops during the first week after fertilization, and is called "embryo" from the second week to the eighth. [1]

In 2001, an ethical report from the European Society for Human Reproduction and Embryology (ESHRE) discarded it as it considered it as an attempt to lower the symbolic value of the embryo, recognizing the concept as a way to make research with human embryos something more acceptable to the public, justifying their destruction and use without requiring unconditional respect for them. [1]

Due to the above, it is necessary to know the different visions that revolve around the concept of pre-embryo in order to weigh scientific research in the early stages of the embryo.

II. PURPOSE

The purpose of the following work is to analyze the different points of view around the concept of pre-embryo, which, despite its brief history, has not been exempt from controversy and bioethical questions. His conception brought to the fore deep questions about the beginning of life as a proper human being, and the respect that these initial forms of human life deserve. Although currently its use has been in decline, the ethical conflicts around the research remain, so the analysis from different angles will allow to address this debate in a more comprehensive way.

III. MATERIAL AND METHODS

A bibliographic review was carried out, for which works were searched in the following databases: PUBMED / MEDLINE, CINHAIL, SCOPUS, POPLINE, British Library Catalog, CENTRAL, WHO Global Health Library, Google Scholar and Scielo, with the following keywords MESH and DeCS (Table I): Embryonic development, Embryonic Developments, Embryogenesis, Embryo developo, Embryo Development, Embryogenesis, Embryo Development, Bioethical issues, Bioethical issue, Bioethics, Humans, Human, Modern Man, Ser Humano, Seres Humans , Human, Humans and Man. Considering that the word pre-embryo is not MESH or DeCS, a separate search was carried out in the Google Scholar database, with the following keywords: Preembryo, Pre-embryo and Bioethics. Finally, useful gray literature was added according to the research group.

The inclusion criteria were: All work published in a journal with an editorial committee available on the internet, including quantitative, qualitative studies, special articles, communications or any other document, which were maximum 10 years old (2008 - 2018), with free access to the article complete, in Spanish and relevant to the topic. The exclusion criteria were: All that work that the use of the concept of pre-embryo was to explain diagnostic processes of any type, infertility treatments and genetic studies of pregnancy. No measurements or meta-analyzes were

Used combinations of MESH and DeCS words:
(Embryonic development OR, Embryonic Developments OR, Embryogenesis OR, Embryo developo OR, Embryonic development OR, Embryogenesis OR, Embryonic development) AND (Bioethical issues OR, Bioethical issue OR, Bioethics) AND (Humans OR, Human OR, Modern Man OR , Human OR, Human OR Human, Human OR, Human OR Man).
Non-MESH or DeCS word combinations used:
(Pre-embryo OR, Pre-embryo) AND (Bioethics)

performed. All searches were carried out during the month of May 2018.

TABLE I. COMBINATIONS OF WORDS USED IN THE SEARCH.

The selection of studies was carried out complying with the limits set out above, marking a process of 2

stages: The first consisted of the search by the research group of the abstracts of the works, then the research group deliberated on the relevance of the works topic for inclusion in this review. The information was extracted by means of the research group electronically using the structured form previously raised.

In total, a total of 17 papers were found with the keywords MESH and DeCS, of which only 5 were in Spanish and were freely accessible, but 4 met the exclusion criteria and were therefore not used in the review. On the other hand, with the keywords not MESH or DeCS, 4 were analyzed that met the criteria, were in Spanish and were freely accessible. Finally, a total of 5 works were analyzed. The entire selection process during the corresponding phases is detailed in Fig. 1.

The presentation of the results consisted of organizing the information in each of the views found with their respective foundations, making a summary table of each one of them.

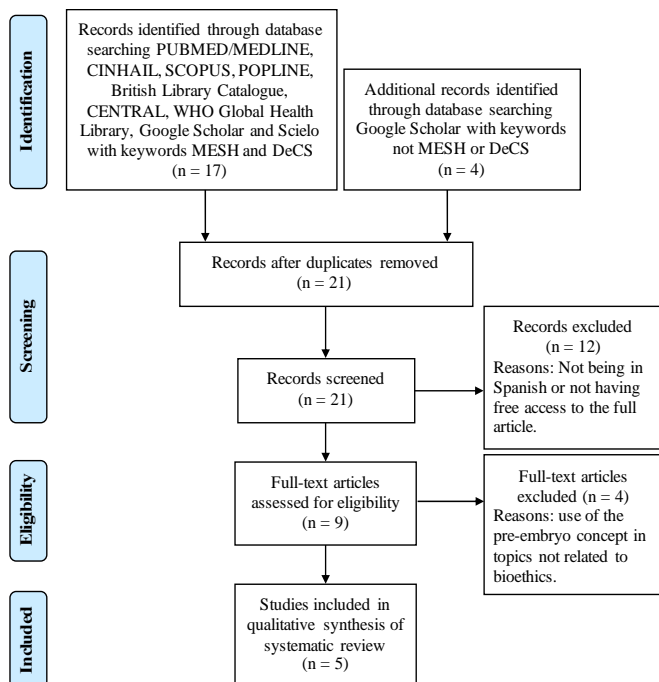


Fig. 1. Flow diagram of the different phases of the study selection process, according to the PRISMA guidelines.

IV. RESULTS

A total of 5 works were analyzed, of which; two correspond to special articles, one is a law, one is an encyclical letter, and finally a thesis report. Below are the most important findings.

A. Scientific Vision of Pre-embryo:

In the thesis report written by García Varela D. It was commented that there was an embryologist specializing in amphibians, named Grobstein, who was deeply involved in the ethical debate of reproductive medicine in the 70's and 80's. He determined that the pre-embryo is not an individual prior to implantation because there is the possibility of twinning, then, it only becomes an individual after 14 days from fertilization where the formation of the primitive line occurs, that is,

an outline of what will be the neural tube; the loss of totipotency and the creation of the relationship of nutritional and organic dependence of the pre-embryo. [2]

In addition, it indicated that it was not possible to occupy the term embryo before 14 days due to the lack of individuality, organization of the embryo, need for implantation, lack of rationality, and lack of power to become a human being and a person. On the other hand, it would be the "external signals" that would indicate the difference between an embryo and a pre-embryo, these signals being those that are recognized as human by other people. Therefore, the pre-embryo has a right to a special status, different from that given to the embryo and fetus. [2]

Thus, the British Research Committee on Human Fertilization and Embryology, in 1984, limited embryonic research after fertilization to fourteen days, accepting the term pre-embryo used by Grobstein. Despite this, the same Committee admitted that embryonic life would begin with fertilization, recognizing that once the ovum has been fertilized and the development process has begun, no particular stage of the development process is more important than another. Thus, research involving the destruction of pre-embryos was authorized, based on the fact that it must be taken into account that progress in the treatment of infertility would not have been possible without the research; and that the appearance of the primitive line is the sign of the beginning of the individual development of the embryo. [2]

B. Legal Vision of Pre-embryo:

In the thesis of García Varela D. It is proposed that the human body when starting with fertilization, the zygote would end in the development of an adult individual, therefore the pre-embryo would be a human being. On the other hand, the appreciation of whether or not there is a human person does not correspond to biology, but to the law because the concept of person is a legal and philosophical concept. Thus defining what is socially acceptable and clarifying what is prohibited and permitted. [2]

On the other hand in the original article of Campos Herrera P, it was suggested that the human being would be the same individual from conception to death, and there would be no biological characteristic that would make an essential difference. Therefore, since fertilization, the zygote is a living being that qualifies it as an individual member of the human race. [3]

So, it is not possible to deny the human nature of the pre-embryo as posited García Varela D. Therefore, it is essential that the law must be related to the protection of the human species and to consider whether the use of pre-embryos for research represents an unlawful instrumentalization of human beings for the benefit of third parties, considering that it is a form of human life that they could give rise to the birth of a human being. Although, it is a human life with increasing gradual protection, from fertilization to birth, at which point it is possible to speak of a proper person

and, therefore, of ownership of rights, this gradualness being what allows us to weigh the research. [2]

However, several legal systems did not agree to give the embryo the same status as a person with rights and obligations, for example: In Austria, embryos are defined as "inseminated eggs and cells developed from them", in Germany defines embryo as "the fertilized human ovum cell capable of developing, from the moment of the fusion of the pronuclei", in Spain the pre-embryo is distinguished from the term embryo and from the fetus, in the United Kingdom the living embryo is defined as "one where fertilization is complete, including an egg in the fertilization process", finally in Chile an embryo is defined as: the zygote in a pronucleus state from the moment of fertilization; the concept of pre-embryo is not considered. Furthermore, within the framework of Law 20.120, It is prohibited to destroy embryos for no other purpose than research or diagnosis. [2] [4]

C. Ethical Vision of Pre-embryo:

In his book "The fictitious embryo: history of a biological myth", Herranz G, criticizes the absence of biological basis and scientific seriousness that support the concept of pre-embryo. According to its author, biologists and embryologists provided philosophers and jurists with a series of apparently scientific "arguments" but convincing enough not to be questioned or critically reviewed. [5]

Herranz questions the process of biological and ethical devaluation that was given to the fertilization process by organisms such as the American College of Obstetricians and Gynecologists, where the conception process is redefined, going from being a synonym of fertilization, to signifying the implantation of the embryo in the mother. Conception, in its new sense, signified and marked the beginning of pregnancy, just 14 days after fertilization, so the first 14 days post-fertilization become pre-gestational, which implies the idea that interrupting pregnancy, (say abortion), in those two weeks it becomes impossible, since gestation has not started, and the loss of embryos less than two weeks old is no longer considered abortion with this redefinition. Herranz also criticizes the fact that fertilization is reduced to one more link, and not the most important, in the continuum of life. [5]

It also questions the scientific veracity of the disproportion of cell populations, where the extra-embryonic is massive and the embryonic itself is almost non-existent; This is due to statistics, without any apparent support in cell counts in human embryos, given by the embryologist Anne McLaren, who in 1987, would have invented the fact that at the beginning of gastrulation, the human embryo represents less than 1 percent of the tissue derived from the fertilized egg, and that the remaining 99 percent goes to the formation of the placenta and other structures of nutrition and support. As almost everything that is seen of the conceived is practically extra-embryonic tissue (placental tissue, amnion, yolk sac, extra-embryonic coelom), that is, a set of materials, which undergo involution in the following weeks, or that they are discarded "as secondary" at the time of delivery; the

pre-embryo would only be a barely visible outline of the embryo, so it would have a more disposable character. [5]

Thus, the author also refutes the ontological inconsistency in the monozygotic twinning process, that of tetragametic chimeras, that is, when two embryos merge into one, as well as that of totipotentiality, which proclaims that all the cells of a young embryo they are capable, each one of them of developing a complete embryo, and, finally, of the massive spontaneous loss of embryos, which appreciably lowers the value of such outdated entities. [5]

At the same time, Campos Herrera P comments in her article that from a personalistic approach in which the dignity of the human being is based on being a person, for which there is a demand for respect from the moment of conception until natural death, therefore denying equal rights to all humans, such as the unborn, is equivalent to denying the equality of being a person, since embryonic life already presents a human condition, since it is a human being with potential of develop all the characters that define a person in maturity. [3]

For its part, in the thesis of García Varela D. suggested that the concept of pre-embryo is a cosmetic trick, that not a single word is said in favor of the term pre-embryo or about the legitimacy of its use in Biology, and that it only eliminates problems; yet ethics focus on the reasons for destroying a pre-embryo, and the risk of abuse for non-medical reasons. [2]

D. Religious Vision of Pre-embryo:

The debate on the use of human embryos for experimentation also involves religion, understood as a set of beliefs and norms of behavior adopted by a human group, with which a relationship with the divinity is recognized and that has great value in today's society, exercising moral authority over human actions and influencing political and legal decisions that society adopts. [2] [6]

Religious views on the acceptability of human embryo research are related to the personhood attributed to the blastocyst. Moral philosophy makes distinctions between what is human life, non-human life, and human persons. Human persons enjoy a maximum moral status, owing them the utmost respect, while human life, despite demanding respect, is not comparable to personality and the rights linked to the concept of person. These distinctions generate differences in the point of view of the different religions. Some consider the human embryo as a person and therefore a subject of rights, such as Catholicism, while others attribute the endowment of the soul to the "personalization" of the embryo, a process that, in their view, it would occur weeks or months after conception, like Islam and Judaism. [2]

Catholicism, the predominant and most influential religion in Chilean society, is emphatic in affirming that human life begins from conception, attributing to the

embryo the same moral status as a person and considering illegal and immoral all kinds of acts that threaten existence of the same. In relation to this, it has issued a series of documents, highlighting the *Donum Vitae* in 1987, which affirms that the pre-embryo has “the right to the same respect that is granted to a child already born and every human person”, and more recently the encyclical *Laudato si'*

published in 2015 by Pope Francis, which rejects all kinds of justification for experimentation with human embryos, alluding to the fact that the inalienable value of the human being is beyond the degree of its development. [2] [7]

Next, in the following Summary Table (Table II) the most relevant of each vision was highlighted.

TABLE II. SUMMARY OF PRE-EMBRYO VISIONS AND THEIR FOUNDATIONS

Summary of Preembryo's visions	
Vision	Basis
Scientific Vision	The scientific vision focuses on setting a limit based on biological characteristics to morally approve the use of pre-embryos in scientific research. It also adopts the term pre-embryo to differentiate it from the concept of embryo, then it would not be taking care of a person.
Legal Vision	The legal vision focuses on accepting that the pre-embryo is actually a human being for which it deserves protection by the law, but does not deserve the same rights as an adult person, so it is right is contrasted with the utilitarian sense of the science.
Ethical Vision	The ethical vision focuses on criticizing that the foundations for defining the concept of pre-embryo were considered to reach a consensus rather than to really investigate whether it is ethically appropriate to occupy the pre-embryo for the purposes proposed by science.
Religious Vision	In particular, the Catholic religion defends human life from conception, attributing the quality of person and therefore, it would consider the pre-embryo as a subject of rights.

V. CONCLUSIONS

After the review carried out, it could be concluded that there is no clear consensus on what a pre-embryo means, since, from a scientific perspective, it could be considered that Grobstein's probable intention was to reduce the moral status of the pre-embryo in order to justify social and legally the experimentation processes that were carried out in the pre-embryo, which could be considered lack of seriousness due to the arbitrary nature of the 14-day decision. Although, the great advances that have been made in reproductive medicine should not be overlooked, giving opportunities to couples that previously had no solution. [2]

On the other hand, the legal view, apparently is the most practical, that despite granting rights to the pre-embryo, considers that the rights of the pre-embryo are weighty, that is, they can be judged to favor some scientific research, establishing that the rights that presents a pre-embryo, they are not the same as those of an adult. However, it accepts the use of the concept of pre-embryo with the arbitrary limits established by science, only that it indicates the legal limits to regulate the activities carried out with pre-embryos such as research. [2]

Due to the above, the ethical position regarding the concept of pre-embryo seems to make sense when

stating that it is an invented concept to allow scientific interventions without being judged. In addition, it considers that the discussion regarding the concept of pre-embryo and the real impact it could have, such as the risk of using the pre-embryo for non-medical reasons. Therefore, as established by ethics, the concept of the pre-embryo becomes a semantic trick, that is, a euphemism, to justify research or other activities. [5]

On the other hand is the religious vision; In this work, the Christian vision from the Catholic Church was highlighted, which supports the idea that from conception, the generated product is a human being, and deserves the rights of any person. This vision agrees, in part, with the judicial vision, however, the religious vision applies the same rights, while the judicial one weighs them. [2] [6]

Therefore, we can conclude that the approach to the concept of pre-embryo involves multiple edges, which are in constant clash throughout the brief history of the concept. Given the accelerated scientific advance and medical, political or social interests around the origin of life as a proper human being, comprehensive look is necessary, developing ethical assessments that allow a balance between what is correct within the norms by which society is governed and at the same time allowing the development of new technologies for the benefit of humanity. [1]

In that sense, the legal vision is the most pragmatic because it considers the concept of pre-embryo, despite the arbitrary definition of the concept, and weighing the rights, for the investigation. In this context, it would be the role of bioethics to ensure that the use is for the correct purposes, while defining the true meaning of pre-embryo.

Finally, it must be considered that in the review made only those works in Spanish and free access were included, excluding those in English and paid, so that part of the information was not considered. Furthermore, the fact that the word pre-embryo is not considered a descriptor for the database search makes it difficult to access works on the subject, relegating the search task to the research group according to the methods they deem necessary, which could lead to biases.

REFERENCES

- [1] Ferrer Colomer M. The preembryo's short lifetime. The history of a word. Cuad Bioét [Internet]. 2012; 3. Available in: <http://aebioetica.org/revistas/2012/23/79/677.pdf>
- [2] García Varela D. Constitutional aspects of bioethics: legal status of the pre-embryo [Internet]. Madrid; 2017. Available in: <http://eprints.ucm.es/43330/1/T38916.pdf>
- [3] Campos Herrera P. The protection of the human embryo in Chilean legislation, based on a personalist perspective. [Internet] JW Nursing; Available in: http://www.enfermeriajw.cl/pdf/embri%F3n_Chile.pdf
- [4] Test regulation of law No. 20.120, on scientific research on human beings, their genome and prohibits human cloning. Ministry of Health; Undersecretariat of Public Health; 2011.
- [5] Ferrer Colomer, M .; Pastor García, LM. Genesis and use of the term "Pre-embryo" in current scientific literature. Person and Bioethics [Internet] 2009; 2. Available in: <http://personaybioetica.unisabana.edu.co/index.php/personaybioetica/article/view/600/1335>.
- [6] Religion [Internet]. Dle.rae.es. 2018. Available in: <http://dle.rae.es/?id=VqE5xte>
- [7] Pope Francisco, Encyclical letter, Laudato si' Laudato Si' of the Holy Father Francis on care for our common home [Internet]. 2015. Available in: <http://www.vidanuevadigital.com/wp-content/uploads/2015/06/Laudato-Si-ES.pdf>