Bioethical dilemmas in using animal in medical research. Challenges and opportunities

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Abstract
Purpose: The study aims to present the main ethical dilemmas that research on animals raised for anyone involved in this process, starting from the idea that there are rights of animals to be known and respected.
Background: The evolution of medicine is inextricably linked to the production of new drugs, the occurrence of surgical techniques; none of these can be possible without the study of experimental animals, in vivo experimentation being part of the process of medical research.
Content: The article analyzes the main ethical dilemmas related to the use of animals in medical research, in the current legislative context and historical perspective of achieving such studies.
Discussion and Conclusions: The use of animals in medical research must be conducted in accordance with clearly established moral rules, which facilitate reducing to the maximum the negative effects on the animals, avoiding unnecessary suffering to them and especially to facilitate progress achievement with the minimum possible animals sacrificed.

Keywords: bioethics, medical research, ethical norms, animals.

Introduction

The outstanding contribution of animal experimentation, which led to the progress of medicine, has evolved within both the scientific and the didactic field. It is well known that the most significant discoveries in medical history were obtained from experiments on animals. However, it is considered that the benefits accruing to science researcher do not absolve responsibility [1], especially since „more than 115 million animals are used each year in experiments or to supply the biomedical industry” [2].

Historical facts

The people’s attitude towards animals has been brought up for the first time in the Greek philosophers’ writings [3]. The use of animals for experiments was first mentioned around 500 BC. Throughout history, anatomists have compared and noticed the similarities between human anatomy and various animals.

Aristotle (384–322 BC) and Erasistratus (304–258 BC) studied living animals, relying also on scientific observation; the first dilemma was due to Aristotle and his theory that animals have souls [4].

Alcmeone of Crotona (500 AC), Hippocrates (460–370 BC) or Herophilus of Chalcedon (335–280 BC) are some of those who founded the observation of structure and function of organs from living animals.

Nevertheless, the who that is regarded as the most complex personality of this view was Galen (Claudius Galen of Pergamon, 130–200 BC), known as the father of experimental medicine, due to the vivisections performed [5].

The Middle Ages will be marked by giving up the practice of vivisection under the influence of the church, the revival of this process taking place only in the XVIth century [4].

In the XVIth century, William Harvey had an important contribution, who wrote the first treaty involving animal studies, “Exercitatio anatomica de motu cordis et sanguinis in Animalibus”, in which he showed blood circulation in the body of over 80 species of animals [5].

In the XIXth century, Antoine Laurent de Lavoisier (1743–1794) was using the animals to test anesthesia or to study respiration; Louis Pasteur (1822–1895) inoculated anthrax in sheep and Emil Adolf von Behring (1854–1917) [4] demonstrated the effect of diphtheria toxin on animals.

The same century brought the first animal protection law in Britain, in 1822, in response to the realization of 250 animal experiments a year before that [4].

The current state of the use of animals in research in the EU

According to the Seventh Report from the Commission to the Council and the European Parliament on the Statistics on the number of animals used for experimental and other scientific purposes in the member states of the European Union COM 2013 [6], in the EU there have been used about 11.5 million copies in 2011, which confirms that it is an issue that must be considered including from the ethical point of view. According to the official data, in Europe, they were using different classes of animals shown in Table 1 [6].
**Regulations on the animal use in medical research**

In the European Union, there have been developed and adopted a series of regulations such as Council Directive 86/609/EEC Commission Decision 90/67/EEC, the European Convention on protection of animals used for experimental and other scientific purposes in 1986 and updated in 1998.

In Romania, the legislation that may be correlated with medical research using experimental animals is represented by Law No. 205/2004, as amended and supplemented, Government Ordinance No. 37/2002 on the protection of animals used for experimental and other scientific purposes or Law No. 305/2006 on the ratification of the European Convention for the protection of animals used for experimental and other scientific purposes.

Law No. 205/2004, states in Art. No. 7 that “animals used for experimental purposes are subject to specific protective rules, without causing them any unnecessary suffering”.

To check the compliance with legislation, a number of national structures have been established, designed to certify how the law is applied. Thus, in the US, Institutional Animal Care and Use Committees (IACUCs) demonstrated that looking through a blind-type protocol, the necessity of using animals in medical research, only 61% of research were really necessary, although the initial percentage, when the analysis was carried out in a conventional manner, was of 98% [7].

**Ethical dilemmas – pros and cons regarding the animal use in medical research**

Throughout time, the dispute between those who wanted to use animals and those who opposed to this fact was sometimes fiery even within families; so if Claude Bernard (1813–1878) was a supporter of vivisection, his wife will set up the first society in France to combat vivisection [4].

Charles Darwin (1809–1882) had a balanced approach. He was distinguished by moderation and advocated for the use of animal experiments only when needed [4].

As we move into an accelerated pace within scientific investigations, new problems (e.g., genetic manipulation of animals), on the care and use of laboratory animals continue to occur. The main question that gives rise to these philosophical debates is whether it is right or moral to carry out research on animals. If most researchers agree that it is not fair, but it is nevertheless necessary, others, such as the case of David Baltimore, a Nobel Prize winner, believe that “testing on animals pose no ethical issue” [8].

In the past, scientists were little concerned about the ethical considerations in relation to animals. Instead, public opinion has evolved steadily from expressions of concern over unnecessary suffering of a large number of animals used in experiments, to intolerance at experiments of superior animals. Animal rights have been recognized not only in general, but there are people who believe that any animal should have the right to live in freedom and not be affected by his physical integrity [9].

Thousands of civic, national and international organizations were formed in the European countries, promoting the spirit of responsibility and respect for life, compassion for all beings susceptible to pain and suffering [10].

To reduce animal suffering, but without sacrificing the scientific results, they use genetic engineering. While it can still achieve total removal of suffering, but reducing it, research progresses [11].

The debate on the use of animals for research or other activities (transport, cosmetic industries etc.) have intensified also due to the Peter Singer’s book, “Animal Liberation” in 1975, the subject of this book being precisely the condition of animals during experimental procedures. The appearance of this book led to the introduction of regulations on animal experimentation in the Declaration of Helsinki of 1975, and in 1978, at a meeting in Brussels, to be announced by UNESCO Universal Declaration of Animal Rights [5].

But, even before this statement, due to the increased number of animals involved in experiments, other people campaigned for abandoning the use of animals in experiments or even for humanizing the conditions under which they were held. They insisted that animal experiments should be replaced by alternative methods such as in vitro tests or computer simulations. They were William M. S. Russell and Rex L. Burch, who in 1959 published a book in which they spoke for the first time about the 3Rs principle [5, 12].

3Rs strategy (reduction, replacement, refinement) was introduced in experimenting on animals. They sought alternative research methods to implement this strategy. These methods were used in the testing of drugs and chemicals up to certain levels [13, 14].

This strategy was accepted in the International Congress of Biological Standardization (San Antonio, Texas, USA, 1979), and then developed under the auspices of the World Health Organization [15], being converted then into the 4R strategy by adding rehabilitation. The 4R is the basis for the ethical review of animal use (Figure 1).

The protection of the animals used as subjects does not only refer to the conditioning and manipulation during the experiments, but also to the maintaining conditions of the animals in farms, which have to correspond to the specific physiological requirements of races and age groups, as provided in the Directive No. 86/609/CEE [16–18].
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According to Vivienne Nathanson, quoted by Moore (2008): “believes animal experimentation is necessary at present to develop a better understanding of diseases and how to treat them, but endorses the concept that wherever possible, alternative experimental methods should be used” [19].

Also, it is considered important for the people that those who will use animals for research must benefit from a special training that would facilitate their use respecting all moral and ethic rules [18].

At the level of the European Union, it is regulated by law that the researcher, when starting a project that may imply the use of vertebrate animals, must first assure that the study cannot be fulfilled by any other means [14].

As Szücs et al. mention: “Deontological positions involve each individual considering their duties when deciding what action to take. Most people who are asked «what was the right course of action in relation to the animal treatment» will say that some actions should never occur but other decisions should be taken according to the balance of costs and benefits” [3].

Pros and cons of animal experimentation can be systematized in Figure 2.
The responsibility of researchers from a moral point of view

The main responsibilities of researchers can be systematized in Figure 3, starting from the general principles of bioethics.

The trend of the last decades for reducing the number of big animals is correlated to the reducing the number of articles published in PubMed by 10%, according to the study done by Ramalli et al., proving once again that the demands have risen in terms of animal use and medical research has become more diversified, as far as using cell cultures [20].

As Ewald R. Weibel mentioned: "Physiologists are bound to test their scientific theories in experiments on the living matter and, ultimately, on living organisms – animals or humans”. The following principles have to be respected both for humans and for animals [21]:

- “Humans as well as animals are members of the living earth community.
- Animals as well as humans have the ability to suffer.
- Animals as well as humans have a striving for life”.

The researchers’ activity is often hampered by the activity of animal protection organizations, which do not accept the use of animals for medical experiments, sometimes even applying moral pressure both directly and through mass-media, often an unbearable one [22]. The situation of the animals is significantly improving when they are viewed more as a “pet” and less as an object [23].

Animal bioethics, as defined in 2000 [15], brings up more and more decisional problems, starting from a truth known since the Andreas Vesalius (1514–1564) analysis was performed on the mistakes done by Galen regarding human anatomy and physiology: there are undisputable differences between species. As Susan Bridgwood Green shows, “clinical investigators accept responsibility for ensuring that the animal data they use is scientifically sound before proceeding with human trials” explaining the undisputed role of animal experimentation [24].

As shown by Dancet et al.: “scientists are advised to inform the public that they adhere to high standards for animal use and care set by international or governmental agencies and that their study protocols are reviewed with great scrutiny in order to receive federal or other funding. Additionally, the public should know that independent agencies regularly subject animal research to monitoring and scrutiny” [25].

Furthermore, it has become necessary to develop alternative methods of research, such as computer simulations [26], especially when it comes to educating future scientists and restoring experiments for educational purposes.

Conclusions

Although the use of experimental animals is an absolute necessity in the medical-pharmaceutical practice, there are many voices that currently are opposed to the use of animals for this purpose, or seeking evidence that this has been achieved only in conditions in which there were no other alternatives for testing drugs or medical procedures. An increased demand for animals has been made for the past years, in order to put more emphasis on the development of regulations to prevent unnecessary repetition of some experiments or the use of communications between researchers aiming to reduce the total number of animals used. The principles of human bioethics, based on the famous “primum non nocere” must be reflected in the practice of medical research on animals, believing that it is very important that one should not do more harm than necessary and, also, that moral and bioethical standards need to rigorously be applied to this absolutely necessary practice.
Conflict of interests
The authors declare that they have no conflict of interests.

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