Commentary

Ethical considerations and challenges associated with euthanasia in laboratory animal research

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Introduction:

Laboratory animals are important tools in medical studies, including biology, physiology, toxicology, etc. Through the years, they have constantly played a crucial role in the advancement of medical sciences (1). Experimental animals should be euthanized at some stage or at the end of a procedure. However, euthanasia should be performed humanely and with minimum pain (2). Research on animals requires the highest level of scientific and ethical responsibility. According to the guidelines developed by international committees on ethics in medical research, laboratory animals should be treated in a humane manner (3). Some researchers do not know how to deal with laboratory animals, and sometimes an underequipped laboratory or lab workers' insufficient knowledge of equipment operation may hamper the humane treat-Ment of animals (4). Researchers should observe ethical issues while working with animals throughout the different steps of the research, including holding, transfer, intervention, surgery, and postoperative care (3). Consequently, it is imperative that ethical considerations be noted when the time comes to end the animal's life.

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Putting an animal to death - known as “euthanasia” - should be a pain-free process (5). Unfortunately, this is not the case most of the time, and the animal suffers pain when put down. Laboratory animals are commonly terminated through either chemical or physical euthanasia procedures. Given the importance of observing ethics in all stages of research, this study aims to direct researchers' attention to ethical considerations in the extermination of laboratory animals.

Chemical Euthanasia Methods

The history of the use of laboratory animals is clear testimony that animal experimentation not only plays a crucial and undeniable role in the progress of medical science but is also an indispensable part of it. The most common chemical euthanasia methods used on laboratory animals include sodium pentobarbital, carbon dioxide (CO_2), and isoflurane. Sodium pentobarbital is considered a humane and effective anesthetic that induces rapid unconsciousness and death when administered intraperitoneally (6) However, recent studies point to possible pain and stress associated with its use, raising concerns about its efficacy and impact on animal welfare (6). CO_2 is also widely accepted and easy to administer, but it can cause anxiety and aversion in rodents, and there is evidence of significant stress responses during administration (7). As an inhalational anesthetic, isoflurane is effective for rapid induction of anesthesia, but can also induce stress and is less preferred in animals due to possible aversion (7). Although these techniques are commonly used, ongoing scientific research emphasizes the need for alternative approaches that reduce suffering and discomfort in laboratory animals. Also, euthanasia with toxic substances is not implemented when the dying process is prolonged, causing significant discomfort to the animals, and is considered unethical by international standards (8).

Physical Euthanasia Methods

If the animal’s carcass and tissue are needed for further studies, a physical (manual) method is the most common practice. The decapitation method may lead to great pain for the experimental animal (9) and lengthen its death due to various reasons, including stress on the user (especially in the case

of amateurs and students), improper pressure on the wrong place, and an inappropriate angle.

Physical euthanasia methods for laboratory animals continue to be a common option due to numerous advantages, such as elimination of the toxicity associated with the use of chemical agents that may affect experimental results, the quick and easy method of execution, and lack of the need for specialized equipment (9). At present, the predominant physical euthanasia techniques include cervical dislocation, decapitation facilitated by a manual guillotine, and blunt force trauma. Cervical dislocation is characterized by the swift disengagement of the uppermost cervical vertebrae. There is a paucity of empirical evidence substantiating the assertion that cervical dislocation yields a consistent and humane cessation of life (10). Moreover, using a mechanical guillotine may result in tissue damage, for instance when parts of the brain tissue such as the brain stem and cerebellum are required for an experiment.

Therefore, further research is needed to find effective innovative modifications to euthanasia methods and to help standardize the techniques (4). This is possible through the potential use of aids/tools to improve accuracy in order to ensure rapid, correct, and ethical decapitation in laboratory rodents.

Discussion

The use of animal models is an important tool in medical research studies and preclinical trials. Sometimes the animal should be disposed of after using its tissue or performing behavioral tests, but ethical principles should be observed in the euthanasia process (11).

Effective euthanasia must focus on achieving rapid loss of consciousness to reduce suffering. The intraperitoneal injection of sodium pentobarbital is a recognized chemical approach owing to its effectiveness and ethical implications. Nevertheless, it has the potential to cause pain and distress, which raises questions about its reliability (6). Physical euthanasia techniques for laboratory animals emphasize the reduction of pain and suffering while conforming to established ethical principles. Although these techniques are intended to be compassionate, there exists a continual discourse concerning optimal practices and ethical implications related to euthanasia within laboratory

contexts. Certain scholars promote alternative approaches that could alleviate stress for both the animals involved and the personnel administering the procedures (9). Physical techniques such as cervical dislocation are occasionally employed, particularly in the case of small rodent species, but they should be administered by adept professionals to mitigate potential distress and pain. Using a manual guillotine lengthens decapitation (12), and user error and stress make the animal suffer great pain (13). The stress experienced by an animal causes biochemical and hormonal changes in blood that interfere with relevant tests (14). Also, in some studies, a manual guillotine is used on a large number of animals, which may result in operator tiredness and increased number of errors. Another disadvantage of working with a manual guillotine is that it is not safe due to the possibility of injury to the hands and fingers of users, especially if they are amateurs or students, and even in the case of experienced persons or their assistants, when the work load is unusually heavy (15,16). Additionally, working with a manual guillotine is stressful for amateurs who have little experience with laboratory animal euthanasia and researchers who cannot kill an animal on moral grounds (16). Decapitation with a manual guillotine can cause stress to the operator, especially when dealing with a live (semi-conscious) animal, due to blood splashing around and on the table, hands, face and clothes of the user. Thus, it is imperative to consider the operator's emotional welfare. The act of terminating an animal's life may induce significant distress, which, when coupled with the inherently direct and non-aesthetic characteristics of certain physical methods, can result in adverse emotional consequences (17).

Therefore, an automatic method/device can be employed to improve user safety, accelerate the procedure, minimize errors, reduce stress during euthanasia, and finally achieve better and more reliable results. This may also lead to a decreased number of laboratory animals used because the frequency of experiments and errors of the researchers, who may lose the desired tissues, will be reduced. In addition, the decapitation will happen faster and both the animal and the researcher will experience less stress. As a result, more coherent studies can be carried out while the goals and recommendations of international

committees related to ethics in dealing with laboratory animals will be observed.

As most of the devices used in modern medicine have gone through the process of evolution and improvement (18), to upgrade the equipment currently used for the euthanasia of laboratory animals, an easy-to-use and safe device should be provided that can be operated by any researcher with minimal stress. Our proposed solution is to make an automatic guillotine machine (Figure 1) for euthanasia, so that laboratory animals can be euthanized with the lowest possible amount of pain and bleeding.

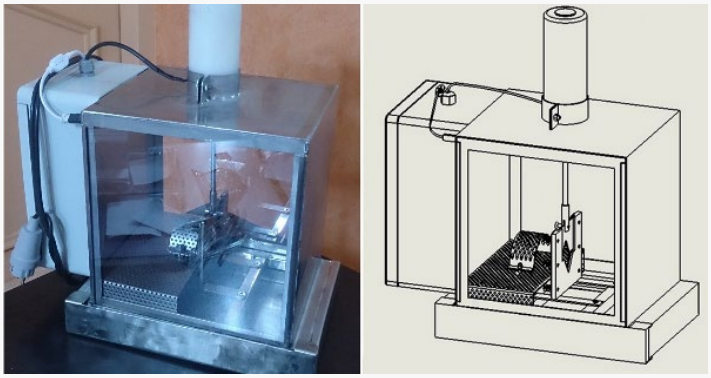

Figure 1. Pictures and schematic presentation of the proposed automatic guillotine.

Upgrading manual animal euthanasia to automated methods has certain advantages. For instance, due to the speed of the automated methods and the rapid decapitation, euthanasia is performed quickly, with minimum anxiety and distress for the animal. Also, these devices are safer to operate and at the same time cause less stress for researchers.

Conclusion

As a rule, utilization of animals in research should be restricted to instances in which no other viable alternatives exist, and laboratory animal euthanasia should be performed using a pain-free method. The practice of euthanasia through administration of toxic substances is predominantly abandoned when

the dying process is prolonged, inflicts significant distress upon the animals, and violates ethical norms. Decapitation is a physical method of euthanasia that may result in considerable agony for the experimental subjects and can also extend the time for the animal to die owing to various factors, including the psychological strain placed upon the operator. An automatic method can therefore be employed to improve and accelerate the procedure, minimize errors, reduce stress during euthanasia, and finally achieve better and more reliable results.

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Conflict of Interests

There are no competing interests to declare.

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