Brønstad A. Current Concepts of Harm-benefit Assessment of Animal Research – A Mini Review. J Infectiology. 2018; 1(1): 16-18

Journal of Infectiology

Journal of Infectiology

Mini Review Open Access

Current Concepts of Harm-benefit Assessment of Animal Research – A Mini Review

Aurora Brønstad*

Department of Clinical medicine, University of Bergen, Bergen, Norway

Article Info

Article Notes
Received: May 22, 2018
Accepted: June 22, 2018

***Correspondence:**
Dr. Aurora Brønstad, Department of Clinical medicine, University of Bergen, Bergen, Norway,
Email: Aurora.Bronstad@uib.no

Use of animals in research for infectious diseases can show a long merit of benefits for better understanding of how to treat and prevent such diseases as well as other field of research. Research in animals provide essential knowledge that could not be achieved by alternative methods. However, the fact that animal experiments have shown to be essential does not justify the use of animals in all cases per se. An ethical qualification must be performed for the particular case and context and the negative impact – harm – to the animals must be weighed against the potential benefits in a harm-benefit assessment.

Harm benefit assessment of animal research is anchored in several international guidelines for research like the Council for International Organizations of Medical Sciences and International Council for Laboratory Animal Science joint document[1], the World Organization for Animal Health – OiE Terrestrial Animal Health Code[2], The Guide to the Care and Use of Laboratory Animals[3] and the European Directive 2010/63[4]. However, how to compare different sizes like harm to animals versus benefits for humans has been questioned by several authors[5-9]. The American Association for Laboratory Animal Science (AALAS) and the Federation of European Laboratory Animal Science Associations (FELASA) set down a joint working group with representatives from animal research field[a]. The tasks for the working group was to review the current literature on harm-benefit analysis, define and describe the concepts and elements of harm-benefit analysis and recommend how it can be addressed by protocol applicants as well part of ethical evaluation. The working group published 2 papers where these issues were addressed[10, 11].

Harm to animals is defined as any negative impact on animal welfare addressed by the domains of the five freedoms[12, 13] i.e. freedom from hunger or thirst, from pain, injury or disease, freedom to express most normal behavior and freedom from fear and distress. The five freedoms were originally defined for farm animals but were adapted by Mellor and Reid as a tool to discriminate between levels of harm for animal research[13]. The approach using the five freedoms better reflect interests of the animal than solely focus on pain and distress.

Means to reduce harm are important to improve the harm-benefit balance and can be summarized by the concept of 3Rs

[a] The other members of the AALAS-FELASA working group were Kathy Laber, Chris Newcomer, Thierry Decelle, Jeff Everitt and javier Guillen

defined by Russel and Burch[14]. Harm reduction is achieved by either Replacing animal experiments by alternative methods when such methods are available. Reducing the number of animals to the minimum need to achieve results of a certain level of precision. Refine procedures to minimize negative impact on animals as well as optimizing their wellbeing. Together with harm-benefit assessment, compliance with 3Rs form a foundation for ethical conduct of animal research.

Benefits can be more difficult to assess as they are something expected to be achieved in the future. Some benefits can be achieved shortly, like educational benefits by for example practicing surgical procedures in animal. Safety test also give information that is beneficial there and then. Knowledge benefits generate by fundamental research are also achieved as soon as studies are concluded. However, how this knowledge is ultimately used must be seen in a long perspective and may be regarded as secondary benefits. It has been discussed if the single researcher actually can be held responsible for long term, secondary benefits[15]. In the evaluation of harms versus benefits it may be tempting to overestimate the benefits to make a more positive balance in favor of support of that experiment. Competition of research founding can be a driving force to overselling benefits of a particular experiment. Benefits for humans, animals or environment are regarded as legitimate benefits. Researchers should be able to define who will likely benefit from a particular study, how will they benefit, what are the benefit and when will the benefits likely be realized. It seems that benefits, in contrast to harm is well less defined when it comes to classification or means to strengthen benefits in operational terms. Quality of experiments, likelihood of achieving defined aims and reliability of a study have been hold as both a harm factor and a benefit factor by different authors. Animal are not more harmed by a poorly designed experiment; however, such use of animals is regarded as unnecessary and unethical if it cannot provide reliable information or benefits cannot be achieved.

Several models for harm-benefit analysis have been discovered by the AALAS-FELASA working group. The Bateson cube[16] is a visual model that in a pedagogic way illustrate the concept of harm-benefit analysis. Harm, benefit but also quality are three different domains that must be evaluated individually, and where combinations of the evaluation guide if the experiment can be ethically justified or not. For example, a low benefit – high harm experiment may be difficult to justify, while high benefit – low harm is easier to support. Interestingly, Bateson regarded quality as a separate dimension, with the implication that even if promised benefits are high and harm low, this cannot be justified if the quality of experiment is poor. The limitation of Bateson's cube lays in how to discriminate between different levels how harm and benefit, which is necessary for practical application of the model.

Other models for harm-benefit analysis include different algorithms[17, 18], where data reflecting discrimination levels for harms and benefits are plotted into arithmetic functions generating a "yes" or "no" for approval as the output. This sounds tempting and may give a useful indication of an experiment's ethical status, but it is difficult to make such algorithms that are relevant or valid for all cases. Others have claimed that you cannot reduce a moral question to an arithmetic exercise[19].

An expert working group by the European Commission has developed guidelines for severity categorization or classification system for discriminating between different levels of harm[20] as well as examples to illustrate the process of severity classification[21]. Discriminating into categories is helpful for simplifying a complex picture and also it should stimulate actions to implement mitigating factors when an experiment is classified as severe. However, the problem with defining distinct categories is that it does not fit for all cases.

Based on the review of the current concept of harm, benefit and the pros and cons with the different methods for harm-benefit analysis, the AALAS-FELASA working group on harm-benefit analysis developed a novel model for harm-benefit analysis[11].

The domain for assessing harm under this model was based on how animal welfare is impacted by assessing the five freedoms. In addition, mitigating and aggravating factors must be identified and included in the score. Impact on benefit is assessed by asking who will benefit, how will they benefit, what are the benefits and when will benefits be realized. Benefits for humans, animals and environment are regarded as legitimate, while economic benefits can be questioned. Also, knowledge and educational benefits are regarded as legitimate benefits with a value in their own.

To discriminate different levels of harms and benefits we suggested a heat-scale from white to deep red or crimson. White reflects high potential benefits or low, trivial harm, while crimson on the opposite reflects low potential benefits or harmful, severe impact on animals. We choose not to use a numeric scale as this could tempt to an arithmetic solution that we were not in favor of. We did not either want to use a green, yellow, red traffic color scale as we think green could give an indication of no moral concern, while the working groups opinion is that there are always some concerns in animal research.

The model is intended to help researcher to identify potential harm and apply mitigating factors to reduce harm. The model also helps to clarify potential benefits and make them more explicit. By this way, the model structures the way relevant information is provided so an informed

decision can be made. The method is transparent in the way that factors that have been considered and the evaluation of them can be traced. We suggest this contributes to harmonization and openness in the question of animal research that is necessary for further support of animal research when there are no alternatives.

References

1. CIOMS-ICLAS, International guiding principles for biomedical research involving animals, CIOMS-ICLAS, Editor. 2012, CIOMS-ICLAS.
2. OIE, Terrestrial Animal Health Code, Use of animals in research and education, W.O.f.A. Health, Editor. 2014.
3. Garber JC . Guide for the Care and Use of Laboratory Animals: Eighth Edition, T.N. Academies, Editor. Committee for the Update of the Guide for the Care and Use of Laboratory Animals; National Research Council: National Academies Press. 2010; p. 248.
4. EuropeanCommission, Directive 2010/63/EU og the European Parliament anf of the council of 22 September 2010 on the protection of animals used for scientific purposes, EuropeanCommission, Editor. 2010.
5. Rickard MD. The use of animals for research on animal diseases: its impact on the harm-benefit analysis. Altern Lab Anim. 2004; **32 Suppl 1A**: p. 225-7.
6. Buning Tde C. Practical difficulties in balancing harms and benefits in the modern use of laboratory animals: biotechnology. Altern Lab Anim. 2004; **32 Suppl 1B**: p. 459-63.
7. Bout HJJM, Vlissingen F, Karssing ED. Evaluating the ethical acceptability of animal research. Lab Anim (NY). 2014; **43**(11): p. 411-4.
8. Grimm H. Turning Apples into Oranges? The Harm-Benefit Analysis and How to take Ethical Considerations into Account. ATLA. 2015; **43**: p. 22-24.
9. Würbel H. More than 3Rs: the importance of scientific validity for harm-benefit analysis of animal research. LabAnimal. 2017; **46**(4): p. 164-166.
10. Bronstad A, Newcomer CE, Decelle T, et al. Current concepts of Harm-Benefit Analysis of Animal Experiments - Report from the AALAS-FELASA Working Group on Harm-Benefit Analysis - Part 1. Lab Anim. 2016. **50**(1 Suppl): p. 1-20.
11. Laber K, Newcomer CE, Decelle T, et al. Recommendations for Addressing Harm-Benefit Analysis and Implementation in Ethical Evaluation - Report from the AALAS-FELASA Working Group on Harm-Benefit Analysis - Part 2. Lab Anim. 2016; **50**(1 Suppl): p. 21-42.
12. FAWC, The Five Freedoms. 1992, Farm Animal Welfare Council: London.
13. Mellor D, Reid C. Concepts of animal well-being and predicting the impact of procedures on experimental animals, in Improving the Well-Being of Animals in the Research Environment, R.M. Baker, G. Jenkin, and D.J. Mellor, Editors. Australian and New Zealand Council for the Care of Animals in Research and Teaching: Australia. 1994; p. 3-18.
14. Russell WMS, Burch RL. The principles of humane experimental technique. London: Methuen. 1959; 238 s.
15. Grimm H, Eggel M, Deplazes-Zemp A, et al. The Road to Hell Is Paved with Good Intentions: Why Harm-Benefit Analysis and Its Emphasis on Practical Benefit Jeopardizes the Credibility of Research. Animals (Basel). 2017; **7**(9).
16. Bateson P. When to experiment on animals. New Sci. 1986; **109**(1496): p. 30-2.
17. Stafleu FR, Tramper R, Vorstenbosch J, et al. The ethical acceptability of animal experiments: a proposal for a system to support decision-making. Lab Anim. 1999; **33**(3): p. 295-303.
18. Porter DG. Ethical scores for animal experiments. Nature. 1992; **356**(6365): p. 101-2.
19. Voipio HM. Nordic-European workshop on ethical evaluation og animal experiments. Scand. J Lab Anim Sci. 2004; **4**(31): p. 251-267.
20. EuropeanCommissionExpertWorkingGrouponSeverityAssessment, Working document on a severity assessment framework. 2012: http://ec.europa.eu/environment/chemicals/lab_animals/pdf/Endorsed_Severity_Assessment.pdf.
21. EUCommssionExpertWorkingGroup, Examples to illustrate the process of severity classification, day-to-day assessment and actual severity assessment. 2011.