



SCIENTIFIC ALTERNATIVES TO ANIMALS IN MEDICAL EXPERIMENTS

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ABSTRACT

Aim: To assess the preference and acceptance of the scientific alternatives to animals in medical experiments in research. **Materials and Methods:** This questionnaire based study was conducted in Sree Balaji Medical College and Hospital, and Madras Institute of Technology (MIT), Chennai, Tamil Nadu, India. The numbers of participants were 100 and the questionnaire was based on Likert scale consisting of five ordered response level. **Results:** The results were analyzed to find out the preference and acceptance of scientific alternatives to animals. Overall, 28% of the participants felt it is ethical to do animal experiment which benefits human beings but violates the rights of animals; 57% participants suggested alternative models like fruit flies, nematodes, zebra fish are less expensive, easy to handle and experimentally more efficient; 60% participants felt human volunteers could be used for microdosing as an important alternative and 73% participants recommended that animal experiments are necessary in medical exp. Further, 74% agreed with 3R's (reduction, refinement and replacement) for performing animal experiments. **Conclusion:** Researchers concluded that animal experiment can be done keeping 3R's in mind and also alternatives to animal testing would be desirable if funding is provided by the Government or any funding agency for the work on alternatives to animal testing.

KEYWORDS: Scientific alternatives, animal testing, Medical experiment, preference, acceptance.



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INTRODUCTION

We have been using animals for a long time to enhance our knowledge of human anatomy and human diseases. Animal research has provided valuable information about many physiological and pharmacological processes that are relevant to humans and has been fundamental in the development of many drugs such as; vaccines, anesthetics, antibiotics, and non-steroidal anti-inflammatory drugs (NSAIDs). To some extent, animals (mammals) and humans behavior, cellular structures, proteins and genes are similar. But the way in which animals and humans react to their environments, both physiologically and behaviorally, and the conditions under which laboratory animals are kept can influence and alter experimental results. The husbandry and treatment of laboratory animals has been and continues to be a major topic of ethical debate¹. In 1954 a scientific technique was proposed by Charles Hume who was the founder of the Universities Federation for Animal Welfare (UFAW). The scientific technique was known as The Three R's (i.e., Reduction, Refinement and Replacement)². The aim of the Three R's was to undertake scientific study of human technique in laboratory animal experiments. W.M.S. Russell, a zoologist, and R.L. Burch, a microbiologist, were appointed to carry out the work, which led to the publication of the book "The Principles of Humane Experimental Technique" in 1959². The 3R's (Reduction, Refinement, Replacement) modulated by W.M.S. Russell and R.L Burch were defined as –

Reduction

Refers to methods which minimizes animal use and enables researchers to obtain comparable levels of information from fewer animals or to obtain more information from the same number of animals, thereby reducing future use of animals³. Further, the examples include; improved experimental design and statistical analysis; modern imaging technique and sharing data and resources.

Refinement

Is "any approach which avoids, alleviates or minimizes the actual or potential pain, distress and other adverse effects suffered at any time during the life of the animals involved, or which enhances their wellbeing as far as possible"⁴. On 24th November 1986, European Directive 86/609/EEC had enforced a law for the protection of animals used for scientific purposes which was again updated on 22nd September 2010. The laws state, an animal experiment shall not be performed if another scientifically satisfactory method of obtaining the result were available, and when an animal experiment has to be performed, the choice of species shall be carefully considered. In choosing the experiment, those which involve minimum number of animals, causing least pain, suffering, distress and harm and which are most likely to provide satisfactory results should be selected. In 1991, the European Centre for the Validation of Alternative Methods (ECVAM) was established by the European Commission to promote the scientific and regulatory acceptance of alternative methods, such as; replacement of animals by other scientific methods.

Replacement

Methods can be absolute replacement, i.e, techniques which do not involve animals at any points, such as computer modelling, in vitro methodologies (e.g, tissue engineering), or human volunteers, and relative replacements which avoid or replace the use of protected animals. The examples include the following, established animal cell lines; animal cells, tissues and organs collected from animals killed by a humane technique [according to Animals Scientific Procedures Act 1986 (ASP)]; invertebrates, such as Drosophila and nematode worms; mammals, birds and reptiles up to half way through gestation or incubation, and larval forms of amphibians and fish, until the stage where they become capable of independent feeding³. A number of organisations around the world are working towards the development and

validation of replacement methods, for example, Medical Advances Without Animal Trust (MAWA), Funds for Replacement of Animal in Medical Experiments (FRAME), The European Centre for the Validation of Alternative Methods (ECVAM) ⁵.

MATERIALS AND METHODS

A questionnaire based study was conducted comprising 100 doctors and researchers from Sree Balaji Medical College and Hospital and Madras Institute of Technology (MIT), Chennai, Tamil Nadu. Prior approval was taken from the Institutional Ethics Committee to conduct the study. The questionnaire was based on a Likert

scale consisting of five ordered response level. The questionnaire contained 10 questions to check their preference and acceptance of the above study. Participants were explained the purpose of the study and were requested to complete and return the questionnaire.

RESULTS

This was a simple observational study. The results were analyzed to find out the preference and acceptance of scientific alternatives to animal experiment by researchers. Response shown by the participants is shown in Table 1 and Fig.1 & 2.

Table 1
Response shown by participants regarding preference and acceptance of scientific alternatives to animal experiment in percentage

Questions	Strongly agree(%)	Agree (%)	Neutral (%)	Disagree (%)	Strongly Disagree(%)
Animal experiments (exp.) necessary in medical exp.	30	43	14	10	3
Animal exp. would be preferable with less invasive techniques	10	52	11	17	10
Is it ethical to do animal experiment which benefits human beings but violates the rights of animals	3	25	19	46	7
Due to biological differences among species, animal test do not really predict outcome in humans.	0	33	27	36	0
Can toxicity test in animals LD ₅₀ be relapsed by a similar in vitro test IC ₅₀ test	6	27	27	27	13
Alternative models like fruit flies, nematodes, zebra fish are less expensive, easy to handle and experimentally more efficient	27	30	20	20	3
In vitro method is faster than animal test	13	53	23	11	0
Human alternatives to animals (microdosing in human volunteer)	20	40	23	14	3
Do you agree with 3R's* while doing animal experiment	13	63	20	4	0
Funding necessary for setting up laboratory for scientific alternatives to animal experiment	57	38	5	0	0

*Note: 3R's- reduction, refinement and replacement

Figure 1
Animal experiment necessary in medical experiments

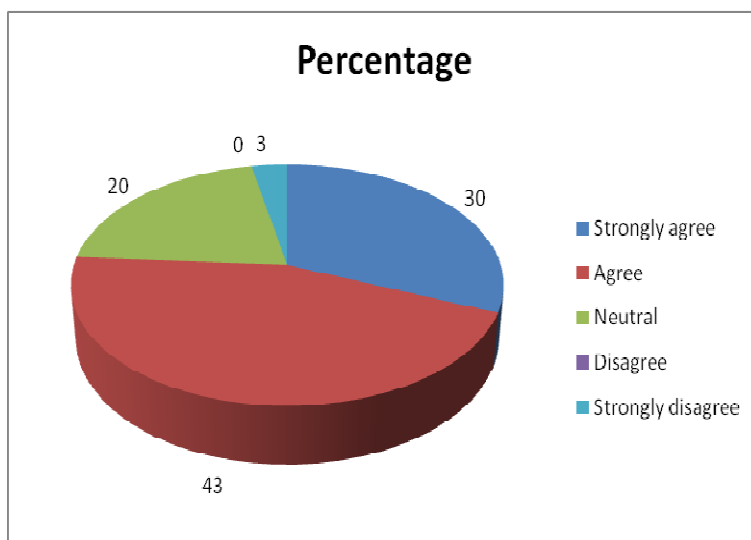
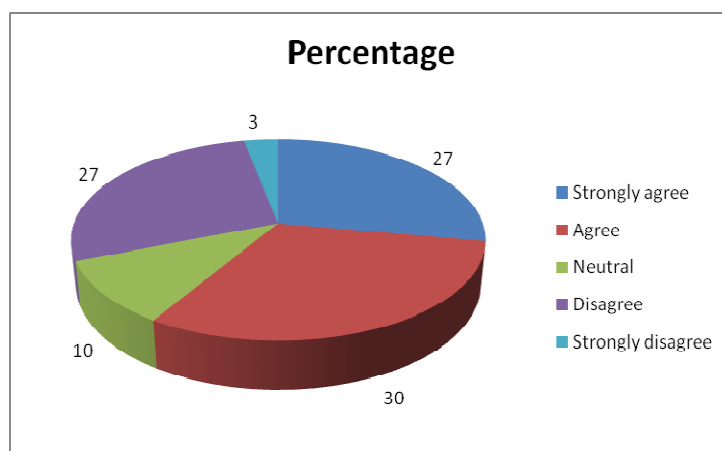


Figure 2
Scientific alternative models are more effective and easy to handle



DISCUSSION

After analyzing the data for preference and acceptance for scientific alternatives, it showed that 73% preferred animal experiments whereas scientific alternative methods were preferred by 57% of the participants. Animal experiments have played a vital role in medical research. According to the US-based Foundation for Biomedical Research, animal research has played a vital role in virtually every major medical advance of the last century for both human and veterinary health. Knowledge of antibiotics, vaccines and other important drugs are based on

research with laboratory animals in the past. Eg. Smallpox eradication (testing with cows), Polio eradication (mouse and donkey), availability of insulin (fish and dog), Tetanus vaccine (horse), and Rubella vaccine (monkey). Nevertheless for every medical research animal model may not be useful. Sometimes outcome in animal model does not show the same picture like that of human subject. In 1963, prospective and retrospective studies of human patients have shown that there is a strong correlation between cigarette smoking and lung cancer but all

experiments have failed to produce lung cancer in animal models^{6, 7}. Another example where animal model had not contributed significantly was AIDS research. AIDS researchers have acknowledge that chimpanzees, an endangered species if inoculated with HIV virus, it rarely develop AIDS like syndrome. So, it is unlikely to prove useful as animal models for understanding the mechanism of infection or mode of treatment⁸. For psychological experiments, animal models were subjected to painful stimuli in order to study their behaviour. But this is strongly opposed by the psychologist as human psychological problems reflect familial, social and cultural factors that cannot be modelled in non-humans. Instead it cause sufferings to the animals⁹.

Even though in the past animal model has helped us a lot in discovering new drugs for various human disease, there is demonstrated evidence of failures of animal models which lead to delay in drug discoveries. Moreover these experiments cause pain and sufferings to the animals. So newer methods has come up where experiments require either minimum number of animals or alternative scientific methods. At the Food and Drug Administration's (FDA's) National Centre for Toxicology Research (NCTR) in Arkansas, scientists are using the embryos and larvae (up to five to six days old) of zebrafish for toxicity testing of various drugs. According to FDA research biologist Jyotshna Kanungo, Ph.D, zebrafish makes terrific preclinical trial subjects as they are vertebrates and share so many common biological pathways with humans. Hearts of both zebrafish and humans have chambers and rhythmically pump oxygen carrying blood through the body. The eyes have retinal structure and they also have a liver, pancreas, kidneys and intestine.

Some effective, affordable, and humane research methods include sophisticated in vitro, genomic and computer-modelling techniques as well as studies of human populations, volunteers and patients, e.g's are – 1) Research laboratory, CeeTox is using human cell-based in vitro toxicity screening to test drugs and chemicals. 2) VaxDesign's groundbreaking Modular Immune in vitro construct (MIMIC) system uses human cells

to create a working dime-sized human immune system for testing the safety and effectiveness of HIV/AIDS vaccines. 3) Researchers are also using advanced human based brain imaging and recording techniques such as MRI, EEG, PET and CT for studying the human brain. These modern techniques allow the human brain to be safely studied down to the level of a single neuron. 4) A research method called microdosing can provide vital information on the safety of an experimental drug and how it is metabolized in humans. Volunteers are given an extremely small one-time drug dose that is well below the threshold necessary for any potential pharmacologic effect to take place and advanced imaging techniques are used to monitor the effect of the drug in the body¹⁰.

From the above study it is seen that there is preference for scientific alternatives to animal experiment. Participants agreed that alternative experiment are more accurate, easy to handle and some alternative experiments like zebrafish, drosophillia, nematodes are more cost-effective than animals. To do in-vitro studies and other human alternatives we need resources. So funding is also an important aspect in the use of alternative methods. There are number of organizations in the world who is working for the development and replacement of alternative methods. Acceptance of alternative experiment by the participants is less than animal experiment. It will take some time for the participants to accept wholeheartedly since they are doing animal experiments for a longer time and moreover they are not much exposed to the alternative methods. Changing their approach requires persuasion, increased communication, training and education in the use of alternatives.

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