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International Journal of Current Research
Vol. 9, Issue, 12, pp.63275-63278, December, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

IS IT A SIN OR BOON TO CONDUCT TOXICOLOGICAL TESTS ON ANIMALS ?

***,[1]Raghavendra Rao, M. V., [1]Sireesha Bala, A., [1]Sateesh Babu, Arja, [1]Samir Fatteh, [2]Jitendra Kumar Naik, [2]Anusha.C.Pawar and [3]Jattavatu Madhavi**

[1]Avalon University School of Medicine, Curacao, Central America
[2]Osmania University, Hyderabad, Telangana state, India
[3]Acharya Nagarjuna University, Guntur, AP, India

ARTICLE INFO

Article History:
Received 24th September, 2017
Received in revised form
23rd October, 2017
Accepted 04th November, 2017
Published online 31st December, 2017

Key words:
Vivisection,
CAT (computer-assisted tomography),
Thalidomide.

ABSTRACT

Experimental research with animals is usually conducted in universities, medical schools, pharmaceutical companies. Animals and human get many of the same illnesses. Animal research usually describes research involving vertebrates, such as cats, mice, frogs, pigs, and primates. All medical research is carefully planned, and this includes medical research with animals. Under federal law, all animals must be treated humanely and undergo the least distress possible. Medical research with animals saves Lives. Dog-discovery of insulin, monkey--polio vaccine, mouse--rabies vaccine, pig---skin grafts for burn victims and computer-assisted tomography (CAT) scans, rabbit-- corneal transplants, rat--carcinogen screening.(National institute of health) (NIH). But by doing experiments on animals, knowingly or unknowingly, willingly or unwillingly we are, Poisoning, shocking, burning, and killing animals is all in a day's work for vivisection. If these atrocious acts were committed outside laboratories, they would be felonies. But animals suffer and die every day in laboratories with little or no protection from cruelty. This is the debate of the article, Is it sin or boon to conduct toxicological tests on animals ?

Citation: Raghavendra Rao, M. V., Sireesha Bala, A., Sateesh Babu, Arja, Samir Fatteh, 2017. "Is it a sin or boon to conduct toxicological tests on Animals ?", *International Journal of Current Research*, 9, (12), 63275-63278.

INTRODUCTION

Man today living in a world created by him that is becoming more and more hostile every day owing to pollution. We talk of air pollution, water pollution, pesticide pollution, heavy metal pollution, noise pollution, radiation pollution so on and so forth. If we clearly examine the current situation, is it possible for us to live with out pesticide, with out heavy metals, with out radio active substances, with out planes, trains, buses, cars which are the noise and air pollution. It is just not possible with out them. So we have to be in and yet be out of it. We have to have the cake and eat it too. So the absence of alternative we have to find out the ways and means of the living in the hostile environment in a friendly manner. We have to subject our self to the toxicants and avoid the toxic impact.This should be practical approach for the environmental management and human adjustments. Man being the crown of creation his welfare is deemed to the welfare of everything. By way of trying to safe-guard man from adverse effects of toxicants treatment can be restored to it if the adverse effects are felt. Say for an instant what we do when a patient comes.

Corresponding author:* **Raghavendra Rao, M. V.
Avalon University School of Medicine, Curacao, Central America

There are incidences where situation evades diagnosis and evil effects manifests after the situation goes out of hands as in case of Thalidomide tragedy of 1950-1960. Heavy metals are essential to normal development of organ systems as well as body metabolism. These are useful to the growth of tissues, synthesis and activity. Many heavy metals like copper, zinc, manganese, chromium etc., are important components of biochemical functions. However, heavy metals at higher concentrations prove hazardous affecting life and life processes. Man has always has been exposed to heavy metals through natural concentration in soil and water. Metals leached from eating-utensils and vessels used for cooking increased the risk. The emergence of industrial age and large scale mining brought occupational hazards caused by various toxic metals. Metalic constituents of pesticides and therapeutic egents are additional sources of hazardous exposure. Heavy metals are believed to exert their influence on the activity of the enzymes playing a vital role in the biochemical transactions of a living system. Embryonic development is characterized by growth and formation of new tissues. The alterations in the activity of enzymes and/or embryonic tissues would invariably influence the developmental processes in viviparous animals as embryonic nourishment is provided by the maternal sources. Shift in the metabolism of either the maternal tissues or the embryos owing to changes in the enzyme activity influenced

by heavy metals can be reflected in the form of deviations from the normal development. The metabolic levels of the embryo can, therefore, be expected to be different from those of the maternal animal. The metabolic state of the embryo relative to that of the mother would be reflected even at the molecular level in the enzymatic activity. Administration of 50, 100, 150 and 200 ppm cadmium chloride to male Sprague-dawley rats, significantly increased aspartate amino transferase (AST or AAT) and Alanine aminotransferase in the kidney, brain and liver tissues (Rajanna *et al*., 1981) The mother of the fetus of mammals have been shown to have different enzyme status. Effects of cadmium at sub-lethal concentration in rainbow trout (*Oncorhynchus mykiss*) have significant responses on growth and biochemical parameters generally followed by an early elevation (or depression) and a return to baseline values in chronic exposure. This pattern is suggestive of acclimation to the toxicant over time. The levels of AST and ALT activity increased in the tissues of *Oreochromis mossambicus* exposed to cadmium chloride due to necrosis and increases in the permeability of cell membrane resulting in the damage of tissues after 7 and 14 days. These heavy metals may cause injury to the organisms and the damaged tissues subsequently causing malfunction. (Thirumavalavan, 2010) Continuous exposure to sub-lethal cadmium concentrations resulted in significantly elevated levels of both AST and ALT activity in *Oreochromis niloticus*. It showed a linear pattern of increasing ALP over time with cadmium exposure resulting in recognizable physiological and functional alterations. In contrast, *Oreochromis niloticus* exposed to 0.05 mg/l cadmium during 30-days showed reduction in ALP activity. (Oner *et al*., 2008) Transaminases like ALT and AST play significant role in amino acid and protein metabolism and they may release into the plasma following tissue damage and dysfunction. Different factors such as life history, water quality, exposure duration and cadmium concentration influence ALP activity. The decrease in ALP activity might be a result of disturbance of the membrane transport system, although the increase in the activity may be related to tissue damage. (Gagnon *et al*., 2006) There is distinctive evidence of significant effect in plasma enzymes (AST and ALT) by exposure to cadmium in marine fish *Mugil seheli* and after a transient reduction during the first few days, with an increase in the activity of enzymes reaching levels similar to the control value (El-Naga *et al*., 2005).

There have been multiple reports in alterations in the level of different enzyme levels apart from ALT and AST. A reduction in the activity of LDH was reported in the teleost fishes, *Channa punctatus* and *Heteropneustes fossilis* when subjected to the heavy metal, mercury (Gupta and Sastry, 1981). Mercuric chloride changed the levels of pyruvate and lactate dehydrogenase and inhibited the dehydrogenase activity in fresh water mussel, Parreysia rugosa (Reddy and Chari, 1985) Exposure of Heteropneustis *fossilis* to a sublethal concentration of 0.3ug/l mercuric chloride inhibited the activity of alkaline phosphatase, adenosine triphosphate and glucose-6-phosphatase, but elevated the activity of succinic dehydrogenase, pyruvate dehydrogenase and cholinesterase in the brain tissue (Sastry, Sarma 1981). Exposure of teleost *Sarotherodon mossambicus* to mercury significantly decreased the activities of the succinate dehydrogenase, lactate dehydrogenase, glucose-6-phosphate dehydrogenase, alkaline phosphatase and acid phosphatase. Similarly, exposure of Tilapia mossambica to cupric chloride decreased the succinic dehydrogenase activity and significantly increased the lactate dehydrogenase activity. (Bala Venkata Subbaiah *et al*., 1984) Heavy metals also have a [profound effect in the embryos. Rao *et al*. (Kazi *et al*., 2008) showed that the sub-lethal lose doses of mercury and lead brought about a reduction in the size of the embryos and even failure of parturition in the scorpion, H.fulvipes. Heavy metals are naturally occurring inorganic elements which are present in very small amounts in the living tissues but are important for the vital processes of life (Kazi *et al*., 2008). Some metals (e.g. magnesium) are known as macro-metals and are found in high amount in the body tissues, therefore they are also called macronutrients (Simsek and Aykut, 2007). Mercury (Hg), Chromium (Cr), Nickel (Ni) and Zinc (Zn) are most naturally occurring whereas lead (Pb), Cadmium (Cd), Copper (Cu) and Arsenic (As) are the direct consequence of human environmental pollution (Chen *et al*., 2016). Heavy metals are involved in a range of physiological processes such as prosthetic groups of many proteins, water balance, cofactors of many enzymes etc. (Fraga, 2005). Heavy metals are known to affect the reproduction and development of organism. They are also believed to have an impact in the biochemical constituents and bring about the decrease in carbohydrate, proteins and lipids. They are linked with the many visible changes in the animal models that can range from the decrease in hepato-pancreatic weight to hepato-somatic index. (Rao *et al*., 2017) The exposure of heavy metals, in particular Pb,Cd,As, and methylmercury (MeHg) directly interfere with brain development and results in cognitive impairment. Several studies have reported that the imbalance of some essential metals might adversely affect pancreatic islet and cause development of diabetes (Chen, 2009). The exact mechanism of their toxicity is still unknown but their synergistic effect is well defined (Karri *et al*., 2016).

The human health risk of heavy metals exposure is a public health problem. In a more recent study, investigators of environmental mercury exposure found that for every 1,000 pounds of mercury release, there is a 3.7% increase in autism rates of school age children living near coal fired power plants (Palmer *et al*., 2008). Severe zinc deficiency, allow copper to reach toxic levels in membranes leading to lipid peroxidation and cell damage (Geier and Geier, 2007). Uncontrolled pollution and industrialization might be a potential source to expose human population against toxic metals such as lead (Pb), nickel (Ni), cadmium (Cd) and arsenic (As). Some of the toxic metals are implicated to disrupt the glucose uptake and alter the related molecular mechanism in glucose regulation (Kazi *et al*., 2009; Serdar *et al*., 2009).

Major advances and discoveries

Animals and human get many of the same illnesses. Medical research with animals is one type of medical research, but other types include experiments with cells and chemicals and simulations on computers. Animal research usually describes research involving vertebrates, such as cats, mice, frogs, pigs, and primates. All medical research is carefully planned, and this includes medical research with animals. Under federal law, all animals must be treated humanely and undergo the least distress possible. Medical research with animals saves Lives. Dog- discovery of insulin, monkey-- polio vaccine, mouse-- rabies vaccine, pig ---skin grafts for burn victims and computer-assisted tomography (CAT) scans, rabbit-- corneal transplants, rat--carcinogen screening.(National institute of health) (NIH). Nearly 60 years ago thalidomide was prescribed to treat morning sickness in pregnant women. What followed was the biggest man-made medical disaster ever, where over

10,000 children were born with a range of severe and debilitating malformations (Neil Vargesson, 2015).

History and mechanisms

The subtle effect of Thalidomide tragedy resulting in phocomalia, apoda etc in the offspring led to untold miseries. The drug Thalidomide caused an estimated 10,000 birth defects and thousands of fetal deaths worldwide. The affected babies typically suffered from phocomelia, a failure of the limbs to develop. These unfortunate babies were cruelly referred to as "Flipper babies". This drug formerly used as a sedative, but with drawn in the early 1960's after it was found to cause congenital malformation or absence of limbs in children whose mothers took the drug during early pregnancy. Thalidomide is a sedative that used to be prescribed to treat anxiety, tension, gastritis and insomnia. It was also used to relieve morning sickness in pregnant women. There are similar good number of cases of fetal deaths, still births, terratogenices etc. The young ones of mothers exposed to toxic ants like pesticides, radiation, heavy metal etc. Can we save innocent lives growing in the wombs of the mother from becoming the victims of hostile environment that cannot avoid. This was the question that was prompted me to choose the topic of my research. Women working in metal industries smelter and other industries where heavy metals are used always run the risk of impact of heavy metals on the fetuses. Doing research with human subjects is illegal and unethical. So I have to go non-human material which stimulates human being. Viviparity is common among est mammals but not many provide long gestation period.

Significant gap in research

There are two major challenges, designing a drug that could potentially target the multiple path ways involved and developing models that would help rapid screening of potential drugs. Most drugs in the pipeline have failed in clinical trails.

Current Debate

To study the long term effects of the toxic-ants on the fetal development.Rats have 21, rabbits 30, dog has 60 days gestation period. Where as gestation period is long as in case of sheep, horses, monkeys, elephants, they are not available because of cost procurement and maintenance. So in this situation scorpion comes handy, cheap, available, viable and reliable, with viviparity and long gestation period. All scorpions have a long gestation period. It goes from several months to a year and a half, depending on species. The young scorpions develop as an embryo in the mother's uterus. During this time, the embryo gets food from his mother. Hence scorpion was chosen as a medical research model. It is not enough, that we discover that the polutant effects the mother and the fetus. In several ways but not to overcome these effects in more important to live in the toxic circumstances with out toxic impact.

Ideas where research go next

It is found in my research, by administering the chelating agents like Dimercaprol (BAL) to the heavy metal exposed mothers the adverse effects of Mercury and Lead on both mother and the fetus could be elevated. Extrapolating to humans, it is possible to protection to the fetus of industrial workers by monitoring the heavy metal lode periodically and administering the appropriate dose of antidote. Of course, much work on these lines is needed before we can carry it over. If I am permitted to suggest, i may say that there is enormous scope for us in the medical field to contribute to science and human welfare by taking research of this type and doing collaborative work with other professors of different universities.

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