Animal models of Tumor: Current Status

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Abstract

Morbidity rate is increasing day by day due to diseases and tumor is the playing a very important role in increasing morbidity rate now a days. It is spreading all over the world in all age groups it is chronic disease. If it remains untreated at the early stages, then it may convert into cancer. So, it important to treat this at the early stage by using different supplements and drugs. An animal model is usually for the preclinical studies that are done before the clinical trials on humans. It is done for the safe use of drug in humans. The most used animal models are rodents. Animal models are very helpful in studying the new drug molecules as life span of animals are short, so they are helpful in conducting the pre-clinical studies. There is different type of animal models which are helpful in inducing cancer and its study like chemical induced model, radiation induced model, genetically modified animal model etc.

1. Introduction

In today's world there are many acute and chronic diseases which are spreading all over the world, tumor is one of the most common and serious disease among them. Tumor is the second largest disease which is spreading more day by day in every age group. It is one of the main reasons for the increasing morbidity rate of the world population because of any disease. It is very common now a days, as it is there in one of the ten persons. It is common with every age group and every part of the body. It is differed from cancer only in the way that it is not spreading to other parts of the body and remain confined to the one part of the body. There are many types of the treatments available for tumor including surgery, chemotherapy, radiations etc. There are many kinds of the allopathic medicines which are available for the treatment of the tumor, but they are having many side effects like alopecia, vomiting, nausea, blurred vision etc. As we cannot study the effects or reactions of drugs which are newly developed directly in the human beings so there are some preclinical studies which are done in animals for checking the accurate effective dose and other reactions of drugs in animals and find the accurate dose with minimal side effects for treating any kind of the disease. To check the activity of the drug firstly we have to induce the disease condition in animal so that we came to know whether the drug is effective to treat the symptoms of the disease or be able to cure the disease. Animals used for the tumor induction are usually rodents. Some of the animal models for cancer development are discussed in this review [1]. Mostly used animal models for the cancer studies are rodents as in them the life span is small, and the results are seen within lesser time. The chemicals which are used to induce cancer in animals are known as carcinogens [2]. There are some chemicals which are so much strong that they do not require any other treatment to cause cancer and these are known as the complete carcinogens. Most of the carcinogens cause DNA damage. There are some agents which are known as the Genotoxic agents, they are carcinogenic in nature and act as "initiating agents" for cancer progression. After the first treating with genotoxic agent further progression is done by using other chemicals which cause damage to the tissues which are earlier exposed to the genotoxic agents. Some non-genotoxic agents are also there which can cause

cancer in both humans and animals [3]. After the tumor development the spread of tumor to other sites takes place and it is known as the metastasis. The greatest achievement in the last decade is that now cancer is easily elucidated in the molecular level. The cancer can be caused by the different agents they can be chemicals, viruses, radiations etc. Animal models are very much helpful in studying the human diseases and identifying the drug targets at the molecular level and giving safe doses in clinical trials is done only through the pre-clinical studies [4].

2. Animal models used for tumour

2.1. Mouse model for the hepatocellular cancer induction: A unique mouse strain was created and inbreeded by mixing the two mouse strains from different mice. All mice were given same kind of environment of temperature and light and diet and were euthanized at different time periods following diet intervention. Male mice of 812 weeks age were fed with western diet (WD) with a high amount of sugar solution (fructose + glucose). Chow diet with tap water was given to control group. Mice fed with WD and sugar water (SW) gains weight and become obese at faster at as compared to group given the CD. Mice which was given the WD SW is showing tanning in liver and control was normal, it was continued for 52 weeks. At the last week the nodule formulation was seen in the mice which are given WD SW and foci of tumours were also there in them and hence the tumor is induced in them. The mice which are provided with the CD are not showing any kind of nodules and are safe [5].

2.2. Chemically induced colon carcinogenesis rat model that mimics human disease: Chemically induced-colon carcinogenesis was carried out in KAD rats [6]. The subcutaneous injection of AOM was given to male KAD rat of 5 weeks. Then after the Aom injection in next first week they were given 2% DSS in tap water. Five rats were used to find the tumor volume and lesions upto week 8. Then these rats were divided into five groups in which colon lesions are same. Tumour bearing rats are treated with the 5FU intravenously at week 9, 10 and 11 with two different doses of 50 and 75 mg/kg. One week withdrawal period was there and after one week again for other three weeks 5-FU was administered. At 16 week the animals were sacrificed. Then the animal was fixed in the neutral 10% formalin solution for at least 24 hours. After that it is observed for the colon tumours and kidneys, stomach and other parts are observed for any kind of abnormalities [7].

2.3. Genotoxic and non-genotoxic induced animal model: Genotoxic agents or chemicals directly interact with the DNA and forms DNA carcinogen complex [8]. One of the best example of the genotoxic agent is DEN. After the administration of DEN it is metabolised in liver and results in DNA damage [9], a repeated dose of pro-fibro genic agent is given it will cause oxidative stress. The pro- fibro genic agent used is carbon tetrachloride [10].

Non genotoxic carcinogens does not interact directly with the cell DNA. They damages the cells and results in hepatic damage by increasing the genetic error. These types of the cancer inducing agents are not used alone, they are combined with the genotoxic agents to induce hepatocellular cell damage and fibrosis in the mice model [11]. In case of the non-genotoxic agent carbon tetrachloride is the best carcinogen model with respect to the development of fibrosis or tumor in mice model [12]. Other chemicals used are thio acetamide

and phenobarbital. They are given repeatedly upto some weeks and at the animal is sacrificed and tumor volume is checked and hence induction is done [7].

2.4. Ehrlich ascites carcinoma model: The phosphate buffer saline was used to dilute the cells. Then the cells were aseptically introduced in the animal through injection. The cells need to be viable to induce cancer so trypan blue was used to check the cells viability. The normal saline was used to dilute the ascetic fluid so that we can get the desired concentration of cells in the body for tumor induction [11]. Now the thirty six mice were taken which were fasted overnight and were given 0.25 ml of the prepared solution to obtain the tumor cysts. The mice were observed for behavioural and other changes at different time intervals the samples were collected from the mice to check the tumor growth and tumor volume. In this way induction of tumour is done [12].

2.5. Lung cancer mouse model based on dye trace method: The mice were taken and all of them are kept constant for breeding at particular temperature. The urethane solution was introduced in the bodies of the mouse intraperitoneally at the dose of 600 mg/kg, it is given for 10 weeks and given only once in a week. The 0.5% solution of CMC-Na was used to dissolve the urethane, it is acting as a vehicle. In first group 2mg/kg of shikonin was injected to mice, second group was given with 0.2 mg/kg of aconitine and the notoginseniside 20 mg/kg was given to third group and fourth group was given with the mixture of the shikonin+aconitine+notoginsenisiden and the dose of these are same as they are given individually and the group which is acting as a control one is given dose of sodium CMC every day for 20 weeks. The physical and the behavioural changes along with death of mice were recorded continuously [11].

2.6. Mouse fibro sarcoma model for tumour induction: In this swiss albino mice were taken which were kept in house as per the protocol, the mice taken were of 20 to 25 grams. They were kept under normal conditions of light and dark cycle and humidity and temperature control. A mouse fibro sarcoma was developed in the mouse which was then further transferable and used as the solid tumor in animal study. The tumour induction was started and then the progression is there in the tumour. After the induction of the tumor the tumour diameters were checked and measured regularly with the help of the vernier calliper. The change in the diameter of the tumor was indicating the progress in the tumor growth. When the tumour increases to a certain limit in mice then they are divided into groups with 6 in each group. The percentage increase in weight of the animal was taken as the increase in the tumour volume. The comparison between the weight of the animal before induction of tumour and after the tumour induction is done to know how much tumour is induced in the animal [12].

3. Discussion

An animal model is usually for the preclinical studies that are done before the clinical trials on humans. It is done for the safe use of drug in humans. Animal model can be of any non-human species but mostly rodents are the ones which are used for the clinical studies. The experiments which are prohibited on human beings are carried out on animals. The most used animal models are rodents. Tumor is the uncontrolled growth of the cells which are of no use. Benign tumor and malignant tumor are the types of the tumor. Benign tumor

is the tumor in which cells remain confined to the part of the body whereas in malignant tumor cells will go to the other areas of the body. When the benign tumor remain untreated it will turn into malignant tumor and causes cancer. There are many drugs available for treatment of the tumor like Priviso, *Relaxium lactium* etc. but they are having several side effects which makes the need of the development of the drugs which will be having minimal side effects. There is a need for the development of the animal models so as the side effects of the drugs will be known to us at the initial levels. Animal models are very helpful in studying the new drug molecules as life span of animals are short, so they are helpful in conducting the pre-clinical studies. Moreover, the anatomy of internal body of animals mimics the anatomy of the human beings and as we know we cannot study the new drug molecules directly onto the humans so they play important role for the testing of the new drugs or modified drugs. As in the case of the carcinogens they are directly or indirectly causes the damage of the DNA by increasing genetic error or by rupturing the tissues. Similarly there are some drugs which can cause the tumor if they are taken regularly such as phenobarbital's so they are used as the cancer inducing agents and induce cancer in animals other than that tumours can be transplanted in the animals also or there can be some genetically modified models also which can induce cancer in patients and can be used to study the anti-cancer drugs.

4. Conclusion

The result of this study is indicating that the animal models are very helpful in inducing cancer and then studying the therapeutic activity of the drugs in treating the cancer. As the cancer is the second largest spreading disease in the world and it is life threatening also so there should be some models in which we can induce cancer and provide conditions as that in humans so that we can check the efficacy of the previous drugs and whether the new drug molecule is showing any effect in any concentration or not. So, it is very important to develop some new models to eradicate the alarming conditions of the disease and helping the people to overcome the problems of tumor. With the advancement or development of the new animal models there will be decline in the morbidity rate all over the world as we can test the new drugs in shorter time in those models. So, there is a dire need of the animal model development for the sake of the people welfare.

4. References

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