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ETHICAL ISSUES IN NANOMEDICINE

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The scientists are moving ahead with their research in nanomedicine but the laws and ethics pertaining to the humanity are lagging behind. It is expected that the time has come to address the social and ethical issues concerning nanomedicine in order to be prepared for the upcoming adverse events. It has also been fully understood that the toxicological analyses in the animals is not fully representative of humans and the potentials risks associated is still untapped. This short review would briefly address the ethical issues related to nanomedicine to hold a short discussion based on science to assess the safety and efficacy of the nanomedicine.

Key words: nanomedicine, bioethics, nanoethics.

Etički izazovi nanomedicine. Znanstvenici napreduju u svojim nanomedicinskim istraživanjima, ali zakoni i etika koji se tiču čovječanstva kasne za njima. Trebalo bi očekivati da će se obratiti pozornost na socijalne i etičke izazove koji su povezani s nanomedicinom, kako bi se moglo suočiti s nadolazećim neželjenim događajima. Trebalo bi se u potpunosti shvatiti da toksikološke analize na životinjama ne mogu savršeno predstavljati analize na ljudima i s time povezane moguće rizike. Ovaj kratak pregled sadrži svojim sažetim upućivanjem na etičke izazove povezane s nanomedicinom znanstveno utemeljenu kraću diskusiju u cilju procjene sigurnosti i učinkovitosti nanomedicine.

Ključne riječi: nanomedicina, bioetika, nanoetika.

INTRODUCTION

Nanomedicine is a term which can be used to define the application of nanotechnology in medicine. It deals with the particles in the size range of 100 nm or lower [1]. It includes a variety of drug delivery systems in the nanosize range such as nanoparticles, liposome, cubosomes and hexosomes, drug delivery systems based on carbon nanotubes, fullerenes, nanoparticles based on chitosan and alginates; there are many examples available in the literature with potential disease fighting strategies.

The European Science Foundation defined nanomedicine as “the science and technology of diagnosing, treating, and

preventing disease and traumatic injury, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body [2]”.

The market analysis reported that market for the nanomedicine is continuously growing at the rate of 28 % with a 35% increase in the revenues generated [3]. The National Science Foundation estimated the market for all nanotechnologies to be \$1 trillion. Huge investments are being made in nanomedicine to develop novel therapeutic deliveries. United States govt. sanctioned an amount of \$3.7 billion for nanoscale and

engineering for the fiscal year 2003-08 and the annual expenditure on nanomedicine in United States has increased from \$117 billion in 1992 to \$366 billion in 2010 [4].

The race is on and all the industrial nations are investing in nanomedicine with varying budgets making it a global business. Currently 38 nanomedicine based products are on the market with estimated sales of \$6.8 billion and the efforts to bring them on the market are increasing continuously [5].

It is understood that nanomedicine has potential solutions to many of the

medical problems but the ethical issues concerning nanomedicine are still untapped.

Science is continuously progressing but the ethical issues are lagging behind and some investments should be made to fill the gap between science and ethics.

This review illustrates some of the ethical aspects concerning nanomedicine such as risks associated to environment and human body and the socioeconomic impacts of nanomedicine.

RISKS AND TOXICITY ASSOCIATED WITH NANOMEDICINE

Nanomedicine is generally formulated out of polymeric materials which are selected on the basis of their biodegradability, biocompatibility and their encapsulation properties [1]. It cannot be generalised that these materials would be safe if long term consideration is taken.

The nanoparticles can have off target effects such as triggering an immune response, crossing blood brain barrier and affecting CNS or can cause tissue toxicity if not properly eliminated [6]. Several toxicological responses of nanomedicine based on *in-vivo* characterization have been reported such as hypersensitivity reactions, element specific toxicity and generation of reactive oxygen species [7]. There is a need for a detailed examination of the physico-chemical properties of nanoparticles such as size, shape and surface chemistry and correlating them with their *in-vivo* behaviour could help in understanding the most important technical issues and also for the development suitable models for studying nanotoxicity [7].

There might be some difficulty in conducting the clinical trials for novel therapeutics because of their complicated nature and the long term pros and cons of

them are still unknown. This will create a problem in getting an informed consent from the subjects. Therefore, it becomes an obligation for the sponsors to follow the subjects for a long time which in turn would increase the cost [8], [9].

In 2006, there was a disaster during the clinical trial phase-I study; 6 healthy volunteers were recruited and administered with TGN 1412 (CD 28 MAB) intended for the treatment of rheumatoid arthritis and lymphocytic leukaemia. It was humanised monoclonal antibody and CD 28 receptor agonist. The drug was administered as intravenous infusion and within half an hour all the subjects suffered from life threatening conditions. So it was concluded that *in-vivo* behaviour in animals is not a true representation of humans and more work is need to be done to reduce the risks involved in the clinical trials [10]. Carbon nano tubes based nanomedicine has triggered such immune responses in animal models [7], [11].

The safety of nanomedicine has to be thoroughly examined due to their unpredictable nature, before coming to the trials in human. Significant side effects could also pop up even after phase-III

clinical trials for e.g. a recent report published in Times of India on 17-May-2012 [12] stating the potential hazards of

azithromycin an antibiotic used in treatment of bronchitis. The learning process continues but should not be at the cost of human lives.

ENVIRONMENTAL RISKS

National Science Foundation and Environmental Protection Agency have raised concerns over potential impact of nanomaterials on the environment and the adverse effects have been reported [13]. The possible excretion mechanisms are suggesting that it would be mainly disposed in water and air. The excretory materials would mostly be suspended in air for longer times due to their small size which can cause respiratory disorders and affect the health of individuals [14].

There is a need to ascertain the behaviour of nanoparticles in the surroundings and its long term impact keeping a question in mind “Are we creating another class of non-biodegradable materials?” as they are not biologically inert. The effects are mostly unique and could be seen in the years to come but it is highly advantageous to constantly follow up the advances in the research to create grounds for future.

SOCIAL ISSUES

There is no doubt that nanomedicine can make a significant achievement in medical science but there will be some socioeconomic issues. Firstly, the prices would be very high as the products would be protected by patents till the patent expiry [15]. This would be for a short term but the patients from the low income groups would be deprived of these novel therapeutics and the developing nations would be affected most.

The products would be manufactured in developing nations because of the cheap labour; it would be difficult to afford medication for them. This will create not only socio-economic barrier but could also

promote radical feelings in the individuals. The intellectual property (IP) is generally acquired by the multinational companies and because of their commercial interest the prices are high and economically poor people could not be provided with the medication. It has been reported that some of the patent laws are providing an unjustified economic advantage for some over others [6].

There is also a need for planning the health budgets for the future, as nanomedicine could increase the life span of the people and the population of elderly would increase and also the expenditure.

DEALING ETHICAL ISSUES

The studies on nanomedicine should not be mainly limited to the biopharmaceutical companies; there should be significant involvement of bioethicists, philosophers and environmentalists and jointly progress the research. The journalists should be involved at an early stage of research so that the information reaches to a common man. They would also prove helpful in forming a public opinion which could prove beneficial in later stages such as for the clinical trial. There may be need for the amendment in the rules by authorities in order to adjust the properties of nanomedicine pertaining to their exposure at work place and also to the environment [14]. As discussed earlier, IP issues creating economic disparity; there is need for harmonisation of the international patent laws to promote global justice and fair pricing schemes to developed and practised [15].

Beauchamp and Childress have proposed a very nice theory on bioethics.

Their theory covers some of the most important ethical aspects concerning nanomedicine such as Autonomy, Beneficence, Nonmaleficence and Justice. According to Beauchamp and Childress, their theory could be find place in every part of world as principles are based on common morality [16]. They also mentioned that application of ethical principles should more situation and context dependent and criticised the direct application of universal principles; without any substantial evidence and the approaches should be narrowed down towards the practical application of principles.

The science is continuously progressing and theories should be amended in accordance with the emerging ethical problems. According to Beauchamp and Childress the principles are to be treated as basic guidelines and situation dependent critical analysis of is to be done in order to enhance their applicability [16].

CONCLUSION

Nanomedicine will be coming up with some ground breaking advances in medical sciences but the current knowledge on the safety profile is very limited.. As there are no specific regulatory guidelines for the approval of the nanomedicinal product; it is suggested that individual applications should undergo risk based

assessment to ensure the safety of the product. The theory given by Beauchamp and Childress signifies the progress on the ethical side and there is possibility to extrapolate it for nanomedicine. Close collaboration of bioethicists with scientists in nanomedicine would prove more beneficial on a long term basis.

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