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Nanotechnology Applications and Approaches in Medicine: A Review

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Abstract

The emerging scientific field of Nanotechnology enabled humanity to manipulate the environment at molecular and atomic level and it promises to revolutionize all scientific fields due to its features. Medicine is one of the prominent fields that witnessed a nanotechnological revolution that ushered medical scientists toward wholly new authentic approaches which study pathologies and explore genuine therapeutic stratagems by utilization of nanotechnology to operate on more specific molecular targets and to reduce the adverse risks and side effects that conventional approaches impose on patients. To take a better view on the impact of nanotechnology on medicine. The ramification of this technology shall be explored in terms of medical outcomes. It will reduce societal and financial expenses related with human services, offer early location of pathologic conditions, decrease the seriousness of treatment, and result in enhanced clinical result for the patient. The most promising treatment for cancer is nanotechnology that can be used in treatment and detection. The current treatments for cancer is ineffective with high chances of tumors to grow again and resistant to the treatment which makes it worse in addition to the severe adverse effect of the current treatments. The early detection of cancer can elevate the chances of curing and prevent recurrence, however the technologies and methods used in detection is limited and ineffective which worsens the condition. Intracellular drug delivery and photothermal ablation are promising treatment for cancer. Prostate cancer affects over 2.5 million Americans, but there is an unmet need for targeted treatment with minimal systemic toxicity, especially for metastatic disease. Prostate cancer tumors are characterized by a mixed cell population which is hard to target one treatment for different kind of cells.

Keywords: Nanotechnology; Nanomedicine; Medical ethics

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Introduction

Nanotechnology in medicine

Nanotechnology revolution is the next giant step in science that sets humankind in control of a wholly new dimensions and enable them to manipulate the environment at molecular level. Gökçay and coauthors stated that nanotechnology will lead to a second industrial revolution due to its potency to be applied in nearly every scientific field [1]. Some of these applications including nuclear reactors, transportation industry, cooling of transformer oil, electrical energy, mechanical, magnetic, cooling of microchips, solar absorption and biomedical fields [2,3]. These technology characteristics of high surface volume ratio, significant magnetic forces and vander wall forces photolytic activity and water solubility permit the treatment and manipulation of situations at atomic level [4]. Furthermore, the significant applications in different sectors of science increased the demand and development of nano systems and nanomaterials and expected to hit $3 trillion across global economy by 2020 [4]. The nanotechnology entered and made major changes that skyrocketed the possibilities to wield the power and control of diseases and extend the understanding of pathogenesis and identify the most microscopic and decisive step in the process and target it for cure and drug delivery which again will be through the use of nanotechnology (nanotherapy). The different view that Nano Medicine provides healthcare workers about pathogenesis of the diseases and the ability to detect the slightest change in blood chemistry or in any organ would call into question what it means to be healthy.

Under what conditions the human would be considered healthy. The ability of Nano Medicine devices to detect and spot the subtle molecular changes and DNA mutations may be not enough to consider that individual is ill. For example, it would be debatable whether an individual can be considered cancerous if a gene mutation that playing role in cancerogenesis is detected [5]. To take a better view on the impact of nanotechnology on medicine. The ramification of this technology shall be explored in terms of medical outcomes. They reduce societal and financial expenses related with human services, offer early location of pathologic conditions, decrease the seriousness of treatment, and result in enhanced clinical result for the patient.

According to a research group in John Hopkins University "In cancer therapeutics, one of the great challenges is finding how to specifically deliver high doses of chemotherapeutics to a tumor but minimize the systemic toxicity" [6]. Nanotechnology in medicine promises a new horizon in diagnosis and treating cancers through targeted delivery of drugs, genes and proteins specifically to the cancerous cells with minimally induced healthy cells injuries through the use of polymeric nanoparticles, liposomes, dendrimers and nano-shells. The possibility of cancer reoccurrence with multi drug resistance (MDR) imposes clinical limitations on the efficacy of the therapy. However, the use of targeted drug delivery and photodynamic therapy (PDT) to modulate the MDR mechanisms (cytotoxic drugs efflux, decrease in drug influx and surface receptors hiding) may be a promising technique to overcome MDR limitations [7].

The ever-increasing cases of diabetic patients worldwide urged researchers to improve the conventional methods of diagnosing and treating the disease. Current scientific endeavors to design and construct an artificial pancreas make utilization of the new possibilities created by the new field of nanotechnology. According to Ramirez et al., nanotubes can be implemented to measure and diagnose diabetes through its modulation of fluorescence emissions upon contacting certain biochemical molecules such as glucose or Langerhans isles-targeting antibodies found in type II diabetes [8]. Nanotubes built-in ability to sense glucose (hydrogen peroxide based detection system that uses glucose oxidase enzyme that catalyze oxidation of glucose to form hydrogen peroxide which is in turn oxidized electrochemically resulting electrons that generate current flow proportional to converted glucose amount) opens up the opportunity to develop artificial pancreas that detect the glucose level and accordingly induce the release of insulin without the need to manually supply it [8]. Nanotechnology application in field of pain managements can potentially alleviate the limitations of current acute and chronic pain managements strategies. Sprintz et al. pointed out that nanotechnology utilization in pain managements aims at improving patients' quality of life by increasing safety and efficacy of drugs with high precision of implanted wireless nano-channel silicon technology that delivers drugs to the noxious stimulation origin in response to biosensors feedbacks regarding blood concentration of pain markers, therefore decreases nearby tissue damages [9]. Furthermore, nonunion fractures and vertebral compression can be source of acute or chronic pain. However, Bio Nano Scaffold (BNS) improved the direction of treatment by creating controllable microspheres delivery system that release osteogenetic factors, antibiotics and stem cells around the fracture and promote directional and precise regeneration [9]. Therefore, nanotechnology established new perspectives and therapeutic strategies that aim to alleviate pain and better tissue regeneration ability with decreased induced healthy tissue damage or drug abuse due opiate prescriptions. Nanotechnology has been a subject of research for utilization in the field of cardiovascular system. Due to the processes of platelet aggregation in myocardial infarction, thrombosis, platelet-targeted liposomal drug delivery may prove to have potential therapeutic applications [10]. Liposomes nano-particles that contain PGE-1 has been designed for the treatment of thrombosis, periphery artery diseases and myocardial infarction due to its properties that allow the reduction of PGE-1 degradation and prolong the outcome of the drug [10]. Cardiovascular magnetic resonance (CMR) is an important non-invasive technique that detects inflammation and myocardial tissue configuration for early diagnosis and prognosis. According to Chandarna et al., gold nanoparticles have shown great promise in north cardiovascular medicine through optical imaging: photoacoustic imaging is based on detection of both ultrasound and optical imaging [10]. Therefore, cardiovascular researches could find their way to utilize nanotechnology-based approaches for diagnostic and therapeutic purposes in the field of cardiovascular system. Genes deficits are responsible for countless diseases and some of them are even lethal. Gene therapy is the medical intervention that replaces the defective gene with new gene in the cell using various methods including RNA interference (RNAi) which leads to defective gene silencing and down-regulation. Massadeh et al. points out that there are extracellular and intracellular obstacles that hinder the new genes and protein delivery to the cells due to rapid enzymatic degradation of the therapeutic materials in plasma, impermeability and off target silencing of genes that may lead to undesirable outcomes and exacerbations or even elicit unwanted immune response through activating interferons [11]. Polymer nanoparticles are non-toxic biodegradable particles with high biocompatibility that are used to overcome such complications. These particles are manipulated in order to fit the condensed DNA and proteins into the Nano structures, to permit their internalization within the cells and later regain their original shape upon internalization into the cell through physiological change in pH [11]. Magnetic nanoparticles made of iron oxide nanoparticles have been implemented as drug delivery system which have been guided using strong magnetic fields to deliver therapeutic materials into the desired site.

An application for using nanotechnology: Nanoparticles enhanced antibiotics

Bolocan and co-authors accentuated that the incorporation of antibiotics into nanoparticles such as hydro-dispersible magnetite nanoparticles (HMNPs) facilitates a better penetration into the tissues, the drugs could be released with a controlled and predetermined rate, for a sufficient period of time to reach the target site, that could significantly increase the therapeutic index and the efficacy of treatment against Gram negative bacteria and reduce the harmful side effects on the target organ [12]. Hasanova and co-authors emphasized the use of Antibiotics such as Ciprofloxacin and Kanamycin with Nanoparticles that was prepared in crystalline size (8-16nm) in self-assembling principles that rendered the antibiotics to be more substantial [13].

Obtained results demonstrated that these nanostructures are able to improve antimicrobial properties and decrease the minimal inhibitory concentration (MIC) of pristine kanamycin and ciprofloxacin antibiotics [13]. A study conducted by Saha et al. showed that the conjugation of Gold nanoparticles (Gnps) with antibiotics such as streptomycin and kanamycin yield a form of these antibiotics that exhibit a significant reduction in minimal inhibitory concentration (MIC), increase in bactericidal efficiency and greater efficiency in the remote area, where proper storage condition is unavailable [14]. Moreover, owing to the different mode of antibiotics mechanisms, the relative bactericidal activity of Gnps conjugated ampicillin was less effective than Gnps conjugated streptomycin and kanamycin whereas the MIC values of Gnps conjugated ampicillin decreased 10%, while the percentage decrement for Gnps conjugated streptomycin and kanamycin were 50% and 60%, respectively [14].

Literature Review

Nanotechnology uncertainty

Nano-objects notoriously possess unexpected new properties in virtue of their small size. Their qualities can be radically, and surprisingly, different from larger particles of the same substance. This scale effect is due to several factors: The surface to volume ratio increases, as well as the proportion of atoms that come in contact with surrounding objects; gravitational forces become unimportant; electromagnetic forces prevail; quantum mechanics laws become relevant; the strong Brownian motion of nanoparticles has significant effects. As a result, the nano-world behaves differently and unpredictably from whatever we may know. Our knowledge of the macro-word is not useful to anticipate the interactions at the nano-scale. In fact, we have to deal with a new kind of uncertainty. As in quantum mechanics, uncertainty and unpredictability are not a result of insufficient knowledge but are constitutive attributes of the situation. They are intrinsic and ontological features not just epistemic ones [15].

Nanotechnology, bioethics and medicine

In 1979, Principles of Biomedical Ethic, written by Beauchamp and Childress was published. It lied the most fundamental ethics based on series of ethical principles that concerned the medical practice and patient care and treatment [16]. It offered a way to approach medical dilemmas that health workers and scientists face throughout their careers. In addition, it was recognized by institutions that are related to medicine and human health to be the guiding principles in their careers whether training medical students and residents to those who participate on hospital ethics committees:

- Beneficence.
- Non-maleficence.
- Respect for autonomy.
- Justice.

These principles are the four pillars that constitute the core of all medical practices and scientists in general. It can be argued that the only possible ethics and moral value in personal life is what the individual finds valuable henceforth; being free from suffering is a condition found valuable by all sentiment creatures, e.g.: “humans” [17]. The respect of autonomy principle (capacity of free choice) in medical ethics is important; the patient (a rational agent) has the capacity to act and make moral decisions voluntary and intentionally without any external controlling influences because moral decision making involves agents that are informed and able to freely act [17].

To ensure transparency and respect for autonomy the patients should be informed of the design process of the device and its foundation and the intended use and function, in addition to the conflicting requirements. These should be documented and signed by the intended individual/patient. Where justice allows the offering of a procedure, and that procedure is not clearly against the patient’s interests, the patient should be offered the procedure and to assess her/him in the evaluation and judgment of whether the benefits outweigh the risks, according to his/her goals and life plans. Therefore, under the respect of autonomy, doctors and researchers have the responsibility of informing the patients of any plans and enough data and consideration of the process and any possible outcomes.

From the previous definition of the autonomy principle, we can predict the impact or the potential violation of nanotechnology to this principle. Technologies that are used in nanomedicine and brain implants raise serious ethical considerations as they are threatening the principles and codes of ethics that the field of medicine is working accordingly. For example, the respect for autonomy of the patients which implies the individual capacity for making choices in accordance with his/her believes and values and lives accordingly. Using neural dust therapies in treatment with the patient’s consent and awareness of the outcomes of this procedure is not the problem, however, the non-voluntary interventions on patients for experiences and mind control purposes are what bring the ethical dilemma. The different view that Nano Medicine provides healthcare workers about pathogenesis of the diseases and the ability to detect the slightest changes in blood chemistry or in any organ would call into question what it means to be healthy. Under what conditions the human would be considered healthy. Another implication that nanotechnology offers to scientists in medical field is Human Implantable Nano Devices (HINDs) that allow us to wirelessly collect data of internal body organs conditions such as temperature, pulse and blood glucose as well as correct organ dysfunction such as vision loss and hearing dysfunctions [18].

The principles of biomedical ethics that Beauchamp and Childress emphasized can come to conflict between each other when nanotechnology is applied in patient diagnosis or treatment. These principles can be Prima facie binding. A prima facie (means on first appearance but subject to further evidence or information) is available when a situation justifies a principle or action as prescriptive without being absolute Therefore justifies a course of action until it is outweighed by other prima facie that is hold to be more true [19].

The four biomedical principles are prima facie binding because all of the rules are equal and must be fulfilled but in some occasions they come to conflict therefore the agent must determine what they ought to do by finding prima facie right that is overriding or outweighs all other principles and act impartially in regard to all affected parties and the decision should not be influenced by morally irrelevant information [20]. Therefore, the biomedical ethics can be applied in order to measure the risks and benefits of nanotechnology utilization in medicine when applied to diagnosis and treatments.

Discussion

FDA and clinical trials

Any new drugs and treatments are set for clinical trials for approval. The drugs go through tests that evaluate the effectiveness and risks associated with the new treatments. The trials are pre-clinical, set on animal tests and then go to clinical double-blind tests. The trials may take several years in order to approve new drugs by FDA. According to Glenn and Boyce, the FDA approval for Nano Medicine devices are troublesome and time-consuming because this technology falls into several FDA categories and each one has its own regulations and criteria for approval [21]. Many limitations have been emphasized on the clinical trials related to Nano Medicine. Animal experimental studies that set for pre-clinical trials for minimizing the risks of nanomedicine have significant limitations. The first of these limitations is that there may be differences in the way that humans and animals react to the same material or substance. Because there may be differences in how animals and humans absorb, distribute, metabolize, or eliminate a substance or material, something that is not toxic to animals at a low exposure might be toxic to humans at a low exposure and vice versa.

A second limitation of pre-clinical research is that animal studies generally last from 28–90 days and rarely investigate the long-term effects of new drugs, biologics, or medical devices. However, some of the harmful effects of materials may only occur after many years of exposure. The three phases of clinical trials are inconclusive as well. Because it takes only seven years and post marketing studies ensues only for few additional years. These data can't give enough insight on future adverse effect. For example, genetic or tissue damage result on disease after 30 years such as lung cancer after exposure to tobacco.

The management of risks in clinical trials involves the identification and assessment of risks and benefits and balance between them through reason and justification of risks. And to have sufficient data and information on both sides of the equation. If the risks of a study are more than minimal, the benefits must also be more than minimal. Additionally, special protections for vulnerable populations, such as children, fetuses, and prisoners, apply to more than minimal risk research. It is important to distinguish between research that offers subjects a medical benefit, such as diagnosis, treatment, or knowledge about their condition, Risks to subjects that are much greater than minimal can be justified only if subjects are expected to receive direct, medical benefits. For example, chemotherapy can involve many different risks, such as nausea, weight loss, nerve damage, anemia, neutropenia, thrombocytopenia, fatigue, hair loss, infections, dizziness, headaches, emotional problems, and even death. Nevertheless, the risks of a phase clinical trial investigating a new chemotherapy agent can be justified if the benefits to the subjects (e.g., treatment) and society (e.g. new knowledge) are expected to be very significant. If the risks are more than minimal and the subjects are not expected to receive direct, medical benefits, the risks will be reasonable only if the risks are not much greater than minimal and the benefits to society are large. For example, the risks to subjects in Phase I drug trials are usually more than minimal, since Phase I studies are designed to study the toxic effects of medications in human beings. Nevertheless, the risks of a Phase I clinical trial involving a new drug can be justified if the risks are not much more than minimal and the benefits to society (e.g. knowledge gained and drug development) are great [22].

Conclusion

Nanotechnology is an emerging field that opens the doors for unprecedented new approaches and novel innovations for future progress and potential applications in various fields. Matters at scale of 1 nanometer (parts per billion of a meter) and 100 nanometer and utilize them in order to intervene and manipulate the atomic properties at molecular levels. scanning electron microscope (SEM), nanoparticle research, supramoleculer chemistry, molecular modelling, quantum computation, microelectronic mechanic systems (MEMS), light-emitted diodes, targeted drug delivery, molecular biotechnology, tissue engineering and more are all inclusive of the nanotechnological research fields list. This technology has been employed by many scientific disciplines. Since the human body works on molecular scales with complicated physiochemical properties. The nanotechnology entered and made major changes that skyrocketed the possibilities to wield the power and control of diseases and extend the understanding of pathogenesis and identify the most microscopic and decisive step in the process and target it for cure and drug delivery which again will be through the use of nanotechnology (nanotherapy). The use of nanotechnology in medicine invented nanomedicine. A field that manipulates nano-scale particles and use it for medical purposes. The medical field was able to bend this technology to its will and use it to explore any potential applications of this technology to overcome the current limitations imposed by contemporary diagnostic and therapeutic strategies. It has been applied in cancer, diabetes, cardiovascular and pain managements diagnosis and treatment by employing nanoparticles that sense the changes in cells' DNA and changes in blood biochemistry for screening as well as targeted drug delivery system to the specific desired site with reduction in induced tissue damage and adverse effects.

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