Chapter 1
Personalized Approach in Nanomedicine:
Understanding Adverse Effects and Their Risk Assessment

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ABSTRACT

This chapter characterizes need for new patient-specific approaches in medicine. The authors here illustrate role of nanomedicine and particularly nanotheranostics, combining diagnostic and therapeutic functions, in the paradigm of personalized disease treatment. This chapter discusses current insights regarding the mechanisms of nano-bio interactions and the origin of adverse effects of nanoformulations. Furthermore, this chapter illustrates possible reasons behind an individual physiological response to a given nanomedicine, such as type and stage of disease, physiological conditions and lifestyle of a patient. Finally, a review of possible approaches for the initial choice of nanoformulation, suitable for a given patient is provided at the end of the chapter.

INTRODUCTION

The current approaches to diagnostics and therapy, where the type of therapy and drug doses are selected according to the data obtained from a large cohort of patients, is accompanied by a number of severe adverse effects as well as cases of ineffective treatments. A need to individualize diagnostics and therapy according to the health status of an individual patient has become obvious and urgent. With the use of individualized medicine, clinical trials are likely to become more efficient by lowering the cost incurred due to drug's side effects or prescription of ineffective or potentially life-threatening drugs to the patients of certain genotype and in a certain physiological condition. Recent developments in nanomedicine offer

DOI: 10.4018/978-1-5225-0754-3.ch001

a great number of tools to achieve the target of personalized medicine. The most advanced creations of nanotechnology –nanotheranostics combine several functions and can be used for individual diagnostics, therapy and monitoring of the therapeutic response. However, due to the structural complexity, administration of nanoformulations can result in unexpected physiological effects. This chapter aims to discuss the current view on the interactions between nanoformulations and human body and to consider the determinants of these interactions. The importance of "personalized protein corona" formation and factors governing this process are reviewed in order to formulate the procedure of nanomedicine risk assessment for an individual patient.

BACKGROUND

Individual variability in disease course as well as in efficacy and safety of therapeutics is one of the main challenges in current clinical practice. Predisposition, progression, severity and recovery from diseases vary from patient to patient. Simultaneously, response of the patients to the same therapeutic agent can also vary significantly although diagnosed with the same disease.

A balance between drug efficacy and adverse drug effects determines clinical outcome of a medication. This balance can be calculated based on the concept of "therapeutic window". The therapeutic window is as a range of medication dosages that lie between a dosage with highest therapeutic effect and a dosage, which shows apparent adverse reactions (Figure 1 A). Smaller dosage gives sub-optimal therapeutic effect with almost no side effects while the higher doses enhance therapeutic effect, but at the same time evoke new or stronger side effects. In other words, within the therapeutic window, patients experience maximal therapeutic effect with minimum side effects.

As a rule, therapeutic window is determined for a large patient population. In current clinical practice, this *averaged therapeutic window* is a base for the choice of therapy. However, for most of medications, there are groups of patients, who have atypical dose-response curves for either therapeutic or adverse effect of the drug, or both. Application of a drug within averaged therapeutic window in these subgroups may result either in non-efficient treatment or in unexpected, undesirable and possibly life-threatening outcomes in these patients (Figure 1B and 1C). It is noteworthy that the probability of successful clinical outcome in current medical approach dramatically decreases in case of application of several drugs simultaneously. The lower probability for a patient to be within average therapeutic window for each of applied drugs can explain this.

Thus, there is a need to change the approach for the disease management from traditional "one treatment fits all" concept towards a more personalized medicine, where the individual health status of the patients defines a choice of the medical treatments. The concept of individual diagnostics and therapeutic strategy can already be found in Hippocrates' works: "Endogenously determined difference of human beings from each other together with age, physique, the season of the year" (Hippocrates, 1931) affect both the progression of the disease and how it responds to the treatment. In modern terms, diagnosis and therapy planning should take into account a combination of genetic, as well as physiological and environmental factors. Patient-specific approach in medicine would significantly increase the efficacy as well as safety of therapies and ensure that the medication is given only to patients who are more likely to respond to this treatment. This approach of personalized medicine can take health care to a higher standard with ultimate goal being "to help *and* do no harm".