Chapter

Risk Management of Zika in Context of Medical Provision and in Favor of Disaster Medicine: New Opportunities for Risk Reduction (The Conceptual Idea)

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Abstract

There is a need for timely medical care to the population for the risk management of Zika nowadays. Although scientists determine the widespread nature of the worldwide outbreak of Zika virus infection, it seems clear that there is a real need for outside help to deal with this disease. The Zika disease affects predominantly negatively the fetus in pregnant women, but cases of severe clinical manifestations are also reported among adults. Irrespective of age, it is known to affect the nervous system in humans. The vector causes epidemiological data to expand its area of expertise. In this light of expression, specialists define and attribute to this disease the type and significance of a worldwide disaster management. This requires an in-depth study and analysis of risk factors and their management as a fundamental approach for their prevention and for the benefit of disaster medicine. Reducing the risk with existing traditional tools and methods is not enough to meet the growing needs of people and territories at risk of Zika infection. New strategy approaches and technologies are being sought, and new risk reduction (RR) options are being interpreted. A framework for an innovative conceptual idea based on nano-biotechnology for risk reduction and prevention for Zika virus infection is presented.

Keywords: Zika, risk management, risk reduction, prevention measures (with SWOT analysis), medical provision of the population, disaster medicine, innovative conceptual idea, nano-biotechnology

1. Introduction

The World Health Organization (WHO) has declared the Zika infection an international threat to public health since the beginning of February 2016 [1–3]. The definition, classification, and analysis of the risk factors of the evolution and spread of Zika virus infection require the proper application in time and space of known preventive measures, as well as measures for the protection and medical provision of the population. The real challenge nowadays is to meet the growing demands of society, expanding the opportunities for highly effective risk reduction (RR) and incorporating new technological and strategic solutions to achieve rapid results.

2. Data and analyses of Zika in favor of risk reduction conception

2.1 Epidemiology and the spread of Zika virus: facts and analyses

It is a well-known fact that the Zika virus belongs to the *Flaviviridae* family of the genus *Flavivirus* [1]. The data indicate that the Zika virus was isolated in 1947 from Macaque monkeys in Uganda in the Uganda Forest to which it is named [1, 4, 5]. Retrospective analysis shows that the Zika virus was first studied by scientists at the Yellow Fever Institute (founded in 1936). Later, in 1948, the Zika virus was isolated for the second time in the tiger mosquito. Scientists have discovered the first manifestations of the infection by observing the effects of the virus on the Macaque monkey. Subsequently, the virus was isolated from the blood serum [4, 5]. During the next few years, the Zika virus underwent serious studies and in 1952 received its name in the virological nomenclature. In the International Classification of Diseases, ICD-10 is described under the code name A92.8 [6]. In humans, the virus is known to be the cause of the disease known as Zika fever or Zika disease, spreading since 1950 from *Africa* to *Asia* [7, 8].

Firstly, the data indicate that in 2014, the virus was *transmitted* across the *Pacific* to *French Polynesia*, reaching the shores of Easter Island. Secondly, the surveillance of Zika virus infection since the beginning of 2016 indicates an intensive *epidemic boom* with increasing prevalence of the disease in El Salvador, Venezuela, Colombia, Brazil, Suriname, French Guiana, Honduras, Mexico, Panama, and Martinique. Thirdly, in 2015 there were reported cases in Central America, the Caribbean, and South America, where Zika caused the development of a *pandemic*. It is also known that *sporadic* cases in Guatemala, Paraguay, Puerto Rico, Barbados, St. Martin, and Haiti are reported. According to the World Health Organization, Zika is spreading explosively and could affect 3–4 million people in the Americas. Furthermore, it is believed that the Zika virus was unknown to the US region prior to 2015. Finally, a retrospective analysis of the data indicates that nowadays Zika fever is a serious socially significant disease in the *US region* for which the resources available for its prevention, treatment, and control are scarce [1, 4, 5, 9, 10].

In 2013, there have been cases reported of the disease in *Europe* as well. From South America, tourists carry the virus to Europe. Ten Zika fever (ZVD) cases have been reported in Germany since 2013. There are four in Italy, three in the UK, and seven in Spain in the Zika virus case, as well as one case each in Sweden and Denmark. It is possible that the number of Europeans infected with Zika is much larger without themselves knowing it. According to the American Center for Disease Control and Prevention (CDCP), only one in five people infected with the virus develops the disease. The southern part of the European continent is generally of moderate risk for ZVD. The risk of Zika spreading in Europe in late spring and summer is described as "small to moderate," according to the WHO. The Zika virus is "highly likely" to spread to three European regions where there are tiger mosquitoes that carry it. These are the Portuguese island of Madeira in the Atlantic Ocean and the Russian and Georgian Black Sea coasts. For the other 18 predominantly Mediterranean countries, including Spain, France, Italy, Croatia, Greece, and Turkey, the risk is mostly considered moderate. According to the data provided by the WHO on the spread of Zika, the territory of Bulgaria is identified to be a moderate-risk country for this disease. Analysis of data from the World Meteorological Organization (WMO), the National Institute of Meteorology and Hydrology (NIMH) in Bulgaria, and the Institute for Atmospheric, Climate and Water Research (IACWR) at BAS (functioning from January 1, 2019) in Bulgaria about humidity, high summer temperatures, and the average altitude of the entire terrain of Southern Europe shows the increasing number of mosquitoes spreading the Zika virus [1, 9, 11–14].

2.2 Vectors facts and analyses of spreading ZVD

The infection is known to be transmitted to humans through the bite of infected mosquitoes of the *Aedes* family, most commonly the species *Aedes aegypti* and *Aedes albopictus* or the "Asian tiger mosquito." It seems that these two species are widespread in the tropical regions of Asia, Africa, and America. In fact, the tiger mosquitoes are native to Southeast Asia. The Zika virus was also isolated from *A. africanus*, *A. apicoargenteus*, *A. furcifer*, *A. hensilli*, *A. luteocephalus*, and *A. vittatus*. Generally, tiger mosquitoes can transmit dangerous viral and parasitic diseases to humans and pets, including *Zika*, yellow fever, St. Louis encephalitis, West Nile encephalitis, chikungunya, dengue, heartworm (in dogs and cats), and others [1, 3–5, 11, 15–19].

In *the USA*, it was proven in 1985 in Texas and Maine; in Hawaii in 1986; in Brazil, Argentina, and Mexico in 1988; in the Dominican Republic in 1993; in Paraguay in 1999; in Panama in 2002; and in Uruguay and Nicaragua 2003 [1–5, 17, 18].

It penetrated South *Africa* in 1990, Nigeria in 1991, Cameroon in 1999, and Gabon in 2006 [1, 4, 5, 10, 19] and *in the Middle East*—Lebanon and Israel in 2003 and Syria in 2005 [4, 5, 19].

The Asian mosquito originates from tropical and subtropical regions of Southeast *Asia* [1, 9, 10, 19]. In the last few decades, it has spread to many other regions of the world mainly through means of transport and intensive commodity trade. It was brought to *Europe* in 1979 in Albania in goods from China and has begun to spread massively along *the Mediterranean coast* since 1990. In 1990–1991 it was established in Italy, transported in old tires from the USA, and spread throughout the country, including the islands of Sicily and Sardinia. In 1999 it reached southern France and the island of Corsica. Other countries affected were Belgium in 2000–2001; Montenegro in 2003; Switzerland and Greece in 2004; Spain and Croatia in 2005; the Netherlands, Bosnia and Herzegovina, and Slovenia in 2006; Germany in 2007; Greece (in areas close to or adjacent to Bulgaria) in 2008; and Malta in 2010 [1, 4, 5, 9–11, 19].

In 2011, the presence of a tiger mosquito in *Bulgaria*, in Sozopol (Burgas region), was first established. In 2014 it was detected in Burgas and Plovdiv. In January 2016, there were also data on the spread of the disease vector in Bulgaria in the districts of Blagoevgrad, Pazardzhik, Varna, Vratsa, Montana, Plovdiv, and Stara Zagora. The risk of expansion of the territory in the Danube Plain and in the Upper Thracian Plain and the valleys of the Struma and Mesta rivers is real and is defined as high for the country during the warm months of the year [11, 19, 20].

According to the WHO, *the Black Sea coast* is among the most endangered areas in Europe in the spread of Asian tiger mosquito. The potential risk is identified in all territories [1, 11, 19, 20].

It is also known that the spread of mosquitoes, which causes the transmission of the Zika virus, develops in places with an altitude of up to 200 m. An interesting fact is that mosquitoes attack during the day, prefer humans over other warm-blooded animals, and hide and breed close to human homes [19, 20].

Research shows that mosquitoes are the only carriers of the pathogen, and the Zika virus infection can mainly spread to humans and monkeys. There is a serious risk of spreading the infection only if the viral infection spreads through humans and mosquitoes from areas of normal habitat to the European continent. This spread can be done by sick people arriving from Africa and America or by the direct infestation of mosquitoes from infected areas [1, 11, 19, 20].

2.3 The Zika fever facts and analyses

Studies show that the incubation period of the Zika virus is about 10 days; mostly it is known that people get infected first and foremost by tiger mosquito *bites* (Zika virus carrier). Some data indicated that ZVD can spread to other people through *sexual contact* and is directly infused and inoculated in the placenta [1, 2, 19].

The first case of a possible Zika virus *transfusion* in 2014 at the Hematology Center at Campinas University in São Paulo has also been reported [2, 7, 19].

The virus has been shown to damage the human nervous system and infect, damage, and kill the cells of the developing human brain even more prenatally, disrupting the localization of a pTBK1-protein, the protein that helps in cell division of the growing brain. The scientific community also discusses the link between Zika and microcephaly or congenital anomalies in newborns whose mothers became ill with the Zika virus during pregnancy. After 2014, the disease is associated with Guillain-Barré syndrome, which has been reported in some of the patients with ZVD [15–20].

2.4 Classification and analysis of Zika-related risk factors (author analysis)

The epidemiological data and the facts and analyses for the development and spread of the Zika vector and Zika virus are a good basis for elucidating Zika-related risk factors. Knowledge of risk factors, in turn, enables us to group them according to their type and nature and to give an idea of their classification. This is in favor of building a concise idea of a concept for the possibilities of the reduction and prevention of ZVDs at different levels and stages according to the specific needs and according to the stage of development of the disease from the moment of entry to the person in the distribution zone of Zika vector to the incidence of Zika virus in the human body.

2.4.1 From current conclusions to the conceptual models of ZVD (author analysis)

Nowadays the knowledge that we have about Zika virus infection provides us with some generalizing current conclusions that promise a better understanding of some conceptual models of Zika virus infection (**Figure 1**).

1. Zika fever is a vector-borne disease [1–22].

2. The Zika virus infection vector is also a vector of many other pathogenic viruses and parasites.

3. Practically, the vector spreads under high humidity and moderately high temperature at low altitude.

4. The vector is adaptive and easily enters new habitats through the transport of goods and passengers, mainly by means of water, rapidly increasing its population in warm and humid weather.

5. Climate change provides new threats to humans and new territories for the spread of the vector.

6. The virus spreads in parallel with the area of development and propagation of its vector but does not necessarily exist in all cases of typical habitat of its vector.

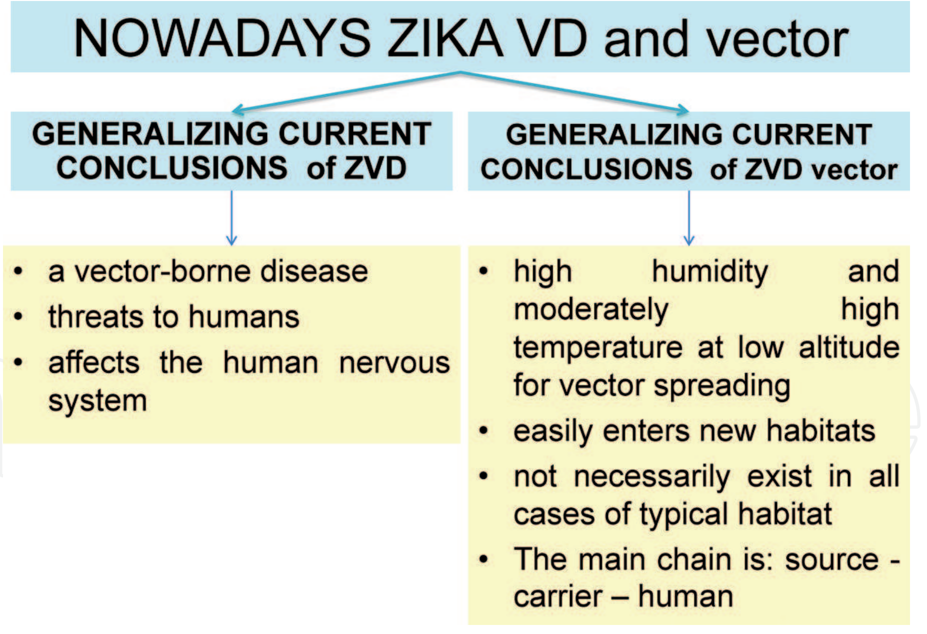

Figure 1.
Zika VD and Zika vector.

7. A prerequisite for the development of Zika fever besides the vector is the presence of a source in a susceptible population by a few chains.

8. The chain of infection with ZVDs can be represented in a few types. The main chain is source-carrier-human. Another chain is also possible: man-man in a vertical and horizontal direction. This is explained by the transplacental transfer (intrauterine infection) of the virus from the pregnant woman to the embryo and fetus, as well as by the transfusion of biological fluids physiologically or mechanically.

9. The virus affects the human nervous system, but not necessarily every person infected with Zika virus infection.

10. Probably the human immune system does not have a good enough response in time and space to stop the damage to the nervous system in every case of infection.

During the study of Zika virus infection, the following several questions arose (**Figure 2**):

1. Is global climate change likely to increase the risk of people with Zika virus infection, and is it possible to reduce this threat?

2. Is it possible to reduce the risk of vector spread of Zika virus infection, and can the population of the vector be reduced by a competitive species or other natural species?

3. Is it possible a mosquito vector to lose its role as a vector?

4. Can the vector be tilted in such a way that it does not affect the person with the bites?

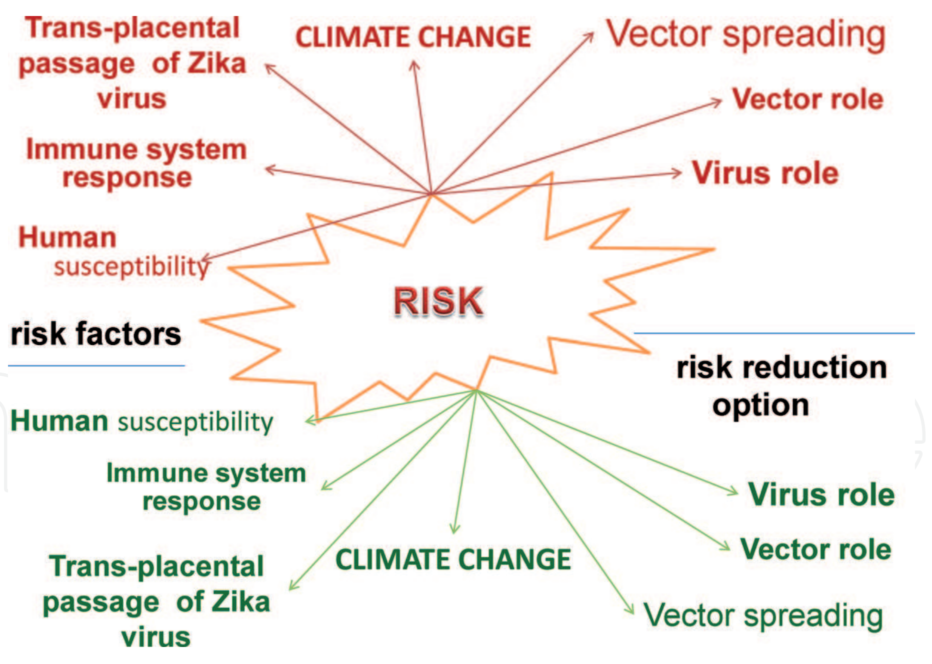

Figure 2.
New risk factors and risk reduction option.

5. Is it possible, if a mosquito bite (as a vector) humans, to stop the entry of Zika virus into the human body?

6. Is it possible to stop the Zika virus that has entered the human body during the bite of the vector?

7. Is it possible to reduce and/or completely stop human susceptibility to Zika virus?

8. Is it possible to understand the mechanism of the immune response in humans in which the Zika virus does not affect the nervous system, and are there other factors that support this course?

9. Is there a mechanism to support a person's immune response in such a way that no damage to the nervous system occurs?

10. Is it possible to prevent the transplacental passage of the Zika virus?

2.4.2 From groups of risk factors to the conceptual framework for modern technological approaches about ZVD (author analysis)

Some of the questions asked seem impossible and even naive in their search for possible solutions. However, the search for an answer, based on risk analysis, led slowly to the idea of a conceptual framework for modern technological approaches, in the hope of increasing the real chance of risk reduction in the process of risk management for the health provision of the population in favor of prevention and in the context of a disaster-prone process.

First of all, some groups of risk factors have emerged from a detailed examination of the available data on Zika virus infection [1–20].

According to the origin of their generation, there are two fundamental groups of risk factors, namely, natural and anthropogenic (**Figure 3**).

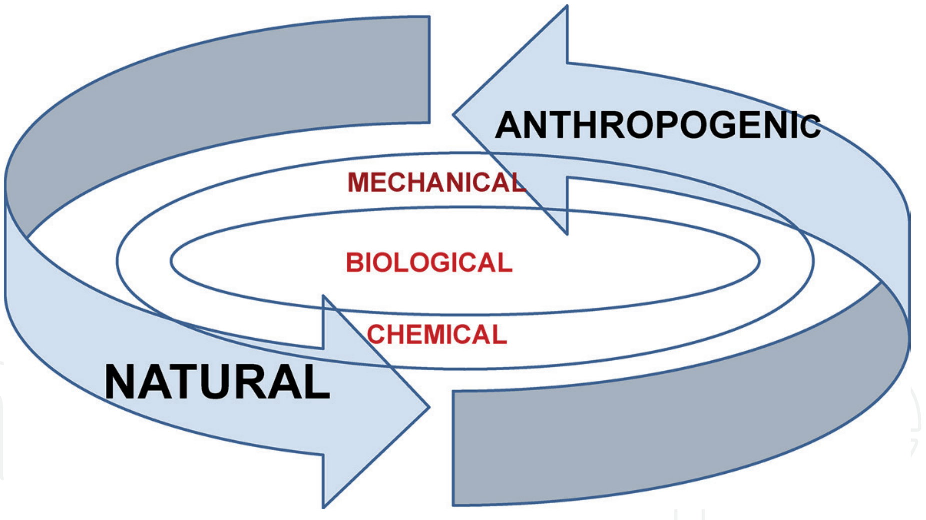

Figure 3.
Groups of risk factors.

Fundamental groups of risk factors can be divided into six main groups according to their type:

1. Risk factors arising from the environment (territorial risk factors, TRFs).

2. Risk factors resulting from the vector (VRFs).

3. Time and weather as risk factors (time risk factors).

4. Risk factors resulting from the population (receptivity, resistance, immune response).

5. Factors arising from human actions and/or inaction.

6. Factors related to knowledge and competence (scientific-cognitive) and the realization of ethical-legal and preventive-therapeutic ideas, methods, technologies, and concepts.

According to their mechanism, the risk factors can be selected as mechanical, physicochemical, and biochemical.

3. The Zika contemporary risk reduction conception

3.1 A brief look at preventive risk management measures (with SWOT analysis): from tradition to the future stage (author analysis)

Zika's strategic approaches about prevention are divided into three groups according to the moment of implementation of the specific tasks: before, during, and after the outbreak of the infection is occurred. In practice, these groups of methods are *strategic time-based approaches* to risk reduction. The timely application of this group of methods is also the responsibility for controlling the risk over time. On the other hand, the application of this approach leads to the reduction of disease territory, regression, and/or complete destruction of the risk areas (the occurrence of a hot and warm zone of infection within a particular territory) at a certain point in time. This is an important element of the health provision of the population (in a certain territory) over a period of time, not just the groups at risk, and is part of the national security. Ongoing control and extreme control are responsible for sporadic Zika infection and for controlling the risk of an epidemic outbreak. The inclusion of additional medical forces and resources when needed at a given time as a health policy results in a reduced response time to the massive nature of Zika disease in the short term. The specific aspects of this approach depend on the seasonality as well as the manifestations of the daily activity of the vector. The time approach is characterized by some cyclicality. Importantly, health-care decision-making considerations based on this approach require firmness, maneuverability, and agility. This strategic approach is a fundamental guarantor for the good control of the risk of Zika virus infection in a timely manner [1–27].

There are some known threats to invoking only these strategic time approaches. They are derived from the nature of the spread of the ZVD and namely through a vector. This requires that the health care of the population be stepped on the basis of *strategic territorial principle* [22] with emphasis on the environment and territory suitable for the development and dissemination of the vector. The control of the vector is possible and also depends on the close transinstitutional interaction, planning, and development of risk maps, as well as their strict updating and upgrading with new methods. Facilitated by appropriate local meteorological and global climate changes, the risk of a hot zone from a Zika virus is present and varies in extent and varies in space. The reduction and even destruction of the natural range of the vector undergo a health-sanitary control in collaboration with various professionals at every level of territorial division of the country—national, regional, and municipal levels. Cross-border cooperation is a fundamental step in the event of a high risk of spreading the disease outside the country. Migration and transoceanic transport of people and goods are factors facilitating the spread of the Zika disease. The globalization of the Zika disease proves the weaknesses of the territorial principle [1–20, 23–27].

Virus-based strategy, a strategic principle based on the viral genesis of the disease, the RNA genome of the causative agent, as well as its genetic variability, is being investigated. Insofar as there is predictability in specific parameters in the previous two principles, it is probabilistic in that. On the other hand, the creation of a specific vaccine and/or specific antiviral drug is a process of unknown duration, and time is proven to be an insufficient resource for the purpose of providing the population with medical care in the face of an epidemic. The laboratory demonstration of the virus both in vectors and in humans is an important step. However, the study and demonstration of Zika virus have its weaknesses, the main one being the recruitment of the necessary and sufficient scope of the study under the specific conditions for the construction of a strictly positive and strictly negative hypothesis for its presence. The process is time-consuming. The reliability of laboratory tests in terms of genomic variability of the virus requires both flexibility and a competitive environment for a prompt response by researchers and experts [1–20, 23–27].

Health education strategy for raising the health culture and awareness of both the population and health professionals is an approach complementary to the above, extending levels of responsibility to each individual except the medical services for the control of the spread of the Zika disease. Difficulties in making such information available to certain sections of the population in a country are defined as a weakness, as well as varying degrees of understanding of information submitted by each person at risk of being potentially affected. Access to health services is not equally available in all cases of the spread of the Zika disease. The levels of literacy and responsibility to one's own health are at different levels of manifestation [1–21, 23–27].

These four strategic approaches are classic approaches in nature. When used in combination, they produce significantly more reliable results (**Figure 4**).

Modern approaches, but with limited accessibility, are immunoprophylaxis approaches. They aim to enhance the immune response of the community, except for any member of the at-risk society. Approaches to *primary*, *secondary*, *or tertiary immunoprophylaxis* take wide limits. Immune protectors are gaining popularity. Immunomodulating herbal remedies complement and extend the boundaries of current immunoprophylactic approaches. Clinical homeopathy or allopathic homeopathy, phytotherapy, herbal medicine, etc. supplement the ability to stabilize and prepare the immune system to meet the Zika virus that is aggressive to the nervous system [1–20, 22–39].

Depending on their type [34], the methods can be grouped into both traditional (classical) and contemporary as well as progressively innovative. If traditional prophylaxis methods [28–31, 34–36] are environment-oriented [22, 37–39], vector-oriented [27, 36–38], or target-specific [21, 22, 35], or targeted at a susceptible population (potentially infected) [22, 38, 39], or a combination thereof, and contemporary to the human body's immune response or to the creation of high public immune status, then all these methods apply to society as a whole and have a group character.

3.2 Progressive-innovative approaches to reducing the risk of ZVD: technologies of the future stage (author's idea)

Innovative technologies excite science—quantum-based as well as nanotechnologies and related software models—supported by mathematical algorithms and block diagrams to model the framework of an innovative idea. In this regard, the Zika RNA virus, with its unknowns, predisposes us scientists to trying to solve the equation from another angle. It turns out that the actual scientific information on Zika is not satisfactory and requires the search for new approaches beyond the known ones in order to achieve more serious results and greater success in solving the equation with such unknowns. This is because if we apply the always known and recognized methods, we will always arrive at the same results. In this case, it means coming up with a specific vaccine and/or specific antiviral agent to deal with Zika disease. This is, of course, an excellent destination and also a well-known area for

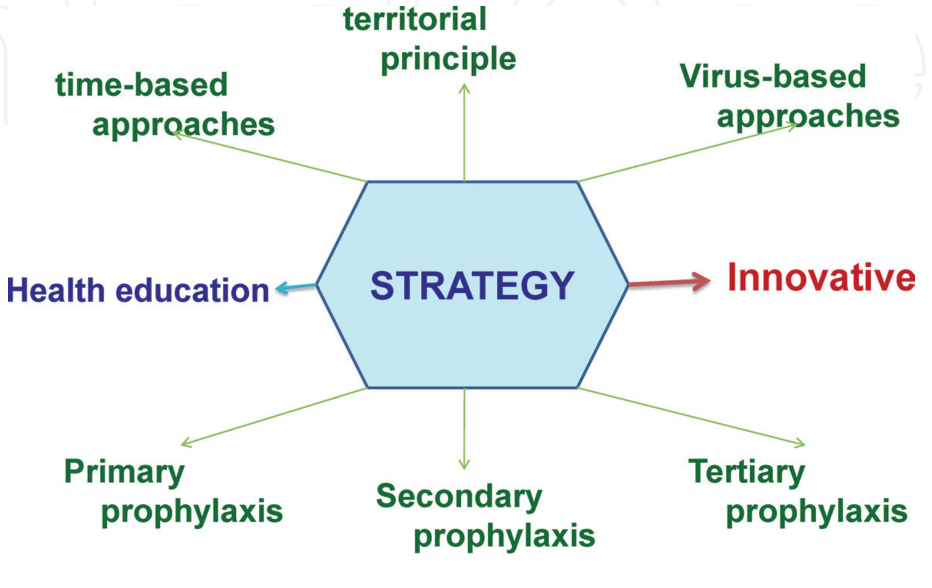

Figure 4.
Contemporary strategy of RR.

dealing with particularly dangerous infections. The high benefits of this approach have been proven, and this is because the world has dealt with diseases such as smallpox. The benefits are undeniable and highly appreciated. However, this is also not an obstacle to look for new approaches that could give another level of solutions. If we manage to integrate a new approach, although it may seem impossible and even absurd in its initial form as an idea, it may 1 day help to fundamentally tackle similar problems.

The thesis of the unrecognizability of Zika virus that has entered the human body appears as a counterbalance (counter thesis) to its recognition. In reality, heretofore, there is no known mechanism to protect the nervous system of the human body that is targeted by the Zika virus. Once penetrated into the body, the Zika virus takes several steps—to multiply, to cover the whole body, to cross the transplacental barrier, and to affect the nervous system and/or destroy it. Although initially recognized as an infectious agent by the immune system, it seems clear that the Zika virus is able to attack the nervous system both in the developing fetus during pregnancy and in some infected adults. The affinity of the virus to the nerve cell leads to its destruction and even to blocking its development in the embryo and fetus in pregnant women during the period of organogenesis. This makes the thesis of the unrecognizability of Zika virus relevant to the study.

The purpose and the tasks set have led us to the idea that biotechnological methods (in their varieties) can work for us in this direction. In reality, biotechnology gives us the opportunity to conduct research in the field of experience, as well as real-world attempts to solve the problem of early specific recognition of the Zika virus incorporated into the human body. The conceptual design covers several stages of its presentation, the most important of which is the targeted recognition of the Zika virus from the moment of the bite (from the mosquito carrier of the virus), through all steps of its incorporation, before it affects the nervous system and/or its development in the fetus.

The different levels of recognition create obstacles due to lack of information about the actual moment of the bite; ambiguity and unrecognition of nonspecific early symptoms; late identification of the disease; inaccessibility to medical services and early medical care; etc.

The invention and production of a nano-biotechnology carrier (as a conveyor) and its intravenous injection in order to determine whether a Zika virus has entered the human body as a key to dealing with the disease, before the virus strikes the nervous system, is a new type of idea. The capture of each virus in the shuttle (at the site of the bite, during their circulation in the body, or during its entry into the human cell) gives us a new opportunity to control the Zika virus. The implementation of this stage is supported by nano-biotechnology. The capture in the Zika shuttle of the virus in the human body requires sufficient durability to allow time for injection of substance “X” solely into the capsule of the virus from the carrier that has captured the Zika virus. This guarantees the destruction of the pathogenic virus only, without affecting the tissue cells in the human body. This is considered within the framework of achieving successful *secondary prophylaxis*, provided that the Zika virus is already incorporated into the human body or has serious clinical and/or laboratory indications of this in humans at risk. The therapeutic result will be available and delivered in a timely manner.

Moreover, the implementation of this approach can also be carried out in advance (as *primary prevention*) for any person who is at risk of being potentially bitten by a Zika virus vector carrier—researchers and scientists working in the field; field medical teams; emergency rescue teams; disaster, accident, and catastrophe field workers; etc. This will generate safety for the teams and enable rescue and rehabilitation activities on the worksite, as well as the successful completion of each mission in a Zika fever area, and will increase the chances of victims of emergency, disaster, accident, and catastrophe at risk of Zika fever. The time factor is in any case the basis for the successful completion of a given mission and/or field task at Zika's risk.

Preliminary studies of "X" substance on the effectiveness of the action to eradicate the pathogenic virus have been made. As far as one can tell, this substance can also be synthesized, except that it can be extracted from the natural sources of a precursor substance. It is assumed that there may be other variants of this substance and that there may be others that are effective, even with more potent action and with faster effect. However, in vivo and in vitro processes can sometimes show surprising results.

4. Conclusion

The idea presented as a theoretical formulation gives new horizons. It is clear that studies are still ongoing in the direction of effective control of the Zika virus. The aim is to demonstrate a mechanism or combination of methods and measures that can reduce the risk of the Zika virus as a possible result in the near future.

Conflict of interest

There are no "conflicts of interest."

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