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Doubled dosage of sofosbuvir is expected for inhibiting Zika virus infection

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ABSTRACT

Sofosbuvir is a new antiviral drug that has been recommended for management of hepatitis C virus (HCV) for a few years. New researches support that sofosbuvir might be useful for the management of Zika virus infection. Based on the pharmacological activity, inhibiting the HCV RNA-dependent RNA polymerase (RdRp or NS5 protein), sofosbuvir is proposed for its effectiveness against Zika virus infection. Here, the authors used a mathematical modelling theoretical approach to predict the expected dosage of sofosbuvir for inhibiting Zika virus infection. Based on the modeling study, if sofosbuvir is assigned for management of Zika virus infection, doubled dosage of the present dosage for hepatitis C management is recommended.

1. Introduction

Zika virus infection is the present global big problem. Worldwide outbreak of this infection becomes a global public health threaten. WHO already declares for the need for collaboration to fight Zika virus infection [1,2]. As an infection that can be transmitted by several routes (mosquito, sexual, *etc*.), the control of Zika is extremely difficult. The lack of specific antiviral drug and vaccine is also another important obstacle for successful management of the infection [3].

There are many ongoing researches focusing on finding new antiviral drug and vaccine against Zika virus infection. Of several candidate, sofosbuvir [4] is a new antiviral drug that has just been approved by FDA for its efficacy against Zika virus [5]. This drug has been recommended for management of hepatitis C virus (HCV) for a few years [4]. Focusing on its activity, Reznik *et al.* noted that 'Sofosbuvir is a uridine nucleotide analog that is converted into a triphosphate metabolite, which then inhibits the HCV RNA-dependent RNA polymerase (RdRp or NS5 protein)' [6]. Here, the authors used a mathematical modelling theoretical approach to predict the expected dosage of sofosbuvir for inhibiting Zika virus infection.

2. Materials and methods

This work was a mathematical modelling theoretical study. The primary agreement was there had to be a specific amount of required energy for reaction between sofosbuvir and its target enzyme and it was hereby called 'X'. Based on bonding theory, the required amount of sofosbuvir was varied to the substrates, sofosbuvir and target enzyme. Here, the simple equation 'A + B →C where A was the target enzyme, B was sofosbuvir and C was end product' could be written.

In case of any virus infection, the difference was the target enzyme. Although the target enzyme was the same, it had different molecular structure and molecular mass. For sofosbuvir, the molecular mass was constant for using in treatment of any viruses. If the final required energy 'X' was fixed, hence, the amount of required sofosbuvir or dosage of sofosbuvir would be varied to the molecular mass of target enzyme in different virus infection. The basic rule of three in arithmetic is hereby used for calculation for required dosage of sofosbuvir in different infections.

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3. Results

The molecular mass of HCV NS5 was 59 885 Da and of Zika virus was 102 968.9 Da. Hence, in the case of Zika virus infection, the required dosage of sofosbuvir was about 2 times higher than that of hepatitis C (1.719 444).

4. Discussion

Basically, sofosbuvir acts against specific enzyme for viral RNA synthesis that is essential for HCV replication and transcription [5,6]. The mentioned enzyme can be seen in both HCV and Zika virus. The use of sofosbuvir for inhibiting Zika virus is based on this observation. In animal model, oral sofosbuvir effectively acts against Zika virus and it is proposed that this antiviral drug is one of the most hopeful antiviral drug candidate against Zika virus [5]. Indeed, sofosbuvir has been already verified as a possible antiviral drug against dengue, the highly similar virus to Zika virus [7].

Acting against the common enzyme is the basic mechanism of sofosbuvir against Zika and dengue viruses. However, the structure and molecular mass of the target enzyme in each virus is not the same. For Zika virus and dengue virus, the similar molecular mass can be seen (about 103 kDa and 104 kDa for Zika and dengue, respectively). But for the hepatitis C, the significant lower molecular mass is observed.

Based on the concept of basic bonding theory, the difference in molecular mass can significantly affect the required dosage to fulfill the require energy reaction. This is the basic concept that can be seen the altered efficacy of antiviral drug in mutant type of virus infection such as bird flu [8]. In the present study, the authors applied the mentioned concept for expecting the required dosage of sofosbuvir in case that it can be used as an effective antiviral drug against Zika virus infection.

Based on the quantum calculation similar to that proposed and used in the previous reports [9–11], it hereby can be seen that the regular dosage of sofosbuvir that is used for management of hepatitis C will not be effective against Zika virus. In case that sofosbuvir is applied for Zika virus infection, double dosage is recommended. Whether this recommended dosage will be effective *in vivo* and cause any side effect or not requires further clinical trial for verification.

In conclusion, based on the modeling study, if sofosbuvir is assigned for management of Zika virus infection, doubled dosage of the present dosage for hepatitis C management is recommended.

Conflict of interest statement

We declare that we have no conflict of interest.

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