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Short Communication

NS2B-NS3-Zika, Therapeutic White for Zika Infection

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Following the American Zika virus pandemic that conditioned the increase of cases of Guillain Barré Syndrome as well as microcephaly associated with Zika congenital syndrome that conditions other fetal alterations, active neurotrophism and teratogenicity, all the global epidemiological alerts have been activated, proceeding to the study of the Viruses, to improve timely diagnosis and treatment strategies [1].

The Zika virus, like the other arboviruses of the genus *Flavivirus*, is single-stranded RNA virus, which consists of 3 structural proteins (C, prM, E) and 7 non-structural proteins (NS1 to NS7). Of the non-structural proteins, the main implicated in viral replication are NS3 and its NS2B cofactor forming an NS2B-NS3-Zika complex which is currently under study with a view to therapeutic pharmacological strategies.

The NS3 protein has two N-terminal domains where the protease and C-terminal form, from which arise enzymes such as RNA-helicase and RNA-triphosphatase (involved in active viral replication), respectively. NS2B acts as a cofactor stimulating NS3 to express the enzymes commented perpetuating replication and viral formation, through the cleavage of structural proteins, release of the RNA for its replication and formation of new viral particles in the cellular endoplasmic reticulum [2].

Having identified this region of viral structure, attention has been focused on it as a possible promising therapeutic target. Organic and non-organic chemicals have been studied, with various possibilities being discovered.

Of the organic substances, 22 compounds related to polyphenols have been identified so far, emphasizing their ability to inhibit the NS2B-NS3 complex, Myricetin, Catechins, Astragalin, Rutin and Luteolin [3].

Regarding the non-organic chemical agents, first known antiviral agents have been evaluated, of which its great activity has been recognized zika virus, being the main ones: Interferon alpha, Interferon beta, Celgosivir (with antidengue properties also), Ribavirina, Brequinar, Dynasore and Chloroquine.

There are other non-antiviral chemical compounds, which have demonstrated Zika anti-virus activity in cellular models, without knowing the exact mechanism of action, these are: 6-azauridine, finasteride and mevastatin [4].

In other cellular models applying inhibition to diverse experimental cells like HuH-7, HeLa, JEG3, hNSC and HAEC and that have inhibited the viral replication in the majority of them (4 to 5 cell lines of study) are: Ivermectina, Mefloquine and Acido Mycophenolic, less than single-cell blockade, are: Azathioprine, Bortezomib, Cyclosporin A, Daptomycin, Pyrimethamine and Sertraline [5].

The concern of a specific population group such as pregnant women, due to the high index of congenital syndrome by Zika that carries fetal microcephaly and other neurological, cardiopulmonary and digestive alterations, makes search for therapeutic options that manage to curb these alterations in the fetus. However, the teratogenicity of various chemical substances, limits this initiative, since coupled with the teratogenicity of Zika virus, could add the chemical teratogenicity of the drugs.

Given the above, substances that could be used during gestation have been identified, being Category B of the drugs recommended by the FDA during pregnancy, and the most representative are: sofosbuvir (monotherapy has not shown teratogenicity and has been shown to reduce the damage (Reduced viral proliferation and cytopathic effect in glial cells and human astrocytes, affecting the neurotrophism of the Zika virus), Bromocriptine (demonstrated to inhibit the protease of the NS2B-NS3 complex, thereby inhibiting Viral replication) and finally daptomycin, with a mechanism not yet clear [6-9].

There are several substances still under investigation, such as CID 91632869 and NITD008, antivirals with promising anti Zika activity, but studies are still required to consolidate as therapeutic options [4].

In conclusion, we can affirm that the research for antiviral treatments with a target the NS2B-NS3 complex, responsible for viral replication has had fruits, demonstrating various drugs that could be implemented both in general population and in vulnerable populations highlighting pregnant women, trying to limit the sequelae of neurotrophism and teratogenicity induced by Zika.

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