BIO_04 - Surveillance of influenza viruses with reduced susceptibility to antivirals in Brazil during the COVID-19 pandemic

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Introduction: Influenza viruses (IV) are major pathogens that act in the respiratory tract and pose as a major threat to humans. One of the main strategies to control these viruses is the use of antiviral drugs. In Brazil, the most available anti-IV drug is the neuraminidase inhibitor (NAI) oseltamivir (OST), which is also distributed by the public health system for high-risk groups of individuals. The recently approved additional anti-IV drug, the cap dependent endonuclease inhibitor (CENI) baloxavir marboxil (BXM), has not yet been licensed in the country. However, point mutations may arise in the genes that encode the target proteins and affect the effectiveness of anti-flu drugs.

Objectives: Therefore, the objective of this study was to monitor, in Brazil, the IVs susceptibility profile to OST and the circulation of IVs bearing mutations associated with antivirals reduced inhibition (RI) between 2020 and 2023.

Methodology: We determined IV isolates OST IC_{50} by measuring NA inhibition and evaluated human Brazilian IVs sequences available at GISAID platform (https://www.gisaid.org/), collected from, which presented at least one of the genes of interest regarding antivirals resistance (PA, NA and MP) through fluserver tool (https://gisaid.org/database-features/flusurver-mutations-app/).

Results: We studied 105 isolates from IVs collected during the studied period comprising isolates of A(H3N2) (n=5) that showed an OST IC_{50} median of 0.06nM (ranging from 0.03 to 0.08nM), A(H1N1) pdm09 (n=20) that had an OST IC_{50} median 0.17nM (ranging from 0.02 to 0.4nM) and IBV-Victoria (n=80) that showed an OST IC_{50} median of 0.06nM (ranging from 0.02 to 4.81nM). Therefore, they were classified as having a normal inhibition profile to OST. Further, we analyzed 4603 Brazilian IV sequences including A(H3N2) (n=2024), A(H1N1)Pdm09 (n=1416) and influenza B Victoria lineage (n=1163). Consequently, we detected the following relevant substitutions associated with antiviral resistance: PA:I38M(n=2) and PA:I38V(n=1) in A(H3N2) viruses. Remarkably, we did not detect mutations associated with NAIs RI in the GISAID included viruses. Moreover, IAV sequences had the M2:S31N adamantanes resistant marker.

Conclusion: These analyses showed that the IVs susceptibility to NAIs in Brazil remains normal indicating that NAIs still remain an option for the treatment of influenza infections in the country. However, surveillance of influenza resistance should be strengthened specially after the beginning of the COVID-19 pandemic. These data may contribute to clinical conduct public health policies for the purchase and stocking of NAIs, and approval of new anti-IV drugs such as BXM in Brazil.

Keywords: Influenza virus; Antivirals; Resistence