P182 VALSARTAN LIMITS PULMONARY AND CARDIAC DAMAGE INDUCED BY SARS-COV-2 IN EXPERIMENTAL MODELS BY REDUCING THE EXPRESSION OF ACE2

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Background: SARS-CoV-2 primarily affects the respiratory system, but cardiac complications also occur very often. The entry of SARS-CoV-2 into host cells is mediated by the interaction between the viral glycoprotein Spike (S) and the host angiotensin-converting enzyme 2 (ACE2) protein. The use of ACE inhibitors (ACEIs) and angiotensin II type 1 receptor blockers (ARBs) might influence both ACE2 expression and viral infection, but our knowledge about these possible interactions is limited. Aim. To evaluate the effects of ACEIs and ARBs during active viraemia.
Methods: We tested the effects of exposure to the ACEI Lisinopril (100nM and 500nM) and the ARB Valsartan (10μM and 50μM) on three different cell types: green monkey-derived epithelial cells (VERO E6) which are used to replicate SARS-CoV-2, cardiomyocytes derived from hiPSC (iPSC-CMs) as heart model and a lung epithelial cancer cell line (16HBE) as pulmonary model. The SARS-CoV-2 wild strain was inoculated on cell lines for 1 hour. Cell viability was measured 72 hours after infection. The supernatants of the infected cells were collected and titrated by the micro-neutralization assay on VERO E6 cells to verify the presence of the virus. Levels of ACE2 mRNA and protein content on cell lysates were quantified after each treatment by RT-qPCR and western blot, respectively.
Results: ACEI and ARB at both concentrations do not affect the viability of the 3 cell lines. Vice versa, viral infection significantly decreases the viability of VERO E6 (-60%, $p < 0.0001$) and iPSC-CMs (-44%, $p < 0.001$), while 16HBE cells do not show a cytopathic effect after infection. Viral titration shows that SARS-CoV-2 replicated in cell lines and was actively released into supernatants. Valsartan 50μM decreased virus release in the three cell lines and increased the viability of VERO E6 (+69%, $p < 0.01$) and iPSC-CMs (+20.5%, $p < 0.05$) after the infection. Valsartan 50μM also decreases both mRNA (-65% in VERO E6, $p < 0.001$; -50% in iPSC-CMs, $p < 0.05$; -60.5% in 16HBE, $p < 0.01$) and protein levels of ACE2 in all 3 cell lines.
Conclusion: The data suggest that ACEIs and ARBs do not worsen the SARS-CoV-2 infection and that Valsartan, by reducing the levels of ACE2 expression, might result protective.