CELL- PERMEABLE SUCCINATE RESCUES PLATELET MITOCHONDRIAL RESPIRATION IN COVID-19 PATIENTS

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The COVID-19 pandemic remains a global health issue since its outbreak. Hyperinflammation with "cytokine storm", endothelial dysfunction, and more recently, mitochondrial dysfunction were identified as main pathomechanisms. Platelet respiratory dysfunction has recently emerged as a peripheral biomarker that could mirror organ mitochondrial dysfunction. NV118, a cell-permeable succinate, is a new prodrug able to support mitochondrial function by enhancing complex II-supported respiration.
The present pilot study performed in platelets harvested from patients hospitalized for various forms of SARS-CoV2 infection was double-aimed: i) to assess the mitochondrial respiratory dysfunction; ii) to investigate whether NV118 can rescue it.
Nineteen patients with moderate (n=5) and severe (n=14) disease were included. Peripheral blood was collected and used for platelet isolation. Platelet respiration was measured at 37°C using high-resolution respirometry according to a SUIT protocol for permeabilized platelets allowing the measurement of the following respiratory parameters: routine, active, non-phosphorylating and maximal uncoupled respiration. Intact platelets (n=15) were acutely exposed to NV118 (*vs* DMSO) and routine, leak and maximal uncoupled respiration were measured.
The severe forms of disease expressed a significant decrease in platelet active respiration for both respiratory complexes and an increase of routine, leak and uncoupled respiration. Moderate forms of disease present only a significant decrease in active respiration, particularly for CI. Cell-permeable succinate elicited a significant increase in routine, leak and maximal uncoupled respiration for both mitochondrial complexes.
In conclusion, COVID-19 differentially impairs platelet bioenergetics, according to the severity of the disease, eliciting mitochondrial respiratory dysfunction that can be rescued by cell-permeable succinate.

Keywords: COVID-19, platelets, mitochondria, high-resolution respirometry, cell-permeable succinate