Topic: THROMBOLYSIS – EXCLUDING CLINICAL TRIAL RESULTS

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Recombinant tissue plasminogen activator reduces phagocytosis of granulocytes and monocytes in vitro.

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BACKGROUND

Stroke induces profound immune alterations which on the one hand influence stroke lesion size and on the other hand promote post stroke infections. Beside mechanical recanalization strategies enzymatic breakup of thrombi by recombinant tissue plasminogen activator (rt-PA) is the only therapeutic option for patients suffering from cerebral ischemia. The aim of this study was to investigate the possible impact of rt-PA on cytokine production and phagocytosis.

METHODS

Cell culture: PBMC from healthy donors EDTA or heparanized whole blood were isolated. Cells were either stimulated with Phytohemagglutinin or anti-CD3/CD28 beads. n=4 per condition. Cells were incubated in RPMI complete medium for 72h (37°C, 5% CO2). The following cytokines were determined in cell culture supernatants by Legendplex Multi-Analyte Flow Assay Kit (Biolegend): IFN-g, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-13, IL-17A, IL17F, IL-21, IL-22 and TNF-a. Phagocytosis was determined by Phagotest Kit (Glycotope) after incubation of healthy donors' whole blood with rt-PA for 4h at 37°C, 5% CO2. rt-PA concentration ranged between 0,5 and 1µg/ml.

RESULTS

Cytokine production was not altered significantly in any of the cell culture conditions by rt-PA. But in vitro incubation of whole blood with rt-PA did reduce the amount of phagocytosed bacteria per granulocyte or monocyte respectively while the percentage of cells that phagocytosed bacteria was not altered.

CONCLUSIONS

Our in vitro experiments demonstrate that rt-PA can affect immune cell function in vitro. Future studies will have to determine whether our finding is of relevance for rt-PA treated patients.