ALTERED NITRIC OXIDE PRODUCTION BY RED BLOOD CELLS DURING EXPERIMENTAL CEREBRAL MALARIA

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Introduction. Cerebral malaria is characterized by severe microvascular dysfunction, reduced cerebral blood flow, and impaired nitric oxide (NO) bioavailability. Although endothelial dysfunction has been extensively studied, growing evidence suggests that red blood cells (RBCs) express functional nitric oxide synthase and can modulate vascular tone, yet their contribution to NO-related alterations during experimental cerebral malaria (ECM) remains poorly understood.

Objectives. To evaluate NO production by RBCs during *Plasmodium berghei* ANKA infection.

Methods. RBCs were isolated from control and *P. berghei* ANKA–infected mice at the peak of disease. To assess NO in RBCs, blood from control and ECM mice were incubated with DAF-FMDA [10 µM] and analyzed by flow cytometry. RBCs were pre-treated with L-NAME or insulin to evaluate modulation of NO production. Nitrite levels were quantified in RBC suspensions using the Griess reaction as an index of NO production.

Results. RBCs from ECM animals exhibited higher basal fluorescence than controls ($p = 0.016$). In control RBCs, insulin increased ($p = 0.03$) and L-NAME decreased ($p = 0.01$) fluorescence, confirming functional NO modulation. In contrast, RBCs from ECM animals showed no significant response to either insulin or L-NAME. Consistently, Griess assay analysis revealed elevated nitrite levels in RBC samples from infected mice ($p < 0{,}0001$).

Conclusion. ECM is associated with altered NO-related signals in RBCs, as evidenced by increased intracellular NO-associated fluorescence and nitrite accumulation. These findings indicate that the parasite modifies NO metabolism in circulating RBCs. While these results suggest that RBC NO production is altered during ECM, the contribution of RBC-derived NO to vascular dysfunction and cerebral hypoperfusion remains to be established.