Background Neonatal asphyxia has significant morbidities including hypoxic-ischemic encephalopathy, necrotizing enterocolitis and acute renal failure. These complications are associated with regional perfusion deficits. During reoxygenation, oxygen free radicals are produced and can activate matrix metalloproteinase-2, leading to cardiovascular dysfunction. There is little information regarding the effect of doxycycline, a known inhibitor of matrix metalloproteinase-2, on regional perfusion. We hypothesized that doxycycline would improve regional hemodynamics during recovery in asphyxiated newborn piglets.

Methods Piglets (1–5 days old) were acutely instrumented for continuous monitoring of blood flow at the left common carotid, superior mesenteric and renal arteries (CAFI, SMAFI and RAFl, respectively). After stabilization, 2hrs of normocapnic alveolar hypoxia (10–15% oxygen) was induced followed by 4hrs of reoxygenation (21% oxygen). Piglets were blindly randomized to receive either normal saline or doxycycline (3, 10, or 30mg/kg) intravenously 5 minutes into reoxygenation (n=7/group). Sham-operated piglets (n=5) received no hypoxia-reoxygenation.

Results All piglets had regional perfusion deficits at 2hrs of hypoxia (CAFI: 76±SD16%; SMAFI: 57±21%; RAFl: 11±10% of respective normoxic baseline). During 4hrs of reoxygenation, doxycycline at 30 mg/kg increased RAFl (p=0.001) and CAFI (p=0.06)at 240min reoxygenation: 66±5% vs. 66±21% (p=0.04) and 92±52% vs. 66±22% (p=0.09) for controls, respectively. Despite attenuating mesenteric hyperemia at 10min of reoxygenation (p=0.03), there was no difference in SMAFI at the end of reoxygenation.

Conclusions In newborn piglets with hypoxia-reoxygenation, post-resuscitation administration of high-dose intravenous doxycycline improves carotid and renal hemodynamics and may attenuate transient mesenteric hyperemia during recovery.

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