**Background and Aims** Oxidative stress contributes to tissue damage after perinatal asphyxia. The thiol-containing free radical scavenger N-acetylcysteine amide (NACA) is a promising new anti-oxidant with good penetration into the mitochondria. The objective was to investigate the protective effect of NACA in a piglet model of birth asphyxia.

**Methods** Anesthetized newborn piglets (n=51) were subjected to global hypoxemia and block-randomized to either

1. intravenous administration of NACA 300 mg/kg and resuscitated with 21% oxygen for 30 min,
2. saline and 21% oxygen,
3. NACA and 100% oxygen or
4. saline and 100% oxygen.

After resuscitation, the piglets were followed for 9 hours and samples for several markers of injury and oxidative stress were collected. Reported here are clinical parameters and measurements of reduced to oxidized glutathione (GSH/GSSG).

**Results** Thirty minutes after end-resuscitation metabolic acidosis was less pronounced in the 100%-NACA group compared to 100%-oxygen-alone (lactate 8.1±2.6 vs 10.9±3.4, p<0.05). This difference was not shown for the 21%-oxygen groups. Mean arterial blood pressure and hemoglobin levels remained similar between the groups. The GSSG values were generally lower. At end-resuscitation GSH was lower in 100%-NACA compared to 100%-oxygen-alone group (164±111 vs 255±113 µmol, p<0.05) and delta-GSH during resuscitation greater (143±49 vs 32±66 µmol, p<0.001).

**Conclusions** The data indicate that NACA may enhance immediate recovery, improve mitochondrial glutathione metabolism and restore the cell to a normal metabolism following asphyxia and resuscitation. Upcoming analyses of histopathology and injury markers will further elucidate neuroprotective effect of NACA treatment following birth asphyxia.