

The long-term effects of a midgestational asphyxial episode in fetal sheep

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Introduction: It is known that fetuses at midgestation can survive a severe asphyxial episode, but by 72h post-asphyxia, they have developed hydrops fetalis^{1,2}. The long-term consequences of such an event are unknown. We hypothesised that the hydrops would resolve by late gestation, however, growth and organ development would be disrupted.

Methods: Fetuses were chronically catheterised under general anaesthesia (1g sodium thiopentone i.v. followed by 1-3% halothane in oxygen). Five days later they were subjected to 30 min of complete umbilical cord occlusion at ~90 days gestation (term ~150 days). At ~130 days gestation in 8 occluded and 10 sham animals, ewes and fetuses were killed with an overdose of pentobarbitone sodium. Nephron number in the right kidney was estimated by an unbiased stereological technique. Cardiac myocyte volume and nucleation were measured using confocal microscopy.

Results: At post-mortem, occluded fetuses showed signs of residual hydrops, i.e. skin fold thickness was increased ($p < 0.01$). Most organ weights were not different between groups, however the brain and lungs weighed 63% and 50% less in the occluded group ($p < 0.01$, $p < 0.001$ respectively). Nephron number, total glomerular volume and total renal corpuscle volume were similar in the two groups. In the heart there was no difference in myocyte nucleation (uni- vs multinucleation) or volume between the groups.

Conclusion: The hydrops that occurred after a 30 min midgestational asphyxial episode did not fully resolve by late gestation. Unexpectedly, the kidney and heart seemed relatively tolerant as there were no obvious residual morphological effects in either organ. By contrast, brain and lung growth were severely impaired. Thus, although fetuses could survive severe asphyxiation, by late gestation the development of the brain and lungs was so profoundly impaired that postnatal survival would be unlikely.

(1) O'Connell, AE et al (2003), J Physiol 552, 933-43.

(2) Lumbers, ER et al (2001), AJP 280(4), R1045-51.