Effect of surgical stimulation on anesthesia induced neuroapoptosis in the mid-gestation fetal ovine brain

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OBJECTIVE

• At 70 days gestation (G70, term=145 days), isoflurane was administered to ewes at 2% for 1 hour (2%Iso x1) or 4% for 3 hours (4%Iso x 3) to simulate anesthetic exposure during in-utero fetal procedures.

• Following induction and endotracheal intubation, a subgroup underwent a midline laparotomy and small hysterotomy.

• Surgical stimulation was performed on the hind limb of the fetal sheep via a femoral vessel cut down and the incision was completely closed.

• Animals were subsequently euthanized, fetal brains harvested and processed for histology.

METHODS

• Purpose of this study was to evaluate the effect of surgical stimulation on anesthesia-induced neuroapoptosis in mid-gestation sheep.

• Hypothesis: Surgical stimulation will decrease the degree of neuroapoptosis compared to unchallenged anesthetic administration.

RESULTS

• Total of 28 fetal sheep brains were evaluated

• Significant decrease in neuroapoptosis was observed in the dentate gyrus of sheep that received 4%Iso x 3hr with surgical stimulation compared to control fetuses and those that received 4%Iso x 3hr without surgical stimulation (Fig 2A).

• All animals that had surgical stimulation demonstrated a significant decrease in neuroapoptosis in the pyramidal lobe (Figure 2B).

• No significant difference in neuroapoptosis was noted in the frontal cortex, endplate and caudate lobes.

CONCLUSION

• Our findings suggests that in contrast to unchallenged anesthetic exposure, surgical stimulation under anesthesia results in decreased neuroapoptosis in the fetal sheep brain in the dentate gyrus and pyramidal lobe.

• No such effect was observed in the frontal cortex, endplate and caudate lobes.

• Studies of neurodevelopmental outcomes of children who have undergone in-utero intervention will be needed to evaluate long-term effects of anesthesia and surgery in this cohort of patients.

Table 1. Study group assignment of fetal sheep

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Group</th>
<th>Isoflurane</th>
<th>Duration</th>
<th>n</th>
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<tbody>
<tr>
<td>70 days</td>
<td>Control</td>
<td>None</td>
<td>1 hour</td>
<td>5</td>
</tr>
<tr>
<td>70 days</td>
<td>Single low dose</td>
<td>Isoflurane 2%</td>
<td>1 hour</td>
<td>6</td>
</tr>
<tr>
<td>70 days</td>
<td>Single high dose</td>
<td>Isoflurane 4%</td>
<td>3 hours</td>
<td>6</td>
</tr>
<tr>
<td>70 days</td>
<td>Fetal Stimulation</td>
<td>Isoflurane 2%</td>
<td>1 hour</td>
<td>5</td>
</tr>
<tr>
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<td>Isoflurane 4%</td>
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