Inhibition of Chondrocyte Death Following Exposure to Commonly Used Anesthetics

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Disclosures

• No disclosures relevant to the content of this presentation.

Background

• Intra-articular injections of local anesthetics such as bupivacaine, ropivacaine, and lidocaine w/wo epinephrine are commonly used to enhance analgesia and reduce bleeding during surgery.
• Intra-articular pain pumps delivering these agents have been shown to cause severe cartilage loss, termed 'post-arthroscopic glenohumeral chondrolysis' (PAGCL) in some patients.

In vitro studies show that anesthetic agents induce apoptosis and necrosis in dose- and time-dependent fashion.
• Inhibition of chondrocyte apoptosis has not been reported following anesthetic exposure.
• Modulation of chondrocyte apoptosis could mitigate chondrocyte loss following anesthetic exposure.
**PURPOSE**

1. Examine the impact of short-term exposure of local anesthetics on chondrocyte viability
2. Determine whether anesthetic exposure results in chondrocyte apoptosis
3. Explore whether apoptosis inhibition results in a significant reduction in chondrocyte death following anesthetic exposure

**METHODS- PART 1**

- Monolayer chondrocytes incubated for 30, 45, 60, 75, 90, 105, or 120 minutes in treatment groups:
  1. 0.9% normal saline
  2. 0.5% bupivacaine
  3. 0.5% ropivacaine
  4. 1% lidocaine

- Cell-viability assayed with LIVE/DEAD staining
METHODS- PART 2

• Chondrocyte monolayer cultures exposed to 90 minutes of 5 anesthetic treatment groups then maintained in fresh culture media
• Protocol repeated with addition of z-vad-fmk, a pan-caspase inhibitor to all incubation solutions
• Apoptosis assayed at 1, 3, 5, and 7 days post-anesthetic exposure
• Apoptosis assessed using TUNEL and anti-activated caspase 3 staining

RESULTS- PART 1

• Bupivacaine caused the highest percentage of chondrocyte death, directly proportional to time of exposure (p<0.001).
• Bupivacaine caused 18.25% increased cell death vs. saline control, 14.8% increased cell death vs. ropivacaine (p<0.001).

RESULTS- PART 2

• Cumulatively, all anesthetic groups resulted in significantly increased rates of chondrocyte apoptosis.
• Caspase-inhibition (CI) effect largest with ropivacaine (40.1% reduced apoptosis, p<0.001).
• Caspase-inhibition (CI) effect smallest with lidocaine (30.2% reduced apoptosis, p<0.01).

RESULTS- PART 2

• Cumulatively, bupivacaine and lidocaine exposure resulted in statistically significant increased rates of chondrocyte apoptosis.
• Caspase inhibition caused a cumulative statistically significant reduction in apoptosis for chondrocytes exposed to all agents relative to control.
CONCLUSIONS

• Chondrocyte viability is directly proportional to duration of anesthetic exposure.
• 0.5% bupivacaine was the most cytotoxic agent tested, causing >60% greater chondrocyte cell death relative to control.
• Epinephrine also results in significant chondrocyte toxicity and may potentiate the effects of anesthetics when used in combination.
• Greatest chondroprotective effect of caspase inhibition occurred with 0.5% ropivacaine.

REFERENCES


CLINICAL IMPLICATIONS

• Use of an apoptosis inhibitor as an adjunctive agent during the administration of intra-articular anesthetics and epinephrine may mitigate chondrocyte loss.
• Further work examining the effects of duration of anesthetic and caspase-inhibitor exposure, concentration, and delivery methods is warranted.