Bupivacaine vs. Ropivacaine: Looking at the Chondrotoxic Effects of Intraarticular Anesthetics in Osteoarthritic Joints

Lauren Price, PA-S and Sarah Burke, PA-S
James Madison University, Harrisonburg, VA

Introduction
Intraarticular injections of corticosteroids used in combination with local anesthetics are a commonly practiced therapy for osteoarthritis. Injections of corticosteroids and local anesthetics can alleviate pain and inflammation in an osteoarthritic joint. Bupivacaine is currently the most commonly used intraarticular local anesthetic due to its long duration of action. Recent experimental studies have suggested that bupivacaine may be toxic to articular cartilage. Ropivacaine, a newer local anesthetic agent, may be a promising alternative to bupivacaine for intraarticular injections.

Results

Objective: To assess the chondrotoxic effects of mepivacaine, ropivacaine, and bupivacaine.
Conclusion: Local anesthetic chondrotoxicity increases with drug type and concentration from ropivacaine to bupivacaine.

Study 2. Apoptosis and Mitochondrial Dysfunction in Human Chondrocytes Following Exposure to Lidocaine, Bupivacaine, and Ropivacaine. Grishko, PhD et al.
Objective: To investigate the effects of lidocaine, bupivacaine, and ropivacaine on human chondrocyte viability and mitochondrial function in vitro and to characterize the type of cell death elicited following exposure.
Conclusion: Bupivacaine and ropivacaine are chondrotoxic to human cartilage through the induction of cell apoptosis.

Study 3. Comparison of Ropivacaine and Bupivacaine Toxicity in Human Articular Cartilage. Piper et al.
Objective: To determine whether 0.5% bupivacaine is chondrotoxic to human articular cartilage and whether 0.5% ropivacaine is a less toxic alternative.
Conclusion: 0.5% bupivacaine is more chondrotoxic than 0.5% ropivacaine. No significant difference in cell viability between ropivacaine and bupivacaine.

Clinical Question
In 40 to 65 year olds with osteoarthritic joint pain, what are the toxic effects of bupivacaine as compared to ropivacaine on chondrocytes?

Methods

Prisma Flow Diagram

Records Identified
Records after duplicates removed
Records screened
Full-text articles reviewed
Screening
Inclusion

Additional records identified through other sources (n = 6)

Records screened (n = 50)

Full-text articles excluded with reasons (n = 13) Excluded if chondrotoxicity study performed in vivo, used cells other than human articular chondrocytes, meta-analysis studies failed to answer clinical question

Studies included in qualitative synthesis (n = 3)

Studies included in quantitative synthesis (meta-analysis) (n = 3)

Table 1. Comparison of Subjects, Methods, and Significant Findings

<table>
<thead>
<tr>
<th>In vivo or in vitro</th>
<th>In vivo</th>
<th>In vitro</th>
<th>In vitro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>4</td>
<td>N/A</td>
<td>3</td>
</tr>
<tr>
<td>Patient population</td>
<td>42-62 year olds</td>
<td>N/A</td>
<td>50 ± 15 years</td>
</tr>
<tr>
<td>OA or intact cartilage</td>
<td>OA</td>
<td>OA</td>
<td>intact</td>
</tr>
<tr>
<td>Bone used</td>
<td>N/A</td>
<td>Femoral condyles and tibial plateau</td>
<td>3 from femoral head, tibial plateau</td>
</tr>
<tr>
<td>Drug concentrations</td>
<td>2 mL Bupivacaine 0.0125%, 0.025%, 0.125%, 0.25%, 0.5%</td>
<td>1 mL Ropivacaine 0.0125%, 0.025%, 0.125%, 0.25%, 0.5%</td>
<td>0.5% Ropivacaine 0.5% Bupivacaine 1% Mepivacaine 0.5% Ropivacaine</td>
</tr>
<tr>
<td>Exposure time</td>
<td>24 hours and 96 hours</td>
<td>1 hour</td>
<td>24 hours</td>
</tr>
<tr>
<td>Statistical significance</td>
<td>P &lt; 0.01</td>
<td>P &lt; 0.01</td>
<td>P &lt; 0.05</td>
</tr>
</tbody>
</table>

Flow Cytometry

At 24 hours and 96 hours:
• Ropivacaine and 0.25% bupivacaine showed no cytotoxic effects.
• 0.25% ropivacaine > 0.5% bupivacaine in cell viability
• Significant cytotoxicity seen after 24 and 96 hours with bupivacaine and 96 hours with ropivacaine

At 24 hours:
• Detectable but not significant decrease in cell viability with 0.5% bupivacaine
• No decrease with 0.25% bupivacaine and 0.5% and 0.25% ropivacaine
• At 120 hours:
• Only 0.2% ropivacaine did not have significant decrease in cell viability

Future Studies:
In order to further define the clinical relevance of these findings, an in vivo experiment would be necessary in order to observe the toxic effects of bupivacaine and ropivacaine on human articular cartilage directly and to better represent the pharmacokinetics of the agents. Future studies should also focus on comparing several equipotent concentrations of ropivacaine and bupivacaine and measuring the effects for longer durations.

Clinical Application
The clinical impact of these results remains unclear. In regards to our clinical scenario, the results of these studies have failed to answer the question: which local anesthetic agent and concentration is the least toxic to chondrocytes? The results did however demonstrate that both ropivacaine and bupivacaine show statistically significant toxic effects to chondrocytes. This is an important revelation that clinicians should be wary of when choosing an anesthetic and which concentration to use. We recommend that orthopedists should use the lowest possible concentration of ropivacaine or bupivacaine to reach therapeutic levels until further studies are performed.

References

We would like to acknowledge Dr. Erika Kandler, Ryan Chico PA-C, Carolyn Schubert, and the JMU Communication Center for their time and assistance with this research project.