Treatment of postoperative pain in shoulder surgery with SABER®-Bupivacaine

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BACKGROUND

- Local anesthetics are an important component of multimodal postoperative analgesia, but are limited by a short duration of action (4-8 hours)
- Relief of postoperative pain with local anesthetics has been shown to reduce the need for opioid treatment, with an attendant reduction in opioid-related adverse events
- For many surgeries, severe to moderate pain lasts for about 3 days

METHODS

Trial Design: Multinational, randomized, parallel, double-blind, placebo and active controlled

Inclusion Criteria:
- Subacromial impingement syndrome, intact rotator cuff on MRI imaging, ≥18 years, male or female (with negative pregnancy test and adequate contraception)

Exclusion Criteria:
- Other shoulder pathology, clinically significant comorbidity, abnormal ECG, QT > 450 msec (M), QR > 470 msec (F), use of drugs contraindicated on bupivacaine label

Study Treatments:
- POSIDUR (5ml, 600 mg), SABER-Placebo (5 mL), or Bupivacaine HCl (20 mL, 0.25%, 50 mg) were deposited into subacromial space through an arthroscopic portal under direct vision

Background analgesia:
- Acetaminophen, 1000 mg qid (wt > 66 kg) or 500 mg qid (wt < 66 kg) for 0-72 hours post-surgery

Rescue Analgesia:
- Morphine 2 mg IV or 10 mg PO as requested for pain relief

Pharmacokinetics:
- When instilled into a surgical incision prior to closure, the product forms a viscous depot that releases bupivacaine over a 3 day period at a rate of about 10 mg/hour

SURGICAL WOUND HEALING

Surgical healing as expected 53 100% 25 100% 29 100% 107 100%

RECOVERY IN OPIOID USE

Proportion of Patients Not Taking Opioids

PATIENT DISPOSITION

Demographics (ITT population)

<table>
<thead>
<tr>
<th>Demographic</th>
<th>POSIDUR</th>
<th>SABER-Placebo</th>
<th>Bupivacaine</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>33 (62.3)</td>
<td>14 (56.0)</td>
<td>17 (58.6)</td>
<td>64 (59.8)</td>
</tr>
<tr>
<td>Male</td>
<td>20 (37.7)</td>
<td>11 (44.0)</td>
<td>12 (41.4)</td>
<td>43 (40.2)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2 (3.8)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>2 (1.9)</td>
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<tr>
<td>White</td>
<td>50 (94.3)</td>
<td>24 (96.0)</td>
<td>29 (100)</td>
<td>103 (96.3)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1.9)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (0.9)</td>
</tr>
</tbody>
</table>

BMI - kg/m²

- Mean 26.77 25.83 26.65 25.52
- Median 26.5 25.76 24.45 26.08
- Min, max 24.0, 40.5 22.6, 38.7 23.7, 39.9 24.0, 38.7

CONCLUSIONS

- The trial was well-conducted and no patients dropped out
- POSIDUR treatment resulted in clinically and statistically significant reduction in post-surgical pain compared to placebo
- POSIDUR reduced pain on each of the 5 days following surgery
- POSIDUR significantly reduced the use of opioid rescue medication by 67% compared to placebo
- 40% of POSIDUR patients took no opioids
- POSIDUR was well tolerated and had no adverse effect on wound healing
- There were no adverse effects due to systemic bupivacaine toxicity