Despite advances in analgesia, patients often experience significant pain in the 72 hours following open surgery. Each of 5 parameters (vital signs, activity level, nausea/vomiting, pain, and surgical bleeding) were evaluated on a 0 to 2 scale, with a value of 1 indicating absence of a parameter regardless of mPADSS score.

Multimodal pain management strategies combine analgesic agents of different classes and routes of administration with the goals of reducing the consequences of inadequate pain control and limiting adverse effects associated with opioid analgesics.

Enhanced recovery protocols that incorporate multimodal analgesia are also evolving to improve pain control, reduce length of postoperative hospital stays, enable earlier return of function, and improve patient outcomes.

Intra-incisional depot bupivacaine (IDB) contains the active ingredient bupivacaine (50 mg in a single 5-mL dose) in a delivery platform comprised of a biodegradable organic matrix (lauric acid, octacosanol, and the solvent benzyl alcohol)

– IDB is instilled via needle-less syringe directly into the surgical incision prior to closure

– The solvent diffuses rapidly on instillation, leaving an extended-release depot that delivers local anesthetic to the surgical site throughout the first 72 postoperative hours

– A randomized, double-blind, controlled study was conducted to extend the existing clinical experience with IDB to patients undergoing major abdominal surgery

METHODS

– This Phase 3, multicenter, double-blind, active-controlled study randomized patients undergoing open laparotomy for a variety of non-emergent indications to receive (in a 3:2 ratio) either:

  – Study drug: IDB (13.2% Fla, 640 mg bupivacaine) instilled directly into the incision just prior to closure

  – Active control: bupivacaine HCl 0.5% (30 mL, 150 mg) infiltrated per-incisionally at closure

  – Efficacy evaluations included postoperative pain intensity, total opioid use, and dischargeability

  – Pattern-assessed pain intensity upon movement was determined using an 11-point Pain Intensity Numeric Rating Scale (PI-NRS) that ranged from 0 (no pain) to 10 (pain as bad as you can imagine)

  – On the day of surgery (day 0), patients entered their assessments into electronic diaries upon awakening from surgery and at 8, 10, 12, and 14 hours post dose

  – On each post-surgery day from 1 to 7, patients completed an assessment at each of 4 time points (00:00, 10:00, 16:00, and 22:00)

  – A repeated measures mixed-effect model ANCOVA was used to compare pain intensity across treatment groups over the first 3 postoperative days, with incision length as the covariate

  – Mean total intravenous (IV) morphine-equivalent opioid medication use for rescue analgesia was calculated for each group

  – Any patient reporting moderate to severe postoperative pain (P-I NRS score ≥6) could receive opioid rescue analgesia

  – Morphine-equivalent opioid doses were analyzed over the 0 to 24, 0 to 48, and 0 to 72 hour post surgery time periods using an ANCOVA model with pooled site and treatment group as factors, and incision length as a covariate

  – Dischargeability was assessed using the modified Post-Anesthesia Discharge Scoring System (mPADSS) for 72 hours following surgery

  – Opioid consumption was lower in patients treated with IDB compared with bupivacaine HCl, enhancing proportion of patients judged eligible for discharge

  – At each time point assessed, the percentage of patients who were considered eligible for discharge was greater in the IDB group than in the bupivacaine group (Figure 3), although the differences were not statistically significant

CONCLUSIONS

– In this open laparotomy model, IDB significantly reduced postoperative pain intensity for 72 hours compared with bupivacaine HCl

– Opioid consumption was lower in patients treated with IDB compared with bupivacaine HCl, enhancing proportion of patients judged eligible for discharge

– Safety results were comparable for IDB and bupivacaine HCl, with no substantial differences in incidence, types, or severity of TEAEs

– IDB is novel, sustained-release local anesthetic formulation, may prove a useful component of multimodal postoperative pain-management strategies for abdominal surgery

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REFERENCES


Table 1. Demographic and Clinical Characteristics – Safety Population

<table>
<thead>
<tr>
<th>Variable</th>
<th>IDB (n=30)</th>
<th>Bupivacaine HCl (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>Median 60 (min, max)</td>
<td>53.6 (22, 80)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male 20 (66.7%)</td>
<td>24 (85.7%)</td>
</tr>
<tr>
<td>Race</td>
<td>African American 12 (40%)</td>
<td>8 (28.6%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Hispanic 4 (13%)</td>
<td>1 (3.6%)</td>
</tr>
<tr>
<td>Incision length (cm)</td>
<td>18 (5.9)</td>
<td>18 (5.9)</td>
</tr>
<tr>
<td>Max severity, all TEAEs</td>
<td>6 (20%)</td>
<td>5 (28%)</td>
</tr>
<tr>
<td>*Not assessed</td>
<td>1 (3.3%)</td>
<td>2 (11%)</td>
</tr>
</tbody>
</table>

SAFETY ASSESSMENTS

– The incidence and severity of reported TEAEs were similar between the IDB and bupivacaine HCl groups (Table 2)

Table 2. Summary of Treatment-Emergent Adverse Events – Safety Population

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>IDB (n=30)</th>
<th>Bupivacaine HCl (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dischargeable</td>
<td>23 (76.7%)</td>
<td>18 (100%)</td>
</tr>
<tr>
<td>Not dischargeable</td>
<td>7 (23.3%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Figure 1. Mean Pain Intensity on Movement Over Time

Figure 2. Readiness for Discharge* as Assessed by the modified Post-Anesthesia Discharge Scoring System (mPADSS) – ITT Population

Figure 3. Readiness for Discharge* as Assessed by the modified Post-Anesthesia Discharge Scoring System (mPADSS) – ITT Population

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<td>0 (0%)</td>
</tr>
</tbody>
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*Patients with an mPADSS score of 0 or 1 were considered eligible for discharge

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Intra-incisional depot bupivacaine reduces pain intensity and opioid consumption for 72 hours following open laparotomy, compared with bupivacaine HCl

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