A new method for treating postoperative pain associated with laparoscopic surgery

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**Objective**

- Despite improvements in analgesic techniques, insufficient postoperative pain control remains a significant problem.
- A recent study reported the presence of moderate to extreme pain after 73% of inpatient and 57% of outpatient surgeries.\(^1\)
- Opioid analgesics, though widely used for postoperative pain control, can cause undesirable side effects (most commonly nausea and vomiting, constipation, and sedation) that delay mobilization, demand more intensive postoperative care, and lower patient satisfaction.\(^2\,3\)
- We sought to develop a sustained-release, locally-acting, non-opioid analgesic administered once at the close of surgery that could provide analgesic coverage directly to the wound bed for the entire 3-day postsurgical period during which pain is most intense.

**Description**

Sucrose acetate isobutyrate extended-release bupivacaine (SABER-Bupivacaine\(^*\))

- A room temperature-stable, transparent, semiviscous solution containing 13.2% (660 mg) bupivacaine base in a single 5 mL dose
- Instilled with a blunt-tipped applicator directly into the port incisions after trocar removal and desufflation, with drug volume divided among the ports
- Forms a viscous depot that releases bupivacaine at approximately 10 mg/h over 72 h
- Also contains sucrose acetate isobutyrate, a biocompatible, biodegradable esterified sugar matrix capable of storing bupivacaine at high concentrations and benzyl alcohol, an antimicrobial solvent

**Preliminary Results**

**Methods**

- We conducted a randomized, active-controlled, double-blind pilot study of 50 patients undergoing elective outpatient laparoscopic cholecystectomy.
- Interventions: SABER-Bupivacaine 5 mL (660 mg instilled into the port incisions, n=30) or bupivacaine HCI 0.5% 30 mL (150 mg infiltrated peri-incisionally, n=20)
- Efficacy variables: 0-72 hour pain intensity on movement and 0-72 hour opioid consumption
- Safety variables: wound healing, adverse events, and 72-hour Holter monitoring

**Efficacy**

- Patients treated with SABER-Bupivacaine had mean pain intensity scores 25% lower than those treated with bupivacaine HCI during the initial 72-hour postoperative period (2.7 vs 3.6, \(P=0.024\); 11-point, 0-10 numeric pain rating scale), with a repeated measures mixed-effect ANCOVA model used for exploratory post hoc data analysis.
- The reduction in pain intensity (below left) was sustained over 72 hours.
- Median total opioid use (below right) was 24% lower for SABER-bupivacaine than for bupivacaine HCI (17.0 vs 22.5 IV morphine mg equivalents, \(P=0.021\)).

**Safety**

- Plasma bupivacaine concentrations (below left) were within established safety margins.
- 72-hour Holter monitoring showed no evidence of cardiac arrhythmias.
- Postoperative wound assessments, excluding discoloration, were similar between groups.
- Treatment-emergent adverse event (TEAE) rates (below right) were similar for the 2 groups, with the exception of application site discoloration (considered treatment related) and headache (considered unrelated).
- Most TEAEs were mild or moderate in severity; 1 serious TEAE (pneumonia) occurred in the bupivacaine HCI group.

**Conclusion & Future Directions**

- This small pilot study in patients undergoing laparoscopic cholecystectomy suggests a clinically meaningful improvement in postoperative pain and reduction in opioid use for 72 hours after treatment with SABER-Bupivacaine, based on an exploratory post hoc analysis.
- A larger, multicenter Phase 3 study of approximately 300 patients undergoing elective outpatient laparoscopic cholecystectomy began enrolling in late 2015 to assess the analgesic and opioid-sparing effects of SABER-Bupivacaine in comparison with placebo control.
- SABER-Bupivacaine, a non-opioid, locally-acting, sustained-release analgesic instilled directly into the laparoscopic port incisions at the close of surgery, may provide important benefits to patients undergoing inpatient or outpatient laparoscopic procedures.

**References**


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