SABER™-Bupivacaine, a novel extended-release formulation of bupivacaine for postoperative pain control demonstrates superior safety and no impact on surgical wound healing following inguinal herniorrhaphy


SABER™-Bupivacaine is a novel extended-release formulation of bupivacaine in a resorbable matrix which allows delivery of bupivacaine at the site of administration over a period of 5 days. The formulation consists of three components: common local anesthetic bupivacaine (12%), organic matrix sucrose acetate isobutyrate, and a chiral, benzyl alcohol. Clinical benefits and safety of continuous infusions of bupivacaine into the surgical wound via elastomer pumps was demonstrated following a variety of surgical procedures (Loo, 2006), including inguinal hernia repair (Loo, 2006, Sanchez, 2004). SABER-Bupivacaine formulations, or transcutaneous fistulation, is designed to provide continuous delivery of bupivacaine once placed in the surgical wound at the same rate of 10-20 mg/hr by elastomer pumps through indwelling catheters. Multiple trials are ongoing to investigate safety and efficacy of SABER-Bupivacaine in various surgical procedures.

A 2-week, randomized, placebo-controlled, double-blind study of SABER-Bupivacaine infilled into the wound in patients undergoing open inguinal hernia repair was conducted at 5 clinical sites in Australia and New Zealand and subsequently extended to include 3 and 6-month follow-up visits to evaluate wound surgical wound healing and scar formation. Initial trial results were reported at the American Hernia Society Annual Meeting (2008, Hernia Repair, Poster 37). This poster describes the new long-term safety data generated during the trial extension and provides an overall summary of trial results.

Methodology

Male or female patients, 18-65 years of age(n=124), undergoing open inguinal hernia repair under general anesthesia were enrolled in a multi-center, randomized, double-blind, placebo-controlled trial. The trial comprised 3 treatment groups (SABER-Bupivacaine 2.5 mL, [330mg], SABER-Bupivacaine 5.0 mL, [660mg], and SABER-Placebo 2.5 or 5.0 mL) in order to evaluate dose-response and the safety of SABER™-Bupivacaine. A follow-up period (post double-blind treatment) included surgical wound healing evaluations at 3 and 6 months after surgery. Patients in all treatment groups had similar demographics, baseline characteristics, and general health profile.

Supplemental rescue analgesia was provided to all patients on demand with oral Tramadol (100 mg maximum 400 mg daily) for treatment of moderate to severe pain or upon request. The tension-free repair was achieved by elastomeric pumps through indwelling catheters. Multiple trials are ongoing to investigate safety and efficacy of SABER-Bupivacaine in various surgical procedures.

All 124 randomized patients underwent elective, open, unilateral, tension-free hernia repair using polypropylene mesh (e.g. Marlex, Angiograft, Atrium, or Nylostran, Covidien, Norwood, MA, 2003) with the exception of one patient who did not have the surgery. Surgical incision length varied between 6 and 10 cm (mean=6.47 cm, median=6.5 cm, SD=0.98 cm). Investigational product was infilled prior to wound closure.

Surgical Wound Healing

During the initial post-operative study period, procedural complications probably or possibly related to study treatment were reported 0% (0/32) in SABER-Placebo group, 2.5% (1/34) in 2.5 mL dose group, and 5.4% [17/30] in 5.0 mL dose group. During the entire study period incidence of these events was 15.6% (5/32) in placebo group, 34.1% (15/44) in 2.5 mL dose group, and 5.4% [17/30] in 5.0 mL dose group, and included reach statistical significance.

Conclusion

Administration of SABER-Bupivacaine by instillation through surgical wound layers in patients with inguinal herniorrhaphy was well tolerated and did not result in significant changes to the surgical routine. Both doses of SABER-Bupivacaine, 2.5 mL, and 5.0 mL, were safe and well-tolerated by comparison to placebo. The higher dose, 5.0 mL, demonstrated effective analgesia in the management of surgical wound pain and significantly improved mean pain intensity on movement AUC on movement compared to placebo for 48 and 72 hours postoperatively. Patients treated with SABER-Bupivacaine required significantly less opioid rescue medications as compared to placebo. Reduction of opioid rescue was associated with reduction of opioid-related side effects (constipation, somnolence, dizziness, nausea and vomiting). Efficacy trends in the SABER-Bupivacaine 2.5 mL group were positive, but not statistically significantly different from placebo. Administration of SABER-Bupivacaine had no impact on surgical wound healing. Evaluation of local tissue, formation of scar and overall healing assessed up to 6 months postoperatively was not adversely impacted by SABER-Bupivacaine or SABER-Placebo in this patient population.

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References


