Historical Selection: Lieblich SE, Danesi H. Liposomal bupivacaine use in third molar impaction surgery: INNOVATE study. *Anesth Prog*. 2017 Fall;64(3):127–135.

David Brooks, a New York Times columnist and author, wrote in his recent book *How to Know a Person: The Art of Seeing Others Deeply and Being Deeply Seen*[1] that there are 2 kinds of people, the illuminators and the diminishers. The illuminators are those who bring out the best in you. They have a persistent curiosity about you and everyone they meet. Illuminators know how to ask the right questions at the right time. They make you feel special and respected, and they allow you to see those talents in yourself that you haven't yet seen. Illuminators help you to become a better version of yourself. They see you, value you, and make you feel your best self. Illuminators embrace your hard work and passion.

Dr Stuart Lieblich was a true illuminator, a real "people person," a gift, and a joy to all who met him. He loved life and shared that love with everyone around him. Stu had a wonderful wit and sense of humor. He enjoyed good food and wine and sharing that pleasure with others. Despite being a man of superior intellect, he never exuded an air of superiority. He was extremely hard working but never seemed overwhelmed. Stu took the tough parts of life in stride and always with grace.

In the spirit of a true illuminator, Dr Lieblich incorporated his passion for mentorship into his professional life. He devoted over 35 years to his multi-doctor private practice, Avon Oral, Facial, and Dental Implant Surgery in Avon, CT, after serving as full-time faculty at the University of Connecticut. Through his example, he positively impacted scores of dental students through the UConn student mentorship/shadowing program, which resulted in several of his most talented students opting to pursue careers in oral and maxillofacial surgery. Dr Lieblich trained dozens of oral and maxillofacial surgery residents, culminating in him being awarded resident teaching awards at both UConn and Cornell University. His intellectual curiosity spawned many innovations within his private practice including creating a culture of anesthesia safety, fostering the responsible use of long-acting local anesthetics and antibiotics with an aim toward reducing community-induced antibiotic drug resistance, and incorporating the judicious use of opioid agonists for postsurgical pain control.

His gracious and giving nature extended throughout his professional life, with countless hours spent in volunteer positions, most notably serving in national leadership positions as president of the American Dental Society of Anesthesiology (1999–2001) and president of the American Board of Oral and Maxillofacial Surgeons (2009–2010). Additionally, his work as a founding board member and director of the Dental Anesthesia Patient Safety Foundation and his text co-edited with Dr Robert Bosack serves as ample evidence of his passion for patient safety.

Published in 2017, Dr Lieblich's study on the use of liposomal bupivacaine for postoperative analgesia following third molar extractions is a tribute to his substantial interest in and care for others and underscores his commitment to patient safety. The drawbacks of opioid analgesia have had long-term adverse effects in our society as evident by the ongoing opioid epidemic. As surgical practitioners in the 1990s, we were instructed on the premise that pain should be considered a vital sign and that it would best be treated with opioid medication.[2] Pharmaceutical marketing representatives would often come to our offices, discuss how the relief of pain using opioids would improve our practices, and leave abundant samples of highly touted opioid analgesics for us to distribute to our patients. However, we never anticipated that the effects of overusing opioids would be so substantial or impactful. As was often the case for vulnerable teenagers undergoing third molar surgery, our well-intentioned efforts as highly ethical and well-respected practitioners seeking to alleviate or relieve pain in our patients often served as their first exposure to highly addictive opioids. Once the horrific effects of opioid overuse were understood, we looked for other ways to relieve post-procedural pain in our daily practices.

Dr Lieblich's curiosity and willingness to entertain creative ideas were most surely behind this study about relieving acute postoperative pain with liposomal bupivacaine in hopes of identifying a safer alternative to opioids. This study aimed to assess the analgesic efficacy and safety of liposomal bupivacaine (Exparel, bupivacaine liposome injectable suspension; Pacira Pharmaceuticals, Inc) vs placebo in patients undergoing bilateral third molar extraction. This unique formulation of bupivacaine produces prolonged local anesthetic effects capable of lasting for 72 hours or longer due to the slow, extended release of bupivacaine from multivesicular liposomes. In this study, the liposomal bupivacaine was administered via local infiltration around the surgical sites in all 4 quadrants (2 mL per side in the maxilla and 3 mL per side in the mandible) at the end of surgery. Pain ratings were assessed through 96 hours along with other outcomes like opioid rescue use, study drug pharmacokinetics, patient satisfaction, and adverse events. After accounting for confounding effects from a large number of protocol violations using an analysis of variance model, the liposomal bupivacaine group had significantly lower pain scores at 24, 72, and 96 hours ($P < .05$). Interestingly, no significant differences were noted between study groups regarding opioid use or patient satisfaction scores, and no major adverse events were documented in either group.

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As part of the study's conclusion, Dr Lieblich et al. state that the results of this study are "encouraging," but they also point out that additional study is needed to better determine the effectiveness of liposomal bupivacaine for dentistry and oral surgery. A follow-up study led by Dr Lieblich was published in 2021, which retrospectively assessed opioid prescribing in patients receiving liposomal bupivacaine after third molar extractions and found those who received liposomal bupivacaine had lower opioid refill rates than patients who did not.[4] However, very few studies to date have examined the use of liposomal bupivacaine for postoperative analgesia in dentistry or oral surgery despite these promising results. Of the few available studies, many report results mirroring those of Dr Lieblich's studies.

Looking through the breadth of Dr Lieblich's publications, we find ample other evidence of his intellectual integrity and willingness to integrate new information and to accept new modes of practice. Dr Lieblich supported and encouraged all of us who had the good fortune of working with him to step out of our comfort zones by remaining open to new approaches and novel innovations. He helped foster within each of us the ability to understand that our practices are constantly evolving.

We invite you to read this article within the historical perspective of the search for alternatives to opioid analgesia for dentistry and oral surgery following the opioid abuse epidemic which began in the 1990s. As you read, please remember our dear illuminator friend and colleague, Dr Stuart Lieblich, and appreciate his efforts to leave the world and our patients in a better, safer place.

Respectfully submitted,

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Figure. (L to R) Drs. Bill MacDonnell, James Tom, and Stuart Lieblich at the 2021 Horace Wells Club Reception and Dinner held at the Town and Country Club in Hartford, CT.

REFERENCES

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4. Lieblich SE, Misiek D, Olczak J, Fleck H, Waterman F. A retrospective cross-sectional study of the effect of liposomal bupivacaine on postoperative opioid prescribing after third molar extraction. J Oral Maxillofac Surg. 2021;79(7):1401–1408.e1. doi:10.1016/j.joms.2021.02.012

Continuing Education Questions

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CE questions must be completed within 3 months and prior to the next issue.

1) In the original study by Dr Lieblich published in 2017, which of the following statements is correct about opioid rescue medication use in the postoperative period following third molar surgery?

   a. Although opioid use in the liposomal bupivacaine group was slightly higher, it lacked statistical significance.
   b. Median time to first use of opioid rescue medication was significantly longer in the placebo group.
   c. The placebo group had a significantly higher rate of opioid use than the liposomal bupivacaine group.
   d. Total opioid consumption through 48 hours was significantly higher in the liposomal bupivacaine group.

2) Which of the following factors of the 2017 Lieblich study severely limited the outcomes and outcomes analysis of the efficacy of liposomal bupivacaine?

   a. A high frequency of adverse events (AE).
   b. Multiple protocol violations in both the study and placebo groups.
   c. Several overdose reports in patients utilizing the opioid rescue medication.
   d. The extremely small sample size utilized in this study.

3) From both Lieblich's 2017 study and the accompanying commentary, what clinically significant outcome was determined by examination of the effects of liposomal bupivacaine use in dental surgery?

   a. A significant increase in the use of nonsteroidal anti-inflammatory drugs was found within the placebo group.
   b. A significant reduction in cumulative pain scores was observed within the liposomal bupivacaine group for the per-protocol population.
   c. A significant reduction in serious adverse events (AEs) was noted in the liposomal bupivacaine group.
   d. A significant reduction occurred in the use of rescue opioids for postoperative pain within the liposomal bupivacaine group.

4) In a follow-up study performed by Lieblich et al, in 2021, what outcomes measure was studied in dental surgery utilizing liposomal bupivacaine?

   a. The frequency of opioid prescription refill rates for patients receiving liposomal bupivacaine infiltrations for postoperative pain after dental surgery.
   b. The incidence of permanent buccal nerve paresthesia produced by liposomal bupivacaine injection for mandibular third molar extraction surgery.
   c. The incidence of tissue necrosis localized to the area of liposomal bupivacaine injection after third molar surgery.
   d. Toxicity reactions associated with therapeutic amounts of liposomal bupivacaine used for postoperative pain control after dental surgery.