Does Liposomal Bupivacaine (Exparel) Significantly Reduce Postoperative Pain/Numbness in Symptomatic Teeth with a Diagnosis of Necrosis? A Prospective, Randomized, Double-blind Trial

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Abstract

Introduction: Medical studies have shown some potential for infiltrations of liposomal bupivacaine (Exparel; Pacira Pharmaceuticals, San Diego, CA), a slow-release bupivacaine solution, to extend postoperative benefits of numbness/pain relief for up to several days. Because the Food and Drug Administration has approved Exparel only for infiltrations, we wanted to evaluate if it would be effective as an infiltration to control postoperative pain. The purpose of this study was to compare an infiltration of bupivacaine with liposomal bupivacaine for postoperative numbness and pain in symptomatic patients diagnosed with pulpal necrosis experiencing moderate to severe preoperative pain. Methods: One hundred patients randomly received a 4.0-mL buccal infiltration of either bupivacaine or liposomal bupivacaine after endodontic debridement. For postoperative pain, patients were given ibuprofen/acetaminophen, and they could receive narcotic pain medication as an escape. Patients recorded their level of numbness, pain, and medication use the night of the appointment and over the next 5 days. Success was defined as no or mild postoperative pain and no narcotic use. Results: The success rate was 29% for the liposomal group and 22% for the bupivacaine group, with no significant difference (P = .4684) between the groups. Liposomal bupivacaine had some effect on soft tissue numbness, pain, and use of non-narcotic medications, but it was not clinically significant. There was no significant difference in the need for escape medication. Conclusions: For symptomatic patients diagnosed with pulpal necrosis experiencing moderate to severe preoperative pain, a 4.0-mL infiltration of liposomal bupivacaine did not result in a statistically significant increase in postoperative success compared with an infiltration of 4.0 mL bupivacaine. (J Endod 2016;42:1301–1306)

Key Words

Bupivacaine, endodontic pain, liposomal bupivacaine, postoperative pain, pulpal necrosis, symptomatic patients

Significance

Although the use of liposomal bupivacaine (Exparel) did not result in a statistically significant improvement in postoperative success when compared with bupivacaine, further research is indicated to evaluate this new drug for effectiveness in endodontics.
CONSORT Randomized Clinical Trial

including bunionection (6), total knee arthroplasty (7–10), total hip arthroplasty (11), implant-based breast reconstruction (12), colec-
tomy (13, 14), ileostomy reversal (15, 16), hemorrhoidectomy (17–19), mammoplasty (20, 21), abdominoplasty (22), and rhytidec-
tomy (23). Postoperative pain was reduced in some studies (9, 12, 17–19, 21), and some studies showed a reduction in the use of postoperative narcotics (6, 9, 11, 13–19, 22, 23). However, other studies showed no difference in pain/and or opioid use postoperatively (7, 8, 10, 20).

There have been no studies on the use of liposomal bupivacaine in endodontics. The theory of using liposomal bupivacaine is that it may provide a 72-hour window of no or reduced postoperative pain and decreased need for analgesics (including opioids). Because the FDA has approved Exparel only for infiltrations, we wanted to evaluate if it would be effective as an infiltration to control postoperative pain. The purpose of this study was to compare bupivacaine with liposomal bupivacaine (Exparel) for postoperative numbness and pain in symptomatic patients diagnosed with pulpal necrosis experiencing moderate to se-
vere preoperative pain.

Materials and Methods

One hundred patients participated in this study. All patients were in good health as determined by a health history and oral questioning. Exclusion criteria were as follows: subjects who were younger than 18 years; unable to take ibuprofen, acetaminophen, or hydrocodone; allergic to local anesthetics or sulfates; pregnant or nursing; had a history of significant medical conditions (American Society of Anesthesiolo-
gists class III or higher); or unable to give informed consent. The Ohio State University Human Subjects Review Committee approved the study (institutional review board protocol number 2013H0421), and written informed consent was obtained from each qualifying patient.

Patients had a clinical diagnosis of a symptomatic tooth with a pulpal diagnosis of necrosis and moderate to severe pain at the time of treatment. Each tooth tested negative to an electric pulp tester (Ana-
lytic Technology Corp, Redmond, WA) and to Endo-Ice (Hygenic Corp, Akron, OH) and had a periapical radiolucency on radiographic exam-
ination using periapical digital radiography. No patients had a draining sinus tract. After the tooth was accessed, pulpal necrosis was confirmed.

Before treatment, patients completed a Corah Dental Anxiety Scale to rate their level of anxiety (24). Each patient also rated his or her preop-
erative pain on a Heff-Parker visual analog scale (VAS) (25). The VAS was divided into 4 categories as described previously (2). To qualify for the study, patients presented with moderate to severe pain as rated on the VAS.

All patients received 1 cartridge of 2% lidocaine with 1:100,000 epinephrine (Xylocaine; AstraZeneca LP for Dentsply, York, PA) by infiltr-
ation for maxillary teeth or inferior alveolar nerve block for mandib-
ular teeth. Because all patients presented with moderate to severe pain, local anesthesia was administered. Additional local anesthesia (maximum of 0.9 mL 2% lidocaine with 1:100,000 epinephrine) was administered for the rubber dam clamp using lingual infiltration anes-
thesia in the maxilla and a long buccal injection for mandibular molars. In the maxilla, a greater palatine (posterior teeth) or nasopalatine (anterior teeth) injection could have been given for lingual anesthesia. However, the lingual infiltrations provided effective anesthesia.

After signs of soft tissue anesthesia (lip numbness in the mandible and cheek numbness in the maxilla), the tooth was isolated with a rubber dam. Access was gained using a number 4 round bur in a high-speed handpiece. Endodontic debridement was performed using 3% sodium hypochlorite irrigation, stainless steel K-type files (Dentsply Interna-
tional, Inc, Johnson City, TN), and rotary files (Vortex, Dentsply Interna-
tional, Inc, Johnson City, TN). A 25-G 5/8-inch irrigating needle attached to a 20-mL sterile disposable Luer-Lok syringe was used for irrigation after every third hand and rotary file. The working length was determined using periapical digital radiographs, which were confirmed with an apex locator (Root ZX II; Morita USA, Irvine, CA). The canals were prepared to a minimum size of 30/04 or 40/04 depending on the tooth and canals treated. The canals were dried with paper points and calcium hydroxide (Multi-Cal; Pulpdent Corp, Watertown, MA) was placed as an intracanal medicament. The teeth were temporized with Cavit (Cavit G; 3M ESPE, Seefeld, Germany), and the patients were scheduled for root canal completion. The senior author (B.G.) performed all anesthetic injections and endodontic treatment.

After endodontic treatment, the patients were randomly divided into 2 groups and received either 4.0 mL (53.2 mg) liposomal bupivacaine (Exparel) or 4.0 mL (20 mg) 0.5% bupivacaine with 1:200,000 epine-
phrine (Marcaine, AstraZeneca LP for Dentsply) by infiltration. Each of the patients in each group was randomly assigned a 6-digit number to blind the experiment (ie, the patient and doctor were unaware of which anes-
thetic solution [liposomal bupivacaine or bupivacaine] was given to them because only the random numbers identified the formulations).

The liposomal bupivacaine was stored in the refrigerator and upon removal was warmed to room temperature. Using a sterile technique, 4 mL of the appropriate anesthetic formulation (liposomal bupivacaine or bupivacaine) was drawn into 5-mL sterile, plastic syringes (Becton-Dickinson & Co, Rutherford, NJ) using a 25-G, 5/8-inch needle (Mono-
ject; Sherwood Services, Mansfield, MA) by trained personnel not directly involved in the study. The syringe was wrapped with opaque tape, and a corresponding 6-digit number was assigned to the syringe to effectively blind the anesthetic formulations. A copy of the master list of 6-digit random numbers was supplied by the lead researcher (M.D.) and was not made known to the investigator during the data collection period.

Patients received a buccal infiltration next to the offending tooth of 4.0 mL of either liposomal bupivacaine or bupivacaine using a sterile 5-
ML syringe (Becton-Dickson, Franklin Lakes, NJ) and a 25-G 1½- inch needle (Monoject). The infiltration was given at least 20 minutes after administration of the initial lidocaine formulation per manufacturer’s instructions for liposomal bupivacaine (4). The senior author (B.G.) administered all infiltrations.

If the patient presented to the clinic already taking an antibiotic, he or she was instructed to finish his or her current regimen if the antibi-
otic and dosage was clinically appropriate. Patients who were not on antibiotics or were not prescribed an appropriate antibiotic regimen received a prescription for an antibiotic (500 mg penicillin; if allergic, 300 mg clindamycin) to be taken every 6 hours for 7 days. Antibiotics were administered because a number of presenting patients were already on antibiotics, and we wanted to eliminate this variable from the study. The patients were given a 5-day supply of 600 mg ibuprofen (take 1 tablet every 6 hours as needed for pain) and 500 mg acetamin-
ophen (take 2 tablets every 6 hours as needed for pain). The ibuprofen and acetaminophen were to be taken together. The patients were in-
structed not to take any other pain or antibiotic medications during the investigation. The patients were given a script for either 5/500 or 5/325 hydrocodone/acetaminophen (escape medication) depending on changes in the available drug formulation at the time of the study. If the ibuprofen/acetaminophen given to the patient was not managing their pain, they were instructed to call an assigned cell phone number of the principal investigator, and the script was then approved to be filled by the pharmacy. The patients were instructed to stop taking the ibuprofen and acetaminophen once starting the escape medication to avoid taking multiple doses. The patient was seen emergently in the clinic if the need arose.

Patients received a diary for the evening of the appointment before going to bed and 5 days postoperatively upon awaking to record

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subjective soft tissue numbness (100-mm VAS with 0 being no numbness and 100 being complete numbness), the pain they were experiencing (170-mm VAS), and the pain medications (study or escape) they were taking. Patients were asked to record soft tissue numbness next to the tooth to capture their perception of soft tissue numbness. Patients were required to return all unused medications upon completion of the study to verify diary results. The time of day was recorded, and any pain was recorded on VASs as described earlier for pain. Success was defined as none or mild postoperative pain and no use of narcotic medications.

The data from this study were collected and statistically analyzed. Comparisons between liposomal bupivacaine and bupivacaine for sex and jaw were analyzed using the chi-square test, and comparisons by age, presenting pain, soft tissue numbness, postoperative pain, and analgesic use were analyzed using the randomization test adjusted with the step-down Bonferroni method of Holm. The patient’s Corah Dental Anxiety Scales were analyzed using a Mann-Whitney-Wilcoxon test. Between-group differences for tooth type were analyzed using the Fisher exact test. Comparisons between liposomal bupivacaine and bupivacaine for sex and jaw were analyzed using the Fisher exact test. Between-group differences in success were evaluated using a repeated-measures logistic regression with group, day, and sex as the independent variables. Between-group differences in pain and the use of non-narcotic pain medications over day 1 to day 5 were analyzed using logistic regression between the 2 groups. The use of narcotic (escape) medication between pain medications over day 1 to day 5 were analyzed using logistic regression with group, day, and sex as the independent variables. Between-group differences in pain and the use of non-narcotic pain medications over day 1 to day 5 were analyzed using logistic regression by group and day. The use of narcotic (escape) medication between the 2 groups was analyzed using the chi-square test. Comparisons were made between liposomal bupivacaine and bupivacaine for sex and jaw. Comparisons were made between the 2 groups with regard to age, sex, presenting pain, Corah anxiety ratings, tooth location, or jaw.

**Results**

A total of 113 patients were recruited for this study. Thirteen patients were disqualified for the following reasons: 2 because of vital tissue in 1 of the canals and 11 for not returning the postoperative surveys. Therefore, the total number of patient data analyzed was 100 (52 in the liposomal bupivacaine group and 48 in the bupivacaine group).

Table 1 shows the preoperative variables. There were no statistically significant differences between the 2 groups with regard to age, sex, presenting pain, Corah anxiety ratings, tooth location, or jaw.

Figure 1 shows mean soft tissue numbness for liposomal bupivacaine and bupivacaine. The liposomal bupivacaine group had significantly more reported soft tissue numbness for days 1 (P = .0030) and 2 (P = .0007). For both groups, numbness decreased over the 5 days (Fig. 1).

Table 2 shows the regression summary for treatment success. There were no significant effects for group, sex, or jaw. Success was

### Table 1. Preoperative Variables for the Liposomal Bupivacaine and Bupivacaine Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Liposomal Bupivacaine</th>
<th>Bupivacaine</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)†</td>
<td>36 ± 10</td>
<td>37 ± 13</td>
<td>1.000</td>
</tr>
<tr>
<td>Sex 16 females, 27 females,</td>
<td>1.788</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presenting pain‡</td>
<td>117 ± 22</td>
<td>119 ± 27</td>
<td>1.000</td>
</tr>
<tr>
<td>Corah Anxiety (median)</td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Tooth location, % (n)</td>
<td></td>
<td></td>
<td>.5782</td>
</tr>
<tr>
<td>Anterior</td>
<td>6 (3/52)</td>
<td>13 (6/48)</td>
<td></td>
</tr>
<tr>
<td>Premolar</td>
<td>15 (8/52)</td>
<td>15 (7/48)</td>
<td></td>
</tr>
<tr>
<td>Molar</td>
<td>79 (41/52)</td>
<td>73 (35/48)</td>
<td></td>
</tr>
<tr>
<td>Jaw</td>
<td></td>
<td></td>
<td>.9744</td>
</tr>
<tr>
<td>Maxilla</td>
<td>46 (24/52)</td>
<td>46 (22/48)</td>
<td></td>
</tr>
<tr>
<td>Mandible</td>
<td>54 (28/52)</td>
<td>54 (26/48)</td>
<td></td>
</tr>
</tbody>
</table>

*There were no significant differences between the 2 groups.

†Mean ± standard deviation.

‡Mean ± standard deviation, Helt-Parker visual analog scale ratings.

**Discussion**

Differences in the preoperative variables of age and sex would be minimized because no statistically significant differences were shown

### Table 2. Logistic Regression Summary for Success

<table>
<thead>
<tr>
<th>Effect</th>
<th>Num DF</th>
<th>Den DF</th>
<th>Chi-square</th>
<th>P value &gt; Chi-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (liposomal bupivacaine vs bupivacaine)</td>
<td>1</td>
<td>84</td>
<td>1.51</td>
<td>0.2187</td>
</tr>
<tr>
<td>Sex (female vs male)</td>
<td>1</td>
<td>84</td>
<td>1.35</td>
<td>0.2449</td>
</tr>
<tr>
<td>Jaw (maxilla vs mandible)</td>
<td>1</td>
<td>84</td>
<td>0.03</td>
<td>0.8666</td>
</tr>
<tr>
<td>Tooth type</td>
<td>2</td>
<td>84</td>
<td>0.51</td>
<td>0.7741</td>
</tr>
</tbody>
</table>

### Odds ratio estimates

<table>
<thead>
<tr>
<th>Effect</th>
<th>Estimate</th>
<th>DF</th>
<th>95% Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (liposomal bupivacaine vs bupivacaine)</td>
<td>1.895</td>
<td>84</td>
<td>0.674</td>
</tr>
<tr>
<td>Sex (female vs male)</td>
<td>0.539</td>
<td>84</td>
<td>0.188</td>
</tr>
<tr>
<td>Jaw</td>
<td>1.097</td>
<td>84</td>
<td>0.367</td>
</tr>
</tbody>
</table>

Den DF, number of degrees of freedom associated with the model errors; DF, degrees of freedom; Num DF, number of degrees of freedom in the model.
between groups (Table 1). The presenting initial moderate to severe pain (Table 1) is representative of emergency patients with symptomatic teeth, a pulpal diagnosis of necrosis, and a periapical radiolucency as shown by Wells et al (1) and Sebastian et al (2). Because patients reported low to moderate Corah scores (Table 1), anxiety may not have played a large role in influencing the pain associated with the use of liposomal bupivacaine or bupivacaine. The influence of tooth location was minimized because the teeth were evenly distributed (Table 1).

The liposomal bupivacaine group showed significantly more reported soft tissue numbness on days 1 and 2 (Fig. 1). This is an indication that the mechanism of slow release of liposomal bupivacaine is operable. However, the clinical effect of soft tissue numbness would be minimal because the mean soft tissue numbness ratings of 28/100 mm and 18/100 mm for days 1 and 2, respectively, would indicate incomplete numbness for the majority of patients.

Although pain was reduced from presenting pain levels, moderate to severe pain was still reported by 51%–59% of the patients the night of the treatment, 40%–53% of the patients on day 1, and 22%–40% on day 2 (Table 3). When evaluating postoperative pain in a similar study (2) of patients with symptomatic necrotic teeth presenting with moderate to severe pain who received endodontic debridement and postoperative ibuprofen and acetaminophen but no postoperative anesthetic, moderate to severe pain was reported by 62% of the patients the night of the treatment, 40%–53% of the patients on day 1, and 22%–40% on day 2. Therefore, it is reasonable to conclude that administration of 4.0 mL of either liposomal bupivacaine or bupivacaine by infiltration would result in a similar incidence of postoperative pain. The decrease in tooth pain over the 5 days (Table 3, Fig. 2) is probably the natural course of the disease process for the clinical condition of a symptomatic tooth with a necrotic pulp and associated periapical radiolucency. Other authors (1, 2, 26–29) showed that the majority of patients started to improve regardless of drug or active treatment protocols on the third postoperative day.

When comparing pain levels from day 1 through day 5 (Table 3, Fig. 2), liposomal bupivacaine statistically ($P = .000$) reduced pain when compared with bupivacaine. Therefore, it would appear that the liposomes are releasing small amounts of bupivacaine over a 5-day period. However, the effect on pain would not be clinically significant because moderate to severe pain was still experienced by 51% of the patients on day 1 and 40% of the patients on day 2.

Although there are a number of studies (30–34) evaluating postoperative pain with bupivacaine, no study has used a postoperative infiltration of 4 mL adjacent to the involved tooth in patients presenting with symptomatic necrotic teeth and moderate to severe pain who received endodontic debridement and postoperative ibuprofen and acetaminophen. Therefore, comparisons with other studies would not be possible.

Table 3. Percentages and Discomfort Ratings of Postoperative Pain for the Liposomal Bupivacaine and Bupivacaine Groups (excluding patients who took narcotics)

<table>
<thead>
<tr>
<th>Group</th>
<th>None, % (n)</th>
<th>Mild, % (n)</th>
<th>Moderate, % (n)</th>
<th>Severe, % (n)</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0*</td>
<td>Liposomal bupivacaine 10 (5/52) 38 (20/52) 40 (21/52) 11 (6/52) 54 ± 38</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Bupivacaine 10 (5/48) 33 (16/48) 42 (20/48) 17 (8/48) 72 ± 47</td>
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<tr>
<td>Day 1</td>
<td>Liposomal bupivacaine 18 (8/45) 42 (19/45) 31 (14/45) 9 (4/45) 50 ± 44</td>
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<tr>
<td></td>
<td>Bupivacaine 7 (3/45) 40 (18/45) 40 (18/45) 13 (6/45) 65 ± 43</td>
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<tr>
<td>Day 2</td>
<td>Liposomal bupivacaine 24 (11/45) 51 (23/45) 15 (7/45) 7 (3/45) 38 ± 44</td>
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<td></td>
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<tr>
<td></td>
<td>Bupivacaine 18 (8/45) 53 (24/45) 27 (12/45) 13 (6/45) 58 ± 45</td>
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<tr>
<td>Day 3</td>
<td>Liposomal bupivacaine 44 (20/45) 40 (18/45) 9 (4/45) 7 (3/45) 23 ± 38</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Bupivacaine 27 (12/45) 35 (16/45) 31 (14/45) 7 (3/45) 46 ± 46</td>
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<tr>
<td>Day 4</td>
<td>Liposomal bupivacaine 57 (25/44) 32 (14/44) 9 (4/45) 4 (2/44) 18 ± 33</td>
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<td></td>
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<tr>
<td></td>
<td>Bupivacaine 36 (16/44) 34 (15/44) 25 (11/44) 4 (2/44) 36 ± 40</td>
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<tr>
<td>Day 5</td>
<td>Liposomal bupivacaine 72 (31/43) 21 (9/43) 5 (2/43) 2 (1/43) 13 ± 28</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Bupivacaine 45 (20/44) 43 (19/44) 11 (5/44) 0 (0/44) 23 ± 30</td>
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</tbody>
</table>

*Night of treatment when local anesthesia wore off.

Table 4. Mean Number of the Combination Medications Taken (excludes patients who took narcotics)

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of patients</th>
<th>Mean no. of tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Liposomal bupivacaine 45 5.3 ± 3.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bupivacaine 45 7.1 ± 4.6</td>
<td></td>
</tr>
<tr>
<td>Day 2</td>
<td>Liposomal bupivacaine 45 3.4 ± 3.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bupivacaine 45 4.8 ± 3.6</td>
<td></td>
</tr>
<tr>
<td>Day 3</td>
<td>Liposomal bupivacaine 45 1.8 ± 3.0</td>
<td></td>
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<tr>
<td></td>
<td>Bupivacaine 45 3.6 ± 3.8</td>
<td></td>
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<tr>
<td>Day 4</td>
<td>Liposomal bupivacaine 45 1.2 ± 2.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bupivacaine 45 2.7 ± 3.8</td>
<td></td>
</tr>
<tr>
<td>Day 5</td>
<td>Liposomal bupivacaine 45 0.7 ± 1.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bupivacaine 45 2.1 ± 3.3</td>
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</tbody>
</table>

Figure 2. Mean postoperative pain as rated on the 170-mmVAS.
Most medication usage was in the first several days and decreased over the 5 days, paralleling the decreasing pain (Table 4, Fig. 3). When comparing medication usage from day 1 through day 5 (Table 4, Fig. 3), liposomal bupivacaine statistically ($P = .014$) reduced non-narcotic medication consumption when compared with bupivacaine. When evaluating 2 similar studies (1, 2) of patients with symptomatic necrotic teeth presenting with moderate to severe pain who received endodontic debridement and postoperative ibuprofen and acetaminophen but no postoperative anesthetic, medication usage (mean number of tablets) was 5.7 to 6.3 tablets (1, 2) on day 1 and 4.5 to 4.9 tablets (1, 2) on day 2. Although the medication use was decreased in the liposomal bupivacaine group (Table 4) when compared with the previous studies (1, 2), patients still required medication. When combined with the results of postoperative pain, the use of liposomal bupivacaine would not be clinically significant because moderate to severe pain was still experienced and the patients still required medications.

Eleven percent of the patients in the liposomal bupivacaine group and 24% in the bupivacaine group took escape medications with no significant ($P = .098$) difference between the groups (Fig. 3). In 2 similar studies of symptomatic necrotic teeth, Wells et al (1) and Sebastian et al (2) reported that 20% and 24%, respectively, of patients used escape narcotic medication. These 2 studies, which included endodontic debridement without long-acting anesthetic supplemental infiltration, had higher percentages of patients who used narcotics than the liposomal bupivacaine group in the current study (Fig. 4) but similar narcotic usage for bupivacaine. Although liposomal bupivacaine had some effect on narcotic use, it did not completely eliminate the need for narcotic medication or reach statistical significance when compared with bupivacaine.

Success was 29% for the liposomal group and 22% for the bupivacaine group, with no significant difference between the 2 groups. The definition of success was defined as none or mild postoperative pain and no use of narcotic medications (ie, if the patient had pain, the non-narcotic medications and/or anesthetic infiltration would be controlling the pain at a mild pain level without the use of narcotics). Because only 22%–29% of the patients had success, we cannot recommend the use of infiltrations of either liposomal bupivacaine, at a cost of $250/20 mL single-use vial, or bupivacaine to control postoperative pain in the group of patients studied.

Why didn’t liposomal bupivacaine increase success? In general, although liposomal bupivacaine had some effect on pain and medication usage (Tables 3 and 4, Figs. 2 and 3), it did not increase success. Furthermore, as stated by the manufacturers, “the rate of systemic absorption of liposomal bupivacaine is dependent upon the total dose of drug administered, the route of administration, and the vascularity of the administration site,” which makes comparison of liposomal bupivacaine in the current study to other medical studies difficult (5). Some of the medical studies showing a decrease in pain and/or a decrease in medication use involved larger surgical sites and the administration of larger amounts (75–532 mg) of liposomal bupivacaine for infiltration anesthesia. However, even using larger amounts, not all the medical studies showed a decrease in pain or opioid use, indicating liposomal bupivacaine may not be effective. In the maxilla or mandible, it is difficult to administer such large amounts for infiltration anesthesia because of the limited anatomic spaces of the jaws and surrounding areas. We felt the amount we administered was appropriate given the limited anatomic considerations of an infiltration.

Another important distinction is that patients in the current study had periapical bacterial involvement and associated inflammation, whereas in the medical studies preoperative infection was not likely present. Perhaps a liposomal bupivacaine product that contains a higher concentration of bupivacaine could be more effective for the oral cavity. Such a product could be injected in a similar 4.0-mL volume but have more potency. The potential safety concern would be if too much bupivacaine was released in too short of a time; there could be an adverse reaction.

Another possible way to increase drug efficacy for mandibular teeth would be to administer liposomal bupivacaine as an inferior alveolar nerve block. However, Exparel is currently not approved for use in nerve block injections by the FDA. If the drug is approved for nerve block, the question is if the small amount (3%) of bupivacaine in the liposomal bupivacaine formulation would be available initially to provide a profound inferior alveolar nerve block and also continue to provide analgesia for 72 hours.

In conclusion, for symptomatic patients diagnosed with pulp necrosis experiencing moderate to severe preoperative pain, a 4.0-mL infiltration of liposomal bupivacaine did not result in a statistically significant increase in postoperative success compared with an infiltration of 4.0 mL bupivacaine.

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