New Knowledge, Innovations, & Improvements

RESEARCH

NK1EO – The organization supports the advancement of nursing research.

Provide one completed IRB-approved nursing research study. Use format presented below:

Introduction

Research question and hypothesis

The purpose of this study was to compare the efficacy of eutectic mixture of local anesthetics (EMLA) cream to 4% liposomal lidocaine cream (LMX4) in managing pain during sharp debridement of wounds. The research questions were:

1) Is EMLA cream more effective than LMX4 in managing pain associated with sharp wound debridement?

2) Do participants believe that one anesthetic agent provides better pain relief over the other?

3) What complications associated with these agents do participants experience?

4) Is the use of EMLA cream more cost effective than use of LMX4?

The hypothesis was that there is a difference between EMLA cream and LMX4 in managing pain associated with sharp wound debridement.

Study rationale

Debridement is the removal of infected or necrotic tissue from a wound and is performed to promote healing (Broadus, 2013). Sharp debridement involves the use of a scalpel or scissors to assist with tissue removal; this method is preferred for deep wounds, when there is a large amount of tissue to be removed, or when significant infection is present with risk of sepsis (Bates-Jensen & Apeles, 2006). Sharp debridement has been found to decrease time to healing over other forms of debridement (Steed, Donohoe, Webster, & Lindsley, 1996; The Wound Healing Group, 2011). Chronic wounds, such as venous leg ulcers and pressure ulcers, are among those most frequently treated by sharp debridement. Broadus (2013) reported 6.5 million Americans are affected by chronic wounds. According to Frykberg and Banks (2015), the cost of treatment for chronic wounds in the United States may be in excess of $20 billion.

Sharp wound debridement has been associated with pain (Rosenthal et al., 2001; The Wound Healing Group, 2011). Minimizing pain is essential, as undertreated pain causes distress. Several topical agents have been studied to determine their safety and
efficacy in producing local anesthesia to manage pain associated with debridement. Two of the most commonly used agents are eutectic mixture of local anesthetics (EMLA) and Lidocaine.

Literature review

Lidocaine

Lidocaine is an effective agent for providing anesthesia in a variety of procedures (Khatahtbeh & Qubain, 2012; Mabee, 2007; Vanichantikul & Charoenkwan, 2013). Lidocaine comes in different preparations and strengths. A common topical lidocaine preparation is 4% gel. This formulation is frequently used to provide topical anesthesia for intravenous cannulation (Goldman, 2004; Koh, Harrison, Myers, Dembinski, Turner, & McGraw, 2004) and procedures of the oral cavity (Donaldson & Meechan, 1995; McMillan et al., 1992; Svensson et al., 1992), prostate biopsy (Galosi et al., 2005), episiotomy, and wound debridement (Kaweski, 2008). Liposomal lidocaine is a newer lidocaine preparation. Liposomal encapsulation facilitates lidocaine delivery, resulting in a more rapid onset of anesthesia (Allen, 2013). Not only is lidocaine an effective topical anesthetic, studies have also demonstrated its safety (Donaldson & Meechan, 1995; McMillan et al., 1992; Nestor, 2005; Svensson et al., 1992), although Randell, Yli-Hankala, Valli, and Lindgren (1992) reported use of a 4% gel increased diastolic pressure during a study of topical anesthesia of nasal mucosa during fiberoptic airway endoscopy.

EMLA

Eutectic mixture of local anesthetics (EMLA) is an emulsion of 2.5% lidocaine and 2.5% prilocaine. It is available as a cream, gel, or disk (Physicians’ Desk Reference, 2014). EMLA is used for dermal anesthesia in sharp debridement of leg ulcers and decubitus ulcers, among other wound types (Blanke & Hallern, 2003). Following application, the site is covered with an occlusive dressing to aid absorption. Time to anesthesia varies by dose, site, and duration of application, but for wound debridement, 30 to 60 minute application times have been shown to produce sufficient anesthesia (Blanke & Hallern, 2003; VanScheidt, Sadjadi, & Lillieborg, 2001). Rare adverse effects in adults have been reported, including allergic dermatitis, and seizure in one patient undergoing 17 debridements (VanScheidt et al., 2001).

Comparison Studies

EMLA was new to the market in the early 1990s, so the majority of studies comparing EMLA to other topical agents were conducted between then and the early 2000s. Few studies were found that compared EMLA to 4% lidocaine or 4% liposomal lidocaine, but of those, EMLA cream was superior to 5%, 4%, and 2% lidocaine in studies of topical anesthesia for oral and nasal mucosa (Donaldson & Meechan, 1995; Svensson et al., 1992). Other studies found no significant difference between EMLA and 4% lidocaine gel (Friedman, Fogelman, Nouri, Levine, & Ashinoff, 1999; Koppel, Coleman, & Coleman, 2000; McMillan et al., 1992; Tang, Goon, & Goh, 2004); or between 4% liposomal lidocaine and EMLA when used for laser procedures and skin micro-needling
(Chiang et al., 2015). However, no studies were found comparing EMLA cream to 4% liposomal lidocaine cream for managing pain during sharp debridement.

**Participants**

**Nurses at the organization who are the principal investigators (PI or co-PI) involved in the conduct of the study**

The PI for this study was Jennifer Perry, BSN, RN, CHRN, Nurse Clinician III, a certified nurse employed at the Center for Wound Healing and Hyperbaric Medicine (WHC) at Advocate BroMenn Medical Center. Co-investigators included: Jessica Lee, BSN, RN, Nurse Clinician II, from the WHC and Wendy Woith, PhD, RN, FAAN, Advocate BroMenn Endowed Professor. Other WHC associates served as research assistants: Melanie Evelsizer, RN, CHRN, Charge Nurse; Michelle Hammer, BSN, RN, Nurse Clinician II; and Melissa Smith, RN, CHRN, Outpatient Wound Care Coordinator.

**Methods**

**Study design**

This study was a randomized, controlled, double-blinded, cross-over trial of EMLA cream (intervention) compared to 4% liposomal lidocaine (LMX4) (control) for the management of pain during sharp wound debridement. Participants served as their own control; they were randomized to order of anesthetic agent application. Forty envelopes were stuffed with treatment protocols; 20 envelopes contained the LMX4 treatment protocol first and 20 contained the EMLA treatment protocol first. Envelopes were numbered from 1 to 40 with a removable label and were then randomized using Research Randomizer, a computerized random-number generator that generated one set of numbers with 40 numbers in the set, ranging from 1 to 40. These numbers were affixed to the envelopes and the new order was the order of distribution to participants.

**Study timeline**

- **Start date:** April 27, 2015 – Screening Initiated
- **October 28, 2015 – First Patient Enrolled**
- **Completed date:** March 7, 2016

**IRB approval date:** The application was approved on October 21, 2014 following expedited review by the Advocate Health Care Institutional Review Board.

**Research sample (study participants and sample size, sampling plan)**

Patients referred to the wound center for sharp debridement were recruited for this study. Flyers announcing the study were posted at the wound center. Following registration, potential participants were approached by a member of the research team about participating. Standard processing of all patients requires that they are admitted to a treatment room for preparation. These rooms are private and sound-proof. When
the patient was comfortably seated, a member of the research team described the study. If the patient expressed interest, the research team member reviewed the informed consent document and obtained the participant’s signature if they agreed to participate. They were randomized to treatment order at that time.

A power analysis (conducted using GPower 3.1) for Wilcoxon signed rank test showed a sample size of 35 was needed for 80% power to detect a medium effect size. We expected to enroll 40 patients, which allowed for 10% attrition.

Inclusion criteria included patients who were 18 years and older; able to give consent; English language speakers; and who had a venous, arterial, lymphedemic, or vasculitic wound; or pressure ulcer that required more than one debriding.

Exclusion criteria included patients diagnosed with neuropathy, patients who were allergic to lidocaine or EMLA creams, people with wounds that did not need to be debrided or were projected to need fewer than two debridings, patients with congenital or idiopathic methemoglobinemia, prisoners, adults unable to consent, pregnant/breastfeeding women, and juveniles. People with diabetes were considered if there was no neuropathy.

Patients who had taken analgesics in the previous 24 hours were considered for inclusion in the study, but the intervention could not be initiated during that appointment. However, they could participate during subsequent visits if they have not used an analgesic in the 24 hours prior to the appointment.

**Data collection methods**

Once a participant was enrolled, the top envelope was assigned to that participant. The research nurse took the top envelope from the stack and all forms inside the envelope were numbered with the envelope number. The registered nurse (RN) assigned to the case opened the envelope to identify the treatment protocol, applied the anesthetic agent to the wound using the method prescribed by the manufacturer, and covered the site with an occlusive dressing. Lidocaine remained covered for 15 minutes and EMLA for 30 minutes prior to debridement. Participants were not informed of treatment order nor the association of preparation time to medication.

To prevent physician bias of results, the physicians were blinded to treatment order. Physicians performed debridement according to the type and location of the wound, and the wound was dressed as per standard care.

Participants were asked at both appointments for debriding to rate their wound pain using an 11 point (0 to 10) visual analog scale prior to topical anesthetic application, before debridement started, during debridement, and following debridement. They were also assessed for any complications from the cream; any complications related to the debridement, such as intolerance of the debridement related to pain; and following the second debridement, if they felt that anesthetic application at the first debridement (T1) or the second debridement (T2) provided better pain relief.
Results

Forty participants (28 women and 12 men) were enrolled; 21 women and 11 men completed the study. The main reason for attrition was the wound healed prior to second debriding (n = 6). Mean age was 64.73 years. Wound types included: vascular 57.5%, lymph 15%, surgical 13%, other 15%. Forty-one percent believed Lidocaine provided better pain relief than EMLA (28%); 32% had no preference. The only complication was that EMLA caused burning upon application, lasting up to 5 minutes (n = 5).

Repeated measures MANOVA revealed a significant effect of time ($\lambda = .369, F(3,28) = 15.964, p = < .001$). Mean pain rating was higher at T1 than at T2 for corresponding assessment points (Table 1). Pain during debridement at T1 was statistically significantly higher than pain at any other point except during T1 admission and T2 debridement. There was also a significant effect of drug by drug order (LMX4 applied at Time 1 or EMLA applied at Time 1) ($\lambda = .796, F(1,30) = 7.677, p = .010$); those who had EMLA at T1 reported less pain at T2 with LMX4, but there was no difference for those who had LMX4 at T1.

<table>
<thead>
<tr>
<th>Time Assessed</th>
<th>Mean Pain Rating</th>
<th>Standard Error</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 before application</td>
<td>2.41</td>
<td>.44</td>
<td>1.51</td>
</tr>
<tr>
<td>T2 before application</td>
<td>1.69</td>
<td>.33</td>
<td>1.00</td>
</tr>
<tr>
<td>T1 before procedure</td>
<td>1.38</td>
<td>.35</td>
<td>0.67</td>
</tr>
<tr>
<td>T2 before procedure</td>
<td>0.94</td>
<td>.27</td>
<td>0.40</td>
</tr>
<tr>
<td>T1 during procedure</td>
<td>3.71</td>
<td>.52</td>
<td>2.65</td>
</tr>
<tr>
<td>T2 during procedure</td>
<td>2.44</td>
<td>.40</td>
<td>1.63</td>
</tr>
<tr>
<td>T1 after procedure</td>
<td>2.44</td>
<td>.37</td>
<td>1.68</td>
</tr>
<tr>
<td>T2 after procedure</td>
<td>1.56</td>
<td>.27</td>
<td>1.01</td>
</tr>
</tbody>
</table>

There was no statistically significant difference in pain ratings between EMLA and LMX4, although the means for LMX4 were lower than the means for EMLA at each assessment point where pain was measured (Table 2). There was no time by drug effect, meaning no statistically significant difference in pain ratings between EMLA and LMX4 at any assessment point measured was identified. There was no time by drug order effect, meaning the order of administration of topical anesthetic (whether participants were given EMLA or LMX4 first) did not affect pain ratings at any assessment point. There was no time by drug by drug order effect, meaning the pain ratings at each assessment point were not affected by either EMLA or LMX4, no matter the order of administration.
Table 2  Pain Rating by Drug by Time Assessed

<table>
<thead>
<tr>
<th>Drug: Time Assessed</th>
<th>n</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>LMX4: before application</td>
<td>32</td>
<td>0</td>
<td>6</td>
<td>1.63</td>
<td>1.86</td>
</tr>
<tr>
<td>EMLA: before application</td>
<td>32</td>
<td>0</td>
<td>10</td>
<td>2.47</td>
<td>2.51</td>
</tr>
<tr>
<td>LMX4: before procedure</td>
<td>32</td>
<td>0</td>
<td>6</td>
<td>0.88</td>
<td>1.58</td>
</tr>
<tr>
<td>EMLA: before procedure</td>
<td>32</td>
<td>0</td>
<td>6</td>
<td>1.47</td>
<td>1.88</td>
</tr>
<tr>
<td>LMX4: during procedure</td>
<td>32</td>
<td>0</td>
<td>7</td>
<td>3.03</td>
<td>2.39</td>
</tr>
<tr>
<td>EMLA: during procedure</td>
<td>32</td>
<td>0</td>
<td>10</td>
<td>3.13</td>
<td>2.99</td>
</tr>
<tr>
<td>LMX4: after procedure</td>
<td>32</td>
<td>0</td>
<td>6</td>
<td>1.84</td>
<td>1.85</td>
</tr>
<tr>
<td>EMLA: after procedure</td>
<td>32</td>
<td>0</td>
<td>5</td>
<td>2.16</td>
<td>1.90</td>
</tr>
</tbody>
</table>

Discussion

Summary of key findings

There was no statistically significant difference between LMX4 and EMLA in managing pain associated with sharp wound debridement, so the research hypothesis was not supported. There were, however, significant differences in pain ratings for the four points in time at which pain was assessed for both topical anesthetics, and for the topical anesthetics by the order in which they were given. Participants believed that LMX4 provided better pain relief than EMLA. Five participants experienced burning on application of EMLA, a common complication associated with this agent (Claeys et al., 2010; Evans & Gray, 2005). This sensation lasted no longer than 5 minutes in any of the episodes. There was no difference in direct cost of the agents; however, participants only needed to wait 15 minutes for LMX4 compared to 30 minutes for EMLA prior to starting debridement.

Analysis of the findings

This was the first known study to compare LMX4 to EMLA for sharp debridement. Other studies comparing various forms and concentrations of lidocaine preparations to EMLA for other types of procedures have had mixed results (Chiang, Al-Niaimi, & Madan, 2015; Donaldson & Meechan, 1995; Eidelman, A., Weiss, J. M., Lau, J., & Carr, D. B., 2005; Friedman, Fogelman, Nouri, Levine, & Ashinoff, 1999; Galosi et al., 2005; Koppel, Coleman, & Coleman, 2000; McMillan et al. 1992; Randell et al., 1992; Svensson et al, 1992; Tang et al., 2004).

Participants in the EMLA group had higher mean pain ratings at every pain assessment point than did the lidocaine group, but the differences were not statistically significant. Chiang et al. (2015) also reported no significant difference between LMX4 and EMLA in their study of people undergoing laser and skin micro needling procedures, although the mean pain rating was higher for EMLA than for LMX4. LMX4 was also found to be equivalent to EMLA in studies of topical anesthesia use prior to intravenous cannulation in children (Kleiber et al., 2002; Eichenfeld et al., 2002).
In this study, there was a significant difference in pain experience for the four points in time where pain was assessed during T1 and T2, independent of topical anesthetic used. Participants experienced more pain prior to the application of anesthetic, and again during debridement. This is not unexpected, as most people would be expected to have more pain prior to application of a topical anesthetic and when undergoing sharp debridement. Although mean pain ratings were not all statistically significantly lower at T2 than T1, they were lower. This difference could be attributed to wound healing, requiring less invasive debriding, or to familiarity with the process and procedure.

An unexpected finding was that participants who received EMLA first reported significantly lower pain during the second treatment when they were given LMX4. One possible explanation is that participants who received EMLA first, as a result of having more intense pain initially, experienced the decrease more acutely. It is also possible that the burning sensation experienced by some of the participants may explain the difference.

**Implications of the findings**

LMX4 and EMLA had similar results in managing pain during sharp wound debridement; however, LMX4 demonstrated clinical advantages that included no burning sensation, lower mean pain rating, and it was faster acting. Based on these findings, the WHC nurses have incorporated LMX4 into their treatment regime for topical anesthesia during sharp wound debridement, especially for patients who have higher levels of pain sensitivity. Other departments where topical anesthetics are used for invasive procedures may want to consider employing LMX4 to manage pain.
References


Mabee, J. (2007). A pilot study: 0.2% vs. 0.5% lidocaine for intravenous regional anesthesia. *The Internet Journal of Anesthesiology, 17*(1).


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