

Comparison of the Analgesic Efficacy of Lidocaine/Prilocaine (EMLA) Cream and Needle-Free Delivery of Lidocaine During Fine-Needle Aspiration Biopsy of Thyroid Nodules

Tiroid Nodüllerinin İnce İğne Aspirasyon Biyopsisi Sırasında Lidokain/Prilokain (EMLA) Krem ve Lidokainin İğnesiz Enjeksiyonunun Analjezik Etkinliklerinin Karşılaştırılması

Alptekin Gürsoy, Cüneyd Anıl, Neslihan Başçıl Tütüncü, Aslı Nar, Semra Aytürk

Baskent University, Faculty of Medicine, Department of Endocrinology and Metabolic Diseases, Ankara, Turkey

Abstract

Objective: Efficacy of eutectic mixture of local anesthetic (EMLA) cream and the needle-free injection of local anesthesia for reducing pain associated with fine-needle aspiration biopsy (FNAB) of thyroid nodules has been previously reported. However, there has not been a direct comparison of the analgesic efficacy of these methods. The aim of this study was to compare the analgesic efficacy of EMLA cream and needle-free injection of lidocaine for FNAB-associated pain.

Materials and Methods: A total of 138 patients having their first ultrasonography-guided thyroid nodule biopsy were randomly assigned to receive either EMLA cream (n=68) or needle-free injection of lidocaine (n=70) before FNAB of thyroid nodules. Four needle passes for biopsy of each nodule were performed. Patients rated pain associated with the procedure according to a 100-mm visual analog scale (VAS), an 11-point numeric rating scale (NRS), and 4-category verbal rating scale (VRS).

Results: There were no significant differences between groups in age, sex, thyroid volume, nodule size, or nodule site. Significant differences between groups were noted in ratings of all three pain scales. When the effectiveness of EMLA was compared with that of needle-free injection of lidocaine, the mean VAS score was 23.4±20.5 mm versus 12.7±15.5 mm (p=0.001), and the mean NRS score was 2.8±2.1 points versus 1.6±1.7 points (p<0.001). There was also a significant difference between groups in VRS score (p=0.001).

Conclusions: Needle-free injection of lidocaine provides more effective and faster analgesia than EMLA cream application during the FNAB. *Turk Jem 2009; 13: 5-7*

Key words: Pain, EMLA, needle-free, anesthesia, fine-needle aspiration biopsy, thyroid nodule

Özet

Amaç: Tiroid nodüllerinin ince iğne aspirasyon biyopsisi (İİAB) ile ilişkili ağrının azaltılması için, lokal anestetiklerin ötektik karışımı (EMLA) kremi ve lokal anesteziğin iğnesiz enjeksiyonunun etkinlikleri daha önce bildirilmiş idi. Ancak, her iki yöntemin analjezik etkinliklerinin direkt olarak karşılaştırılması henüz ortaya konmamıştır. Bu çalışmada İİAB ile ilişkili ağrı için EMLA kremi ve lidokainin iğnesiz enjeksiyonunun analjezik etkinliklerinin karşılaştırılması amaçlanmıştır.

Gereç ve Yöntem: Ultrason eşliğinde tiroid nodülü biyopsileri ilk defa yapılan toplam 138 hasta, EMLA kremi (n=68) ya da lidokainin iğnesiz enjeksiyonunu (n=70) İİAB'den sırasıyla 1 saat ve birkaç dakika önce uygulamak üzere çalışmaya alınmışlardır. Her nodüle dört defa biyopsi yapılmıştır. Hastalar, işlemle ilgili ağrılarını '100-mm visual analog scale (VAS)', '11-point numeric rating scale (NRS)', ve '4-category verbal rating scale (VRS)' olarak bilinen üç ağrı derecelendirme sistemine göre skorlamışlardır.

Bulgular: EMLA grubu lidokain grubu ile karşılaştırıldığında; yaş, cinsiyet, tiroid hacmi, nodül boyutu, ya da nodül yerleşimi açısından anlamlı fark bulunmamıştır. 2 grup arasında, her 3 ağrı skalasına göre ağrı skorlarında anlamlı farklılıklar saptanmıştır. EMLA ve iğnesiz lidokain enjeksiyonunun etkinlikleri karşılaştırıldığında; sırasıyla ortalama VAS skoru 23.4±20.5 mm'ye karşı 12.7±15.5 mm (p=0.001), ortalama NRS skoru 2.8±2.1 puana karşı 1.6±1.7 puan (p<0.001) idi. VRS skoruna göre her gruptaki mutlak sayılar da anlamlı olarak farklı idi (p=0.001).

Sonuç: Tiroid İİAB sırasında iğnesiz lidokain enjeksiyonu, EMLA kremi uygulamasından daha etkin ve daha hızlı analjezi sağlamaktadır. *Turk Jem 2009; 13: 5-7*

Anahtar kelimeler: Ağrı, EMLA, iğnesiz, anestezi, ince iğne aspirasyon biyopsi, tiroid nodülü

Address for Correspondence: Alptekin Gürsoy, MD, Başkent University, Faculty of Medicine, Department of Endocrinology and Metabolic Diseases, Ankara, Turkey

Phone: +90 312 212 29 12 E-mail: alptekingursoy@hotmail.com **Received:** 23.02.2009 **Accepted:** 16.05.2009

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Introduction

Fine-needle aspiration biopsy (FNAB) of thyroid nodules has long been established as an effective, reliable, and safe procedure causing minor discomfort and slight temporary pain (1). It is intuitive that a potential painful procedure should require some form of anesthesia. FNAB is sometimes perceived as an uncomfortable and stressful procedure, especially for those who are pain phobic. Efficacy of the needle-free injection of lidocaine and eutectic mixture of local anesthetic (EMLA) cream, which consists of a combination of lidocaine 2.5% and prilocaine 2.5%, for reducing the pain associated with cutaneous procedures and FNAB of thyroid nodules has been established in prospective, randomized placebo-controlled trials (2-5). However, obstacles were present for each form of medication. EMLA requires a longer application time (at least 1 hour); needle-free application of lidocaine requires only a few minutes. Although a very tiny amount of anesthetic material (0.3 mL) is sealed inside, a major concern related to needle-free injection of lidocaine is tissue swelling at biopsy site after injection. This might interfere with subsequent imaging and the targeting of an underlying thyroid nodule resulting in inadequate tissue sample.

The objective of the present study was to compare the effectiveness of the needle-free injection of lidocaine and EMLA cream in reducing the pain associated with the FNAB of thyroid nodules and to compare the nondiagnostic rate of FNAB with each form of anesthesia.

Materials and Methods

This study was conducted in patients with one or more thyroid nodules who were scheduled to undergo FNAB. The Baskent University Ethics Committee for Human Studies approved the protocol. Subjects received verbal and written information about procedure and informed consent was obtained. A total of 138 adult patients with thyroid nodules biopsied for the first time were enrolled. Newly diagnosed patients requiring only one biopsy were included to obtain a uniform study population, since as the number of biopsy attempts increase, pain scores change significantly. All patients had nodule size of 1 cm or more and normal thyroid-stimulating hormone levels. Exclusion criteria were altered mental status or an inability to comprehend questions; long-term opioid or analgesic use or allergy to the trial drug; atrophic or fragile skin resulting from long-term steroid use; extreme old age; and bleeding disorder or anticoagulation therapy.

Patients were assigned by hospital identification numbers via a computer based system. Those assigned an even number were allocated to the group receiving needle-free injection of lidocaine, those assigned an odd number were allocated to the group receiving EMLA. EMLA 5% cream (Astra Zeneca, Istanbul, Turkey) in a dose of 2.5 mL (~ 2.5 g) was uniformly applied in a thick layer over the nodule selected for FNAB 60 minutes before the procedure was performed. The needle-free system of local anesthetic administration is a pneumatically powered pain-free injection system that delivers medications either intradermally or subcutaneously. The needle-free system used was the Injex needle-free medication delivery system (Rösch Medizintechnik, Berlin, Germany). The needle-free system was loaded with 0.3 mL (6 mg) of lidocaine (Jetokain simplex ampule, Adeka Pharmaceutical Company, Istanbul, Turkey).

According to the standard practice at our institution, 4 aspirations were made with 4 different 25-gauge needles at different sites in each nodule. The same endocrinologist (A.G.) performed each ultrasonographically guided FNAB by means of a 10-MHz linear probe (Logiq 5 Pro, GE Medical Systems, WI, USA). A pain survey form was filled out in which the patient was asked to rate his or her pain according to the following 3 pain rating scales:

1. A horizontal 100-mm visual analog scale (VAS) anchored with the words "no pain" on the left border and "worst possible pain" on the right border.
2. A horizontally depicted 11-point numeric rating scale (NRS) that ranged from zero to 10, with zero representing "no pain" and 10 representing the "worst pain imaginable".
3. A 4-point verbal rating scale (VRS) in which a score of zero represented no pain; 1, mild pain; 2, moderate pain; and 3, severe pain. As previous studies have shown, category scales for pain intensity classify a VAS score of zero to 4 mm as no pain; 5 to 44 mm as mild pain; 45 to 74 mm as moderate pain; and 75 to 100 mm as severe pain. An NRS score of 1 to 4 indicates mild pain; 5 to 6, moderate pain; and 7 to 10, severe pain (6-8). The relative merits of 3 scales (VAS, NRS, and VRS) often used to assess pain have been well studied, and their usefulness has been validated by several investigators (8,9).

Statistical analysis

All continuous data were expressed as means \pm SD. Data were analyzed with SPSS software (version 11.0, SSPS Inc, Chicago, IL, USA). Differences in baseline characteristics between patients and controls were assessed by means of the Student *t* test for continuous variables. An independent-samples *t* test was used for nonparametric data to determine if there was a significant difference in pain scores between the two groups of patients. The absolute numbers according to VRS score in each group were compared with chi-square test. *P* values less than 0.05 were considered statistically significant.

Results

A total of 138 patients were randomly assigned to receive either lidocaine (*n*=70) or EMLA cream (*n*=68). The two groups did not differ significantly with respect to age, sex, thyroid nodule size and volume, or nodule site.

As shown in Table 1, the mean VAS score was 12.7 \pm 15.5 in the lidocaine group and 23.4 \pm 20.5 in the EMLA group (*p*=0.001). The mean NRS score of the lidocaine group (1.6 \pm 1.7) was significantly lower than that of the EMLA group (2.8 \pm 2.1) (*p*<0.001); VRS scores were also significantly different between groups (*p*=0.001). The percentage of patients with "no pain" or "mild pain" in the lidocaine group was significantly higher than that in the EMLA group (*p* = 0.001). Similarly, the percentage of patients with "moderate-to-severe pain" in the EMLA group was significantly higher than that in the lidocaine group (*p*=0.001). No local or systemic adverse effects were observed. Four patients in each group had a nondiagnostic biopsy result.

Discussion

FNAB is generally a well-tolerated procedure, and interruption of the procedure because of unbearable pain is not common. Pain at the site of the needle insertion during FNAB is usually not usually severe; therefore, routine use of local anesthesia is usually not recommended (1). However, in our opinion, even if patients do not fit into

Table 1. Patient characteristics and analgesic efficacy of EMLA versus needle-free injection of lidocaine during the fine-needle aspiration biopsy of thyroid nodules. All data are given as mean±SD

	EMLA (n = 68)		Lidocaine (n = 70)		p value			
Male/Female	13/55		12/58		>0.05			
Age	47.5±9.9 y		50.1±12.1 y		>0.05			
Nodule size	18.3±7.6 mm		20.6±10.6 mm		>0.05			
Thyroid volume	20.8±9.8 mL		22.1±10.1 mL		>0.05			
VAS	23.4±20.5		12.7±15.5		0.001			
NRS	2.8±2.1		1.6±1.7		<0.001			
Category scales for pain intensity (%)								
	EMLA				Lidocaine			
	No pain	Mild pain	Moderate pain	Severe pain	No pain	Mild pain	Moderate pain	Severe pain
VAS	17.6	69.1	10.3	2.9	44.3	51.4	4.3	0
NRS	13.2	72.1	7.4	7.4	35.7	58.6	4.3	1.4
VRS	17.6	50.0	25.0	7.4	41.5	54.2	4.3	0
VAS Pain Scale: Zero-4 mm, no pain; 5-44 mm, mild pain; 45-74 mm, moderate pain; 75-100 mm, severe pain. NRS Pain Scale: Zero, no pain; 1-4, mild pain; 5-6, moderate pain; 7-10, severe pain. EMLA, eutectic mixture of local anesthetic; VAS, visual analog scale; NRS, numeric rating scale; VRS, verbal rating scale.								

a category thought to warrant anesthesia (non-anxious and pain tolerant patients, patients with previous history of non-painful biopsy), we think that there is abundant evidence suggesting that anesthesia should always be used (4,5). Some physicians who believe that the use of an injectable anesthetic is as painful as the biopsy procedure administer no local anesthesia. Most patients, however, prefer a nonpainful, effective, and noninvasive topical anesthesia. Effective use of local anesthesia for other neck masses have previously been reported (9).

The ideal method for inducing local anesthesia before a cutaneous procedure such as FNAB should be effective, fast, and portable. It should not disrupt the usual department routine or cause an additional biologic or physical risk to the patient. Previous reports have shown that both needle-free delivery of lidocaine and EMLA cream decreased the discomfort and pain related to FNAB when compared to placebo. The main disadvantage of EMLA cream is that EMLA must be applied a minimum of 1 hour before FNAB, which may render its use impractical in a busy clinic, whereas lidocaine, administered by needle-free delivery, takes effect within 1-3 minutes. The rapid onset and ease of use decrease the time associated with FNAB and enable the routine use of the needle-free delivery of lidocaine in busy clinics.

Although both forms of topical anesthesia are effective, there has not been a direct comparison of the needle-free delivery of lidocaine and EMLA cream. Minimal tissue swelling underlying the biopsy site after the application of a lidocaine might interfere with subsequent imaging and the targeting of an underlying nodule for FNAB, especially in a patient with a superficial nodule or nodule size less than 1 cm. This might decrease the diagnostic yield of FNAB, which is not a problem for EMLA application.

Our results showed that the use of needle-free delivery system was more effective than EMLA cream. Local anesthesia with needle-free delivery of lidocaine is less time-consuming than the EMLA cream. Our previous experience has taught us that the pain of needle insertion of local anesthesia was as bad as or worse than the needle biopsies themselves. The needle-free injection system eliminates pain related to needle insertion of local anesthesia. Both applicati-

ons of local anesthesia were demonstrated to be safe, and the nondiagnostic aspiration rate was similar in both groups.

In our opinion, successful pain control is essential in making ultrasonography-guided FNAB tolerable, and yet even recently few physicians routinely used pain-control techniques. Our findings indicate that needle-free delivery of lidocaine application is superior in respect to analgesic efficacy compared to EMLA cream application. In daily practice, needle-free delivery of lidocaine can be easily and safely performed without changing the diagnostic rate FNAB procedure.

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