EFFECTIVENESS OF LIDOCAINE/PRILOCAINE CREAM ON PERCEIVED PAIN DURING MAMMOGRAPHY: A PILOT STUDY

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ABSTRACT

Background: Mammography (MG) is an important imaging method in the diagnosis of breast diseases. However, pain during MG is an uncomfortable factor for the majority of women. Aim: The aim of this study is to determine the effectiveness of lidocaine/prilocaine cream on reducing pain during mammography. Methods: This is a prospective clinical study. A total of 60 female patients who had mammographic examination were equally divided into three groups; patients receiving 10 g EMLA cream (EMLA group), patients receiving 10 g Bepanthen cream (placebo group), and patients not receiving any cream (control group). Pain levels were assessed by using visual analog scale (VAS) before and after MG. Results: Each group was statistically similar regarding fundamental patient characteristics. There was also no significant difference between the pre-MG VAS scores of the three groups (p = 0.996). On the other hand, VAS scores during MG was found significantly different between the groups (p = 0.001). When the groups were compared in pairs, the patients in EMLA group had considerably less post-MG VAS score than the Bepanthen and control groups (p = 0.001). There was no significant difference between Bepanthen and control groups (p = 0.678). Conclusion: To our knowledge, this is the first study demonstrating that a topical anesthetic, EMLA, provides an efficient analgesia during MG. Reducing the pain can change women’s preconceptions regarding MG.

KEYWORDS: Lidocaine/prilocaine cream, mammography, pain, visual analogue scale

Introduction

Breast cancer is the most frequent type of cancer in women worldwide [1]. Although its mortality rates have been declined in recent years due to the early detection and improvements in treatment modalities, breast cancer is still the second leading cause of cancer-related death among female population after lung cancer [1-3].

Mammography (MG) is one of the most commonly used diagnostic methods in the management of patients with breast diseases. It is also the primary basis for screening programs which ensure a significant reduction in breast cancer-related mortality with estimated rates of 15% in women of 40-49 years and 22% in women above 50 [4].

However, many women cannot regularly participate in these screening programs due to various factors such as socioeconomic reasons; false beliefs regarding the relationship between cancer and radiation from MG, and procedure-related pain. Despite the modern less painful mammographic techniques, it is the fact that pain due to the compression of the breast is a significant factor in the women’s unwillingness in participating in regular screening programs or diagnostic MG for any reason.
In this study, we aimed to determine the effectiveness of a lidocaine/prilocaine cream on reducing pain during MG.

Patients and Methods

Study Design

A total of 60 female patients who had mammographic examination between May 2015 and July 2015 were included in this prospective placebo-controlled study. The study population consisted of women presenting with breast pain with or without any other breast-related symptoms. The patients were equally divided into three groups; patients receiving 10 g EMLA (EMLA, AstraZeneca, UK) cream (EMLA group), patients receiving 10 g Bepanthen cream (placebo group), and patients not receiving any cream (control group). Age under 40, chronic liver disease, chronic renal failure, pregnancy, active breastfeeding, use of continuous medication such as oral contraceptive, previous breast surgery, the presence of mastitis or breast abscess were the exclusion criteria. The written informed consent form was obtained from all patients before the study. Firstly, the application method of the topical creams and how to fill out the 10 cm visual analog scale (VAS) score (0=no pain and 10=worst possible pain), which is one of the most frequently used indicator for evaluating pain in general practice, were explained in detail to all participants at the MG unit. Before MG, all patients were asked to record their pain values on VAS to reveal their breast pain levels (pre-MG VAS score). Later on, the patients applied creams on their breasts 90 min before MG, and completely covered both breasts with a stretch film to avoid the loss of efficacy of the drugs through absorption by the clothes. Immediately after MG, all patients marked their pain levels during the procedure on VAS scale (post-MG VAS score). The patients did not know the name of the topical cream they used.

Statistical analysis

Statistical analysis was performed by using the SPSS (version 15.0, SPSS, Inc., Chicago, IL). The results are presented as mean ± SD/percentages for continuous variables and number/percentage for categorical variables. Kruskal-Wallis test was used for investigating the differences between three groups according to VAS scores. Mann-Whitney U-test was used to compare the groups in pairs. The level of statistical significance was set at p<0.05.

Results

A total of 60 women with a mean age of 50.1 y (range 40 to 65 y) participated in the study. Each group has consisted of 20 patients and was statistically similar regarding underlying patient characteristics. The mammographic findings of all patients were BIRADS 1-3. No malignant lesion was detected by MG. There were nine patients with a pre-procedural pain rating of 9 and two patients with a post-procedural pain rating of 9. There were no significant differences between the pre-MG VAS scores of the three groups (p = 0.996). In the statistical assessment of post-MG VAS scores, a significant difference was found between the three groups (p = 0.001). When the groups were compared in pairs, the patients in EMLA group had significantly less post-MG VAS scores than the placebo and control groups (p = 0.001). On the other hand, there was no significant difference between placebo and control groups (p = 0.678). No adverse effects due to the use of EMLA cream were observed in the study population. All the patient characteristics and statistical analyzes of the groups were presented in Table 1.

Discussion

Breast cancer accounts for 23% of all cancer cases and 14% of cancer-related deaths [5]. According to World Health Organization (WHO): International Cancer Research Agent (ICRA), about one-quarter of all cancer cases can be prevented by occurrence and three-quarter of cases can be successfully treated thanks to existing knowledge on cancer behavior, technological advances and the control-based initiatives in the near future [4, 6, 7]. Nevertheless, there is not a universal standard for the implementation of mammographic screening programs between the countries, due to various factors such as enormous variations in human populations and socioeconomic problems. It should be stated here that possible risk-benefit ratio also seems to be an important element in this situation [8].

Besides the screening programs, MG is also an important part of a diagnostic tool for the patients presenting with any mammary symptom and/or finding. Our study population was composed of patients presenting with breast pain, and each group in our study had similar initial VAS scores before the procedure, indicating similarity regarding breast pain level. It should be stated here that there were nine patients with a pre-procedural pain rating of 9 in all three groups which seem to be quite high. It is well known that VAS scoring system is entirely dependent on the patient’s perception. All patients in each cluster had breast pain in addition to other breast-related symptoms, and this might cause those high pain scores. The education level of our cases might also affect pain scoring because approximately half of our patients were elementary school graduates.

MG is applied by compression of the breast between two transparent plates, which is necessary to flatten and reduce the breast. Also, clear mammographic images can only be obtained by implementation of compression. Although only lasts a few seconds, MG can be painful and uncomfortable for some women. This painful condition varies from person to person due to the presence of mass in the breast, menstrual cycle period, technical characteristics of the device, and anxiety status of the individual [9]. Whatever the reason, procedure-related pain is a substantial handicap of MG, and a straightforward and reliable method to reduce pain may resolve the patients’ concerns regarding this issue. Some authors proposed a pain-preventing strategy focusing on limiting the compression of the breast when the patient considered the procedure too painful [10, 11]. Also, some MG devices with an automatic pain-prevention feature that can limit the compression were proposed to reduce MG-related pain [12]. Recently, a new pain-preventing strategy on the limitation of compression according to breast size has been reported. In that strategy, the compression is personalized because small breasts will reach the target pressure at a lower force than large breasts do [13]. In our opinion, all those methods are widely user- and device-dependent. However, it is well known that topical local anesthetics are routinely used for various painful conditions or for providing an analgesia before any surgical intervention for a long time. Pain related to MG is also a mechanical pain caused by compression, and application of topical local anesthetics can reduce the pain, as in the treatment of other painful disorders such as myalgia and arthralgia. These topical drugs reach to their effective tissue concentrations when used in appropriate doses. Also, a certain period following the application of the
Table 1 Basic patient characteristics and statistical analyses of the three groups.

| Characteristics              | EMLA group (n=20) | Placebo group (n=20) | Control group (n=20) | P   |
|------------------------------|-------------------|----------------------|----------------------|-----|
| Age (year)                   | 50.5±6.71 (41-63 y) | 48.3±4.72 (40-57) | 51.7±6.5 (40-65) | 0.260 |
| Marital status               |                   |                      |                      | 0.927 |
| Single                       | 3 (15%)           | 3 (15%)              | 3 (15%)              |     |
| Married                      | 15 (75%)          | 16 (80%)             | 16 (80%)             |     |
| Divorced/widowed             | 2 (10%)           | 1 (5%)               | 1 (5%)               |     |
| Educational status           |                   |                      |                      | 0.910 |
| Elementary                   | 10 (50%)          | 11 (55%)             | 11 (55%)             |     |
| High school                  | 7 (35%)           | 7 (35%)              | 6 (30%)              |     |
| University                   | 3 (15%)           | 2 (10%)              | 3 (15%)              |     |
| Menopausal status            |                   |                      |                      | 0.638 |
| Premenopausal                | 8 (40%)           | 11 (55%)             | 9 (45%)              |     |
| Postmenopausal               | 12 (60%)          | 9 (45%)              | 11 (55%)             |     |
| Employment status            |                   |                      |                      | 0.731 |
| Housewife                    | 15 (75%)          | 13 (65%)             | 15 (75%)             |     |
| Employed                     | 5 (25%)           | 7 (35%)              | 5 (25%)              |     |
| Severity of breast pain      |                   |                      |                      |     |
| Mild                         | 1 (5%)            | 1 (5%)               | 0                    |     |
| Moderate                     | 3 (15%)           | 6 (30%)              | 9 (45%)              |     |
| Severe                       | 16 (80%)          | 13 (65%)             | 11 (55%)             |     |
| Pre-MG VAS score             | 6.75±1.37 (3-9)   | 6.70±1.5 (3-9)       | 6.75±1.3 (4-9)       | 0.996 |
| Post-MG VAS score            | 3.05±1.05 (1-3)   | 5.90±1.86 (3-9)      | 6.10±1.12 (5-8)      | 0.001 |

Data are presented as mean ± SD for age, pre-MG VAS score and post-MG VAS score; n (%) for other variables.
drug is required to obtain the better analgesic effect. The topical anesthetic drug utilized in the present study is a combination of two local anesthetic agents, lidocaine, and prilocaine, and shows its analgesic effect through blockage of Na+ channels. Lidocaine and prilocaine are among the amide-type local anesthetics with less allergic reaction profile and metabolized in the liver. It has been recommended that its maximum dose should be 10 g at one time in adults with open wounds such as leg ulcers [14]. Several adverse effects such as cutaneous allergic reactions, hypoxia-induced tachycardia, headache, fainting and mental status changes, arrhythmia, methemoglobinemia, coma, and death have been reported to date [15, 16]. However, no significant adverse effect was observed in the present study. Methemoglobinemia may be congenital or acquired; however, most of the cases are developed due to a side impact of a drug [17]. Among all local anesthetic agents, prilocaine is the most frequent cause of methemoglobinemia. The doses of 10 mg/kg carry a high risk of this dangerous condition. Methylene blue, 1-2 mg/kg intravenously, is used in the treatment [18].

A period of 90-120 min is required for the full analgesic effect after the application of the drug. It provides an analgesia for approximately 3 hours. In accordance, our patients also applied EMLA cream on their breasts 90 min before MG.

In the literature, there are many clinical studies concerning the analgesic effect of using EMLA cream in various diseases. Akan et al. [19] showed in their study including patients who underwent excisional biopsy for breast lump under local anesthesia that use of EMLA cream reduced the pain during surgery. The need for the analgesic drug after surgery was also decreased in that clinical trial. In another study, better pain control was reported by using EMLA cream in patients with skin graft donors [15]. Taddio et al. [20] also found that patients receiving EMLA cream on the penis 60-80 min before circumcision had less pain compared with patients not receiving that cream. Shiaw et al. [21] applied lidocaine/prilocaine anesthetic cream to the patients who underwent hemorrhoidectomy and used neomycin pomade to the other group, and they operated both groups under local anesthesia. They found that the VAS scores were significantly lower in lidocaine/prilocaine group than the neomycin pomade group, during and after the operation. In another study including patients undergoing fine needle aspiration biopsy of the thyroid, the patients received 2.5 g EMLA on the thyroid 60 min before the procedure. It was shown that the patients receiving EMLA experienced less pain [22].

Although the effectiveness of EMLA cream on pain relief has been studied in many different painful diseases, diagnostic methods and surgical procedures, to our knowledge, there is no clinical study regarding the use of this topical anesthetic for the MG-related pain. However, similar to our study, Lambertz et al. [23] showed in their work that pain associated with MG was reduced by the application of 4% lidocaine gel in addition to the premedication of patients.

Conclusion

MG is considered as a painful procedure by the majority of women. Also, pain during MG may be a deterrent factor for some patients. Therefore, reducing the MG-related pain may allow more women to participate in the mammographic examination. According to data obtained from the present study, EMLA cream seems to be an efficient and safe topical analgesic tool in reducing pain during MG. However, this is a pilot study, and multicenter studies with larger sample size and different patient groups should be needed to verify the effectiveness of EMLA cream in reducing the pain during MG.

Authors’ Statements

Competing Interests

The authors declare no conflict of interest.

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