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ORIGINAL ARTICLE

Comparison of the use of the Valsalva maneuver and the eutectic mixture of local anesthetics (EMLA®) to relieve venipuncture pain: a randomized controlled trial

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Abstract
Purpose Intravenous cannulation is a painful and stressful procedure. The objective of this study was to compare the analgesic efficacy of the eutectic mixture of local anesthetics (EMLA®) with that of the Valsalva maneuver in adult patients during i.v. cannulation.
Methods One hundred ninety-five patients were randomized prospectively to three groups. The dorsum of the nondominant hand was covered with a thick paste of 2.5 g of EMLA® cream in the EMLA® group (group E) and left for a minimum of 30 min before venipuncture. In the control group (group C), the same procedure was applied except that Vaseline® was used instead of the EMLA®. The Valsalva group (group V) were punctured during a Valsalva maneuver. The patients were placed in the supine position during venipuncture. The patients then scored the amount of pain on cannulation using an 11-point numerical rating scale (NRS; 0 = no pain, 10 = extreme pain).
Results Thirteen patients were excluded from the analysis due to failed cannulation. There was no difference in the demographic profiles of the groups ($p > 0.05$). The success of VP was significantly higher in group V than in groups E and C ($p < 0.001$). The median pain score as assessed by the NRS after venipuncture in group C was 3 (range 0–9), whereas the median pain values in groups E and V were 2 (range 0–7) and 2 (range 1–8).
Conclusions The Valsalva maneuver yields similar results to the EMLA® in terms of pain reduction during venipuncture.

Keywords EMLA® · Pain · Topical anesthetic · Valsalva maneuver · Venipuncture

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Introduction

Aside from the physiology of the patient, emotional and psychological factors are equally important for the perception and subjective characteristics of pain [1]. Venipuncture (VP) is a prerequisite for the administration of safe general anesthesia. Patients usually feel distressed due to the anticipated pain arising from injections [2, 3]. Needle phobia affects at least 10 % of the population and may cause avoidance of medical care in its severe forms [4]. A number of methods to reduce VP pain, including the use of various local anesthetics, ethyl chloride, ice, optimization of patient comfort, and even distraction of the patient's attention, have been reported [5–7]. Examples of local anesthetic combinations that have been used to decrease VP pain include lidocaine/prilocaine cream, liposomal

lidocaine cream, the lidocaine/tetracaine patch, and lidocaine iontophoresis. However, their use is limited by relatively slow onset times, inconvenient and messy application methods, side effects regarding vasoconstriction, or the requirement for complex specialized equipment and training [8].

The EMLA® is a eutectic mixture of 2.5 % lidocaine and 2.5 % prilocaine cream which is used as a local anesthetic [1, 4, 9]. It facilitates the local absorption of each drug without the need to use organic solvents, thus leading to high local concentrations of lidocaine/prilocaine in the skin, which in turn makes it an effective agent for surface anesthesia of the skin. Therefore, EMLA® cream has been successively used as a local anesthetic for procedures such as VP, intravenous catheter placement, and vaccinations in humans [1, 9, 10].

The Valsalva maneuver performed before venous cannulation reduces the incidence and severity of pain associated with VP [2, 6]. It works through the stimulation of the vagus nerve [11]. Sensory fibers from many organs such as the oropharynx, upper gastrointestinal tract, abdominal and thoracic cavities send information along the vagus to the tractus solitarius [12, 13]. The vagus nerve carries fibers for nociception along with these pathways. The Valsalva maneuver increases intrathoracic pressure, leading to baroreceptor activation, which stimulates vagal response. Consequently, stimulation of the vagus nerve induces an antinociceptive effect in human beings [2, 12, 13].

The Valsalva maneuver is easy to perform and cost-effective during venous cannulation [2]. Although many studies have demonstrated the efficacy of the EMLA® [1, 3, 14] and the Valsalva maneuver [2, 6, 15], the two techniques have never been compared in adult patients in terms of their capacities to reduce VP pain. Here, we aimed to compare the Valsalva maneuver with the application of EMLA® cream for the relief of pain associated with VP in adults.

Materials and methods

Ethical committee approval from our university was obtained before the study was conducted. Adult patients (>18 years old) with ASA I–III who applied to the anesthesia outpatient department to undergo various surgical procedures were enrolled in this study. Patients with skin diseases at or around the VP site, such as scars, infection, psoriasis, eczema, active dermatitis, etc., patients with a history of drug addiction, a history of peripheral neuropathy, chronic consumption of analgesics, allergy, or sensitivity to local anesthetics, and patients with verbal communication problems were excluded. The patients who qualified for the study were informed about it and written consent was obtained from them. None of the patients were given any premedication. They were randomly allocated to one of three groups. In group E, the dorsum of the hand was covered with a thick paste of the EMLA® (Astra Zeneca, Eczacıbası Ltd., Luleburgaz, Turkey) 30 min before VP. In group C, the same procedure was performed with Vaseline® (Merkez Medikal Ltd., Istanbul, Turkey). In group V, the patients received VP during the Valsalva maneuver. VP was performed by healthcare professionals using a 20G venous cannula, Plusflon® (Mediplus, Haryana, India). The patients in group V were instructed to perform the Valsalva maneuver just before the VP. In brief, they were asked to inhale deeply and then to vigorously hold their breath after application of the tourniquet. The VP was performed during the Valsalva maneuver, and the patients were allowed to breathe after the venous cannulation. The Valsalva maneuver did not last longer than 20 s in any of the patients in group V. Patients with failed cannulation at the first attempt were excluded from the study. Patient parameters including heart rate (HR) and mean blood pressure (MBP) were recorded before and 5 min after venous cannulation to detect a sympathetic response to pain. The complications of the procedures, such as skin changes, allergic reactions, and syncope, were all recorded.

The primary end-point measurement was the pain felt during VP. All patients were asked to verbalize the pain intensity of VP using a numerical rating scale (NRS; 0 = no pain, 10 = extreme pain). Effect size was calculated using data (NRS values) from previous studies [6]. The sample size was calculated as 53 for each group, assuming an effect size of 0.25, $\alpha = 0.05$, and power = 0.80. The post hoc power was calculated as 0.86. Power analysis was performed using G*Power (G*Power version 3.1.2, Franz Faul, Universitat, Kiel, Germany). However, we allocated 65 subjects per group to cover the number of patients lost to follow-up. The χ^2 test was used to compare the categorical variables. Values of categorical variables are shown as counts and percentages. Shapiro–Wilk's normality test was used to check the normality of the continuous variables. Kruskal–Wallis analysis of variance or one-way ANOVA was used to compare continuous data among groups (the Bonferroni-adjusted Mann–Whitney *U* test was used for post hoc comparisons). The paired sample *t*-test was used to compare the MBP and HR before and after VP. Repeated measures two-way ANOVA was used to compare the alterations in MBP and HR among three groups. Variables are presented as the mean ± standard deviation or median (range). p values of <0.05 were considered statistically significant. Analyses were performed using statistical software (PASW ver.18, ID: 33478001, SPSS Inc., Chicago, IL, USA).

Results

The study started with 195 patients. Thirteen patients (6.7 %) in whom cannulation failed at the first attempt were excluded from study (seven patients were excluded from group E and six patients from group C). The statistical analysis was performed on 182 patients who completed the entire clinical trial. There were no differences in the demographic profiles and the clinical characteristics of the patients among the different groups ($p > 0.05$) (Table 1). The success of VP was significantly higher in group V than in groups E and C ($p < 0.001$). The pain intensity, as assessed using the NRS [median (range)], after VP in group C was 3 (0–9). A significant reduction in the NRS-assessed pain intensity was noted in groups E and V compared to group C: 2 (0–7) and 2 (1–8), respectively ($p < 0.001$). There was no difference in pain intensity between group E and group V ($p > 0.05$) (Table 1). There was no difference in HR or MBP among the groups, either before or after VP ($p > 0.05$).

Local pallor was seen in ten patients and redness in one patient due to EMLA® application in group E, whereas side effects like bradycardia, hypotension, or fainting were not observed during or after the Valsalva maneuver in the operation room for group V.

Discussion

Venipuncture is an uncomfortable and painful situation for patients [3, 4]. There are many contributory factors such as anxiety, previous unpleasant experiences, cultural background, individual variability of pain threshold, and so on that can contribute to this discomfort. Many studies in which different pharmacological agents were administered to alleviate the intensity of this pain in patients have been conducted. However, these agents are expensive and have potential side effects [5–11]. In the present work, we obtained a similar reduction in pain intensity during VP using a simple technique, the Valsalva maneuver, to that obtained using the well-described method of EMLA® cream use.

Many reports have shown that vagus nerve stimulation (VNS) has an antinociceptive effect, resulting in a reduction in pain perception in humans [2, 6, 16–18]. They suggest that pain relief by VNS occurs through central inhibition with contributions from the noradrenergic, serotonergic and endogenous opioid systems, rather than through the alteration of primary afferents [16, 17, 19]. The nucleus tractus solitarii, nucleus raphe magnus, and locus coeruleus and subcoeruleus have been identified as central relay stations for VNS-induced analgesia. The vagus nerve is stimulated via baroreceptors during the Valsalva maneuver [20]. In experimental pain studies, performing the Valsalva maneuver before venous cannulation decreased the incidence and severity of pain associated with VP in humans [2, 6, 15]. The Valsalva maneuver may be a method of distracting attention [6, 15]. Lal et al. [21] compared the use of EMLA® cream and distraction therapy in children who underwent VP. In one group of children they used EMLA® cream and in the other group they taught the children to blow a toy windmill to distract their attention. They found no difference between the groups in terms of their pain scores. The main result of our study is clearly consistent with this finding (in children).

Mohammadi et al. [24] evaluated spinal puncture pain in 90 adult patients who used either the Valsalva maneuver or a distraction technique. The Valsalva group showed significantly less NRS regarding needle pain comparing to the distraction and control groups, but there was no difference among the groups in terms of their HR and MBP measurements. In some studies, the Valsalva maneuver was shown to be an effective simple and inexpensive way of reducing VP pain, with no side effects [3, 6]. Although it has been stated in the literature [25] that fainting may occur during the Valsalva maneuver in patients with impaired autonomic function, we did not encounter this in our patients.

Local anesthetics are commonly used in pediatric patients to decrease VP pain [8, 10]. It has been shown that the application of the EMLA® cream—made from water, oil, and a eutectic mixture of two local anesthetics (2.5 % prilocaine and 2.5 % lidocaine)—is more effective than a placebo [1, 9]. The lidocaine and prilocaine in the cream passes through the subcutaneous tissue and binds to the free nerve ending receptors in the subcutaneous tissue, leading to local anesthetic effects [26]. A meta-analysis by Fetzer et al. [27] included 20 studies and recommended the use of EMLA® cream for VP due to its potential to reduce VP pain. Although it is routinely used in children before venous cannulation, it is not justified in adults [3, 10, 28]

Table 1 Comparisons of gender, age, height, weight, BMI, and NRS among the groups

	EMLA ($n = 58$)	Valsalva ($n = 65$)	Control ($n = 59$)	p
Gender (male/female)	28/30	28/37	19/40	0.196
Age (year)	38 ± 16	42 ± 16	39 ± 14	0.353
Height (cm)	166 ± 9	164 ± 8	164 ± 8	0.425
Weight (kg)	77 ± 14	72 ± 15	73 ± 15	0.327
BMI (kg/m^2)	28 ± 6	27 ± 6	27 ± 6	0.567
NRS[a]	2 (0–7)**	2 (1–8)**	3 (0–9)	**<0.001**

** Statistically significant reduction compared to the control group ($p < 0.05$)

[a] Median (range)

due to its increased cost and because it is impractical [4, 9]. Moreover, it generally requires more than 30 min to become effective, limiting its use in the emergency setting [27, 29].

The side effects of EMLA® are generally mild, and are seen as local reactions, such as paleness, erythema, urticaria, contact dermatitis, or purpura. Rarely, serious side effects like methemoglobinemia are seen [1, 9, 30]. In this study, local pallor was seen in ten patients and redness was seen in one patient due to EMLA® application.

It should be emphasized that both the analgesic effect of Valsalva and the success rate of venous cannulation were higher in group V. The higher success rate of venous cannulation in the Valsalva group can be attributed to increased venous vessel diameter, which facilitates entry at the first attempt [18, 22, 23].

The limitation of the present study lies in its unblinded nature, since the two experimental arms of this study required completely different application techniques. This can be accepted as unavoidable bias in adults. In one arm of the study, a cream was applied physically, whereas a technique was taught to the patients in the other arm.

In conclusion, we have shown that the Valsalva maneuver is as effective as EMLA® application at reducing VP-induced pain. The Valsalva maneuver does not need any equipment. It is easy for patients to learn, and it increased the success rate of venous cannulation. Therefore, we recommend the use of the Valsalva maneuver as an alternative to EMLA® for reducing pain and related stress during venous cannulation in adults.

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