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## **EMLA (Eutectic Lidocaine/Prilocaine) Cream to Reduce Pain during Arteriovenous Fistula Puncture in Adult Patients Undergoing Hemodialysis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials**

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**Objectives :** Patients with end-stage renal disease requiring hemodialysis undergo life-sustaining renal replacement therapy to maintain physiological homeostasis. Intradialytic discomfort represents the predominant physical and psychological source of pain associated with hemodialysis procedures, with intensity noted particularly during cannulation of the arteriovenous fistula, which remains the gold standard modality for vascular access. These individuals perpetually endure procedural pain, substantially compromising the quality-of-life metrics and, in the extreme, refraining from adhering to this life-preserving therapy. Thus, pain management is of paramount importance. The eutectic mixture of local anesthetics (EMLA) cream is a topical formulation comprising 2.5% lidocaine and 2.5% prilocaine, designed for enhanced dermal penetration to provide effective local analgesia during percutaneous procedures. This study aims to systematically analyze the safety and efficacy of EMLA cream as pain control in patients undergoing hemodialysis.

**Methods :** This review was conducted in adherence to the PRISMA guidelines. The literature search was performed across electronic databases, including PubMed, ScienceDirect, and Scopus. Forest plots were generated to illustrate the pooled effect estimates for each outcome of interest using R software and Review Manager 5.4.

**Results :** Seven randomized controlled trials were deemed appropriate for review and meta-analysis, amounting to 1,375 patients. In comparison to placebo and alternative local anesthetics, pain intensity was lower in the EMLA group (mean difference [95% CI] of -2.58 [-3.22,-1.94],  $p < 0.00001$  and -0.99 [-1.57,-0.42],  $p = 0.0007$ , respectively). EMLA provided similar pain reduction as nonpharmacological approaches did, although this comparison did not reach a statistical significance (mean difference [95% CI] of -0.26 [-1.98, 1.45],  $p = 0.76$ ). Concerning safety considerations, EMLA showed an acceptable adverse event profile with a low incidence of local cutaneous reactions (pooled proportion of 7% [95% CI 0.00–0.15],  $I^2 = 75.1\%$ ,  $p = 0.0012$ ).

**Conclusions :** EMLA cream provides effective pain management during arteriovenous fistula cannulation in adult hemodialysis patients while demonstrating favorable patient tolerability and simple application in clinical practice.

Graphical Abstract of EMLA (Lidocaine:Prilocaine) in Reducing Pain in HD Patients.png



Graphical Abstract

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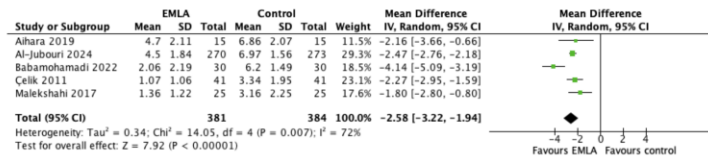


7 RCTs

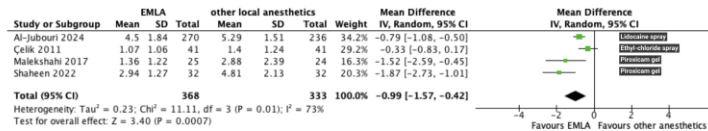


1,375 patients  
on hemodialysis

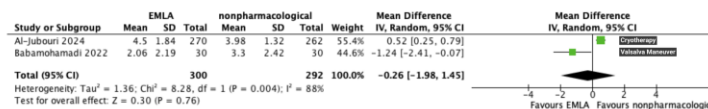
**EMLA  
vs control**



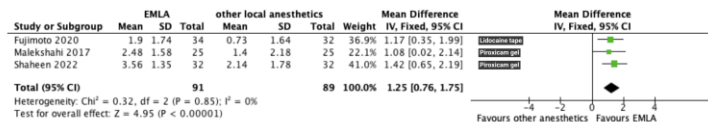
**EMLA vs other local anesthetics**



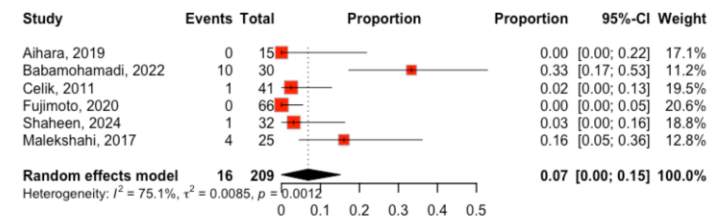
**EMLA vs nonpharmacological management**



**Pain Reduction of EMLA vs other local anesthetics**



**Local Side Effects of EMLA**



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# **EMLA (Eutectic Lidocaine/Prilocaine) Cream to Reduce Pain during Arteriovenous Fistula Puncture in Adult Patients Undergoing Hemodialysis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials**

Table 1. Characteristics of the included studies and the patients.

Author (year of publication)	Study design	Setting	Sample Size	Intervention	Pain Measurement	Age, in mean and SD (years)	Duration of hemodialysis, in mean and SD (months)	Concomitant Kidney Diseases	Diabetes
Ahura et al. (2019)	Randomized, placebo-controlled, crossover trial	A dialysis unit in a hospital in Japan	30 patients EMLA: 15 patients, Placebo: 15 patients	<b>EMLA cream</b> (1 gram) was applied to a 10 cm <sup>2</sup> area above the stenotic lesion of the skin 40-120 minutes before the AVF puncture. <b>Placebo</b> (hypoallergenic cream) was applied to a 10 cm <sup>2</sup> area above the stenotic lesion of the skin 40 to 120 minutes before the AVF puncture.	VAS from graded 0-100 mm horizontal line was assessed <b>immediately</b> after AVF puncture	68±11	32±50	Diabetic nephropathy (9%) Hypertensive nephropathy (27%) Chronic glomerulonephritis (17%) Polycystic kidney disease (2%)	63%
Al-Jaboori et al. (2024)	Randomized, controlled, open-label trial	4 dialysis centers in Iraq	191 patients EMLA: 170 patients, Cryotherapy: 20 patients, Lidocaine spray: 236 patients, Control: 273 patients	<b>EMLA cream</b> (1.5 gram) was applied to a 4 cm <sup>2</sup> area on the AVF for 20 minutes before the AVF puncture. <b>Cryotherapy</b> was applied by placing five cubes of ice (14x2x2 cm) in a plastic bag and covering with a type of cotton cloth for 5 minutes on the site of the AVF before the AVF puncture. <b>Lidocaine spray</b> was applied thrice on the AVF 5 minutes before the AVF puncture.	VAS from graded 0-100 mm horizontal line was assessed <b>immediately</b> after AVF puncture	47.7±13.5	Not reported	Not reported	15.30%
Bakarmohamed et al. (2022)	Randomized, controlled, open-label trial	A dialysis unit in a hospital in Iran	90 patients EMLA: 30 patients, Valiula maneuver: 30 patients, Control: 30 patients	<b>EMLA cream</b> (5 gram) was applied on the skin and covered with a transparent dressing by the patients 1 hour before the dialysis session. <b>Valiula Maneuver</b> was performed through the instruction of blowing in a plastic tube connected to a mercury barometer after taking a deep breath, raising the mercury column to 20-25 mmHg for 14-20 seconds before the AVF puncture. <b>EMLA cream</b> (2 ml) was applied to the two puncture sites under an occlusion dressing 45-60 minutes before the AVF puncture.	NRS (0-10) was assessed <b>2 minutes</b> after AVF puncture	54.11±12.49	58.03±45.80	Not reported	55.50%
Celik et al. (2011)	Randomized, placebo-controlled, crossover trial	A dialysis unit in a university hospital in Turkey	41 patients were randomly assigned to different interventions: EMLA, ethyl chloride spray, and control, in consecutive dialysis treatments	<b>Ethyl-chloride (isopocooland) spray</b> was sprayed at the distance of approximately 10 cm for 2 seconds. The liquid sprayed in the skin was allowed to evaporate for 10 seconds and the AVF puncture was performed 20 seconds later.	VAS from graded 0-100 mm horizontal line was assessed <b>immediately</b> after AVF puncture	57.0±15.3	70.5±57.4	Unknown etiology (61.5%) Diabetic nephropathy (24.4%) Hypertension (14.4%) Glomerulonephritis (9.8%) Amyloidosis (2.2%) Lupus nephritis (2.4%)	26.40%
Fujimoto et al. (2020)	Randomized, open-label, crossover trial	6 dialysis centers in Japan	66 patients EMLA followed by lidocaine tape: 32 patients, Lidocaine tape followed by EMLA: 34 patients	<b>Placebo</b> cream was applied to the two puncture sites under an occlusion dressing 45-60 minutes before the AVF puncture. <b>EMLA cream</b> (2 gram) was applied using a fluffon tape at each puncture site 1 hour before the AVF puncture.	VAS from graded 0-100 mm horizontal line was assessed <b>immediately</b> after AVF puncture	65.94±10.57	73.17±52.08	Not reported	65.15%
Makdashi et al. (2017)	Randomized, double-blind trial	A dialysis unit in a hospital in Iran	75 patients EMLA: 38 patients, Pilocainum: 25 patients, Placebo: 25 patients	<b>EMLA cream</b> (2 gram) was applied on the skin and covered with a transparent dressing by the patients 1 hour before the dialysis session. <b>Pilocainum gel</b> (2 gram) was applied on the skin and covered with a transparent dressing by the patients 1 hour before the dialysis session.	<b>Visual scale</b> (a 10-cm ruler) was assessed <b>immediately</b> after AVF puncture	≥ 50 (73%) 30-49 (24%) ≤ 30 (4%)	Not reported	Not reported	Not reported
Shahen et al. (2022)	Randomized, double-blind, crossover trial	A dialysis unit in a military hospital in Palestine	32 patients EMLA followed by piroxicam gel: 16 patients, Piroxicam gel followed by EMLA: 16 patients	<b>EMLA cream</b> 5% was applied as a thick film without rubbing into the skin and covered with an adhesive tape 1 hour before the AVF puncture. <b>Piroxicam gel</b> 0.5% was applied as a thick film without rubbing into the skin and covered with an adhesive tape 1 hour before the AVF puncture.	NRS (0-10) was assessed <b>immediately</b> after AVF puncture	46.44±11.58	38±28.89	Not reported	25%

AVF=arteriovenous fistula, EMLA=eutectic mixture of local anesthetics, NRS=numerical rating scale, SD=standard deviation, VAS=visual analogue scale