Lidocaine (Lignocaine) for local anaesthesia 2023

Newborn use only

Alert	Clinicians should consider other established non-pharmacologic (e.g. breastfeeding, skin-to-skin care) and pharmacologic interventions (e.g. oral sucrose) prior to lidocaine analgesia. 1% solution is recommended for local anaesthetic injection in neonates to minimise toxic effects.[1] Lidocaine with adrenaline combination is not used in the neonatal population. Methaemoglobinemia has been reported to be associated with EMLA cream.[2] EMLA cream/patch is not recommended for preterm infants <37 weeks gestation.(6) LMX4 cream contains benzyl alcohol.
Indication	1. Local infiltration anaesthesia (e.g. intercostal drainage, lumbar puncture) 2. Topical anaesthesia (e.g. IV catheter insertion, blood sampling, vaccination)
Action	Lidocaine (lignocaine) stabilises all potentially excitable membranes and prevents the initiation and transmission of nerve impulses. This produces a local anaesthetic effect.[1]
Drug Type	Amide local anaesthetic
Trade Name	1% Lidocaine-Baxter solution for injection 1% Pfizer Lignocaine hydrochloride injection Xylocaine 1% (lidocaine hydrochloride) EMLA (Eutectic Mixture of Local Anaesthetics – lidocaine + prilocaine) Numit (lidocaine + prilocaine) LMX4 cream (Liposomal lidocaine)
Presentation	1% solution for injection (10 mg/1 mL) ampoules or vials – lidocaine (lignocaine) hydrochloride (preservative free) EMLA cream for topical analgesia – 5% eutectic mixture containing lidocaine 25 mg (2.5%) and prilocaine 25 mg (2.5%) per gram (preservative free) LMX4 cream for topical analgesia – Liposomal lidocaine 4% w/w. Contains benzyl alcohol.
Dose	For infiltration 0.2-0.5 mL of 1% solution 5 to 8 minutes prior to the procedure.[3-5] Other suggested dosage: Up to 0.3 mL/kg (3 mg/kg per dose) of 1% solution.[1] Topical cream EMLA cream – NOT recommended for preterm infants <37 weeks.[1] 0.5-1 gram (1 g = 3.5cm length of cream squeezed from tube) to be applied for 60 minutes prior to the procedure.[1, 2, 6] LMX4 cream – 0.5-1 gram (2.5 cm – 5 cm of cream squeezed from the 5 gram tube; 2-3.5 cm of cream from 30 gram tube) to be applied 30-60 minutes prior to the procedure.[4, 7, 8] (ANMF consensus)
Dose adjustment	Not applicable – however toxicity from accumulation may develop with repeated or prolonged administration in patients with impaired renal and hepatic function.
Maximum dose	Injection: The dose at any one time should not exceed 3 mg/kg.[1] Topical cream: Up to 1 gram at any one time.[2]
Total cumulative dose	Not applicable.
Route	Infiltration Topical
Preparation	Not applicable
Administration	Injection - First administer the needle intradermally and inject drug to raise a wheal and then advance the needle further into desired interspace to inject the remaining dose, being careful not to inject into a blood vessel or a subdural space if lumbar puncture.[9] Topical cream – Apply the cream and cover with an occlusive dressing and leave the cream in situ for 60 minutes prior to the procedure. Remove the cream prior to the procedure.
Monitoring	Methaemoglobin levels if a preparation containing prilocaine is used
Contraindications	Hypersensitivity to prilocaine, lidocaine or any amide-type local anaesthetics, or any of the excipients. Topical cream/patch - Babies <37 weeks CGA.
Precautions	Local inflammation or infection at the proposed site of injection. Coagulation disorders or receiving anticoagulants.

Drug Interactions	EMLA may intensify the formation of methaemoglobin in patients treated with methaemoglobinaemia-inducing drugs (e.g. sulphonamides). The risk of further systemic toxicity should be considered when high doses of lidocaine are applied to patients already using other local anaesthetics.
Adverse Reactions	Methaemoglobinaemia and seizures with EMLA cream. Local bruising, redness. Transient local reactions at the application site such as redness, oedema, paleness, itching or rash. Arrythmias.
Compatibility	Not applicable
Incompatibility	Not applicable
Stability	Vials or ampoules for injection are for one dose in one patient only, discard any remaining contents
Storage	Store below 25°C.[1]
Excipients	Baxter and Pfizer lidocaine for injection – Sodium chloride and water for injections.[1] Xylocaine – Hydrochloric acid, sodium chloride, sodium hydroxide, water for injections. EMLA cream – Carbomer 934P, polyoxyethylene hydrogenated castor oil, sodium hydroxide, purified water. LMX4 cream – Benzyl alcohol, carbomer 940, cholesterol, hydrogenated lecithin, polysorbate 80, propylene glycol, triethanolamine, dl-alpha tocopheryl acetate, purified water.
Special Comments	
Evidence	**Background** Local anaesthetics offer the advantage of providing local anaesthesia without systemic effects. Local anaesthetics can be injected subcutaneously or applied topically on intact skin. Injections of local anaesthetics are utilised for more invasive procedures, whereas topical local anaesthetics are utilised for less invasive procedures.[4] Currently, the most widely utilised local injectable anaesthetic is lidocaine hydrochloride 1%.[4] **Efficacy** <u>The evidence for local infiltration analgesia in neonates is limited to lumbar puncture. There is lack of evidence on its efficacy for other invasive procedures such as intercostal chest drain insertion.</u> <u>Lidocaine injection for lumbar punctures (LP)</u> Pinheiro et. al. conducted a randomised controlled trial (RCT) in neonates requiring LP. Study neonates received no anaesthetic or 0.2-0.5 mL of 1% lidocaine (from subcutaneous to intervertebral space) using a 1mL syringe with 25-gauge needle prior to spinal needle insertion. Mean birthweight among lidocaine treated group was 1774 g, with 69% less than 2 kg. The injection of lidocaine induced an increase in struggling motion in neonates (P = 0.04). But on insertion of the spinal needle, struggling scores were significantly less in lidocaine treated group, with 15% of neonates in the lidocaine group and 51% of control neonates had moderate or severe struggling at the time of spinal needle insertion (P < 0.001). There were no significant differences in the number of LP attempts, LP failure rates or traumatic LPs.[3] Carraccio et. al. conducted a randomised controlled trial in children younger than 3 years of age requiring LP. Mean age of lidocaine treated group was 5 months (range 0.3-35 months). Ease of obtaining the CSF, as measured by number of attempts and traumatic CSF, did not differ between lidocaine and placebo groups.[10] <u>EMLA cream</u> A 2017 Cochrane review evaluated the efficacy and safety of topical anaesthetics in neonates requiring needle puncture of skin and other tissues. Eight clinical trials enrolling 506 newborn infants met the inclusion criteria. Overall, this review found no good quality evidence that topical local anaesthetics relieve pain during needle punctures in neonates. For EMLA – (a) 2 studies reported a statistically significant reduction in pain during lumbar puncture and venepuncture, (b) 3 studies found no statistical difference during heel lancing, (c) 1 study reported no statistical difference for successful venepuncture at first attempt and (d) risk for local redness, swelling or blanching was significantly higher with EMLA, although these were short-lasting.[11]

A systematic review by Taddio et. al. evaluated the efficacy and safety of EMLA in neonates for procedures including circumcision, heel lancing, venepuncture, arterial puncture, lumbar puncture and percutaneous venous catheter placement. The dose of EMLA used was 0.5 g to 2 g in most studies. The duration of application ranged from 10 minutes to 3 hours. This review found that EMLA diminishes pain during circumcision, but the efficacy data for other procedures are limited. Based on this review, EMLA can be recommended for the treatment of pain from circumcision but not for other procedures.[2] Methaemoglobin concentrations did not differ between EMLA-treated and placebo-treated infants. The incidence of clinically important methaemoglobinaemia was 0% after a single dose. There was insufficient data to assess the risk with multiple doses of EMLA.

Liposomal lidocaine cream

Taddio et. al. conducted a double-blind RCT of 330 healthy term newborns. Before venipuncture for the newborn screening test, neonates received (1) 1 g of liposomal lidocaine cream topically, (2) 2 mL of 24% sucrose solution orally, or (3) sucrose and liposomal lidocaine. Facial grimacing scores were lower in the sucrose group compared with those in the liposomal lidocaine group and for the sucrose plus liposomal lidocaine group compared with those in the liposomal lidocaine group. The mean (SD) plasma lidocaine level was 44.6 (55.3) ng/mL. In conclusion, Sucrose was more effective than liposomal lidocaine alone for reducing pain during venipuncture in newborns. The addition of liposomal lidocaine to sucrose did not confer any additional benefit to sucrose alone. There was no evidence of harm from liposomal lidocaine or sucrose.[7]

ANMF consensus: Clinicians should consider other established non-pharmacologic (e.g. breastfeeding, skin-to-skin care) and pharmacologic interventions (e.g. oral sucrose) prior to lidocaine analgesia. Routine topical anaesthetics including EMLA and LMX4 are not recommended/required in neonates.

Analgesic effect of lidocaine injection and lidocaine-prilocaine (EMLA) cream

In an experimental study in volunteer adults, lidocaine produced total sensory block almost immediately (within 8 minutes) after injection. With EMLA cream, (a) the analgesic efficiency of EMLA cream increased with longer application times (60 to 120 minutes); the effect after 2 hours of application was similar to lidocaine infiltration, (b) the analgesic effect is increased after removal of the cream - total sensory block was reached 20 minutes after removal of application for 80 minutes or immediately after removal of the cream after it was applied for 100 or 120 minutes. Pain block was achieved 30 minutes after removal of cream applied for 30 minutes, 15 minutes after removal of cream applied for 60 minutes and immediately after applications for 80, 100, or 120 minutes.[12]

Analgesic effect of EMLA cream, tetracaine gel and liposomal lidocaine gels

A narrative review by Lehr et. al. summarised the results of various studies on analgesic effects of various creams. EMLA cream takes approximately 1 hour for clinical effect and its depth of penetration is variable and have been reported to be associated methaemoglobinaemia due to prilocaine metabolites. Tertracaine gel doesn't lead to methaemoglobinaemia and has an onset time of 30-40 minutes. Liposomal lidocaine gel (LMX4) offers the advantage of a short onset of action and lacks serious local or systemic side effects.[4]

ANMF consensus on dosing recommendations is the pragmatic summary extrapolated from above studies.

Lidocaine gel for urethral catheterisation

In a RCT by Poonai et. al., children 0 to 24 months requiring urethral catherisation (UC) were randomised to Non-anaesthetic lubricant (NAL) or topical and intraurethral 2% lidocaine gel. Compared with NAL, topical and intraurethral lidocaine was not associated with significant pain reduction during UC, but significantly greater pain during instillation.[13] Similarly, another RCT in 45 children aged 2-24 months requiring urethral catheterisation found that intraurethral lidocaine did not fully alleviate discomfort associated with urethral catheterisation.[14]

	AMF consensus: Current practice of using NALs (e.g. KY Jelly/Optilube) for urethral catheterisation is the preferred method and there is no advantage of lidocaine gel over non-anaesthetic lubricants. **Safety** Methaemoglobinaemia - There have been case reports of EMLA use and methemoglobinaemia from prilocaine metabolites that can oxidise haemoglobin. However, systematic reviews did not find any studies reporting methaemoglobinaemia with EMLA.[2, 11] The efficacy and safety of EMLA and other topical anaesthetics, in preterm infants, is not established. CNS toxicity was also reported following topical EMLA cream.[15, 16] **Pharmacokinetics** Analgesic effect of injection is almost immediate.[12] EMLA cream may take approximately 1 hour for clinical effect, but for total sensory blockade immediately after the removal of cream, a minimum application time of 100 minutes is necessary.[12] It's depth of penetration is variable and increases with increasing application time up to approximately 2 to 3 mm after 1 to 2 hours and 6 mm after 3 to 4 hours.[4]
Practice points	
References	1. Lidocaine (lignocaine). MIMS online. Accessed on 15 November 2022. 2. Taddio A, Ohlsson A, Einarson TR, Stevens B, Koren G. A systematic review of lidocaine-prilocaine cream (EMLA) in the treatment of acute pain in neonates. Pediatrics. 1998;101(2):E1. 3. Pinheiro JM, Furdon S, Ochoa LF. Role of local anesthesia during lumbar puncture in neonates. Pediatrics. 1993;91(2):379-82. 4. Lehr VT, Taddio A, editors. Topical anesthesia in neonates: clinical practices and practical considerations. Semin Perinatol; 2007: Elsevier. 5. Stang HJ, Gunnar MR, Snellman L, Condon LM, Kestenbaum R. Local anesthesia for neonatal circumcision: effects on distress and cortisol response. JAMA. 1988;259(10):1507-11. 6. EMLA cream. MIMS online. ACcessed on 19 January 2023. 7. Taddio A, Shah V, Stephens D, Parvez E, Hogan M-E, Kikuta A, et al. Effect of Liposomal Lidocaine and Sucrose Alone and in Combination for Venipuncture Pain in Newborns. Pediatrics. 2011;127(4):e940-e7. 8. LMX4. Perrigo Australia. MIMS online. Accessed on 16 November 2022. 9. Mittiga MR, Ruddy RM. Chapter 141. Procedures. In Bachur, Richard G., and Kathy N. Shaw. Fleisher and Ludwig's Textbook of Pediatric Emergency Medicine, Wolters Kluwer, 2015. ProQuest Ebook Central, http://ebookcentral.proquest.com/lib/csuau/detail.action?docID=4786250. 10. Carraccio C, Feinberg P, Hart LS, Quinn M, King J, Lichenstein R. Lidocaine for lumbar punctures. A help not a hindrance. Archives of Pediatrics & Adolescent Medicine. 1996;150(10):1044-6. 11. Foster JP, Taylor C, Spence K. Topical anaesthesia for needle-related pain in newborn infants. Cochrane Database of Systematic Reviews. 2017(2). 12. Arendt-Nielsen L, Bjerring P. Laser-induced pain for evaluation of local analgesia: a comparison of topical application (EMLA) and local injection (lidocaine). Anesthesia and Analgesia. 1988;67(2):115-23. 13. Poonai N, Li J, Langford C, Lepore N, Taddio A, Gerges S, et al. Intraurethral Lidocaine for Urethral Catheterization in Children: A Randomized Controlled Trial. Pediatrics. 2015;136(4):e879-86. 14. Mularoni PP, Cohen LL, DeGuzman M, Mennuti-Washburn J, Greenwald M, Simon HK. A randomized clinical trial of lidocaine gel for reducing infant distress during urethral catheterization. Pediatric emergency care. 2009;25(7):439-43. 15. Rezvani M, Finkelstein Y, Verjee Z, Railton C, Koren G. Generalized seizures following topical lidocaine administration during circumcision: establishing causation. Paediatr Drugs. 2007;9(2):125-7. 16. Rincon E, Baker RL, Iglesias AJ, Duarte AM. CNS toxicity after topical application of EMLA cream on a toddler with molluscum contagiosum. Pediatric Emergency Care. 2000;16(4):252-4.

VERSION/NUMBER	DATE
Original 1.0	9/2/2023
REVIEW	9/2/2028

Authors Contribution – current version

Author/s	Srinivas Bolisetty
Evidence Review	Srinivas Bolisetty
Expert review	
Nursing Review	Eszter Jozsa, Renae Gengaroli
Pharmacy Review	Stephanie Halena, Michelle Jenkins
ANMF Group contributors	Nilkant Phad, Bhavesh Mehta, Rebecca Barzegar, Rebecca O'Grady, Mohammad Irfan Azeem, Martin Kluckow, Kerri Knox, Karel Allegaert
Final editing	Thao Tran
Electronic version	Cindy Chen, Ian Callander, Thao Tran, Helen Huynh
Facilitator	Srinivas Bolisetty