National Essential Medicine List Medication Review Process
Adult Hospital Level
Component: Anaesthesia

Date: 17 July 2015

Medication: Topical preparation of lignocaine 2.5% /prilocaine 2.5%.

Indication: Topical anaesthesia for repeated invasive procedures.

Introduction
After skin application under an occlusive dressing, topical lignocaine 2.5%/prilocaine 2.5% provides dermal analgesia after one hour with a maximal effect at 2–3 hours following application. Onset and duration is variable, depending on the site of application (on the genital mucosa, for example, the onset time is faster and the duration of action is shorter)[1]

Recommended dosages: [1]

Age / weight	Maximum Total Dose	Max Application area	Max Application time
Adults	60g	400cm^2	4h

Reason for Inclusion on the Essential Medicines List
Oncology patients who require repeated invasive procedures (venepuncture, LP's etc)

Current Essential Medicines List Alternatives
None.

Search Strategy:
Oncology Patients Requiring Repeated Invasive Procedures.

Excluded Studies
- Paediatric patients.
- Topical preparation of lignocaine 2.5% /prilocaine 2.5% for any other indication other than repeated procedures in oncology patients.

Selected Studies

1. **Articles relevant to improving venous cannulation in adults**

Reference	Type of trial	Intervention	Primary outcome	Results	Comments
Hallen et al 1985, BJA [4]	Blinded, randomized, cross-over, n=31	Topical lignocaine 2.5% / prilocaine 2.5% prior to venepuncture vs placebo	Pain on venepuncture	28/31 had lower pain scores	Topical lignocaine 2.5% / prilocaine 2.5% reduces pain associated with venipuncture
Celik et al 2011, Int J Med Sci [5]	Randomized, placebo-controlled. n=41	Topical lignocaine 2.5% / prilocaine 2.5% vs ethyl chloride vapocoolant vs	Pain on venepuncture	Topical lignocaine 2.5% / prilocaine 2.5% more effective at reducing pain	Topical lignocaine 2.5% / prilocaine 2.5% effective

		placebo for venipuncture in haemodialysis patients		score compared to ethyl chloride and placebo	
Vaghadia et al 1997, Can J Anaesth [6]	Double blinded, randomized, placebo-controlled, n=51	Placebo vs topical lignocaine 2.5% / prilocaine 2.5% patch	Pain on venepuncture, incidence of vaso-vagal side effects	Reduced pain on intravenous cannulation, lower rate of vaso-vagal events	
Watson et al 1988. Nephrol Dial Transplant [7]	Double blind, randomized. n=26	Topical lignocaine 2.5% / prilocaine 2.5% vs placebo in haemodalysis patients for AVF cannulation	Pain on cannulation	Lower pain scores (verbal and visual scales) with topical lignocaine 2.5% / prilocaine 2.5%	Provides pain relief. Improved ease of venepuncture
Nott 1990. Anaesthesia [8]	4 groups: Topical lignocaine 2.5% / prilocaine 2.5% 60min before, 5 min before, placebo, no treatment N=120	Topical lignocaine 2.5% / prilocaine 2.5% applied for either 5min or 60 min pre venous cannulation	Pain scores – visual and verbal – on venepuncture	Lower pain scores at 5 min compared to no treatment	Effective even at 5 min prior to injection

2. Articles relevant to improving lumbar puncture satisfaction

Reference	Type of trial	Intervention	Primary outcome	Results	Comments
Whitlow et al 2015. Paed Blood Cancer [9]	Randomized. placebo vs intervention. Blinded. N=25	Topical lignocaine 2.5% / prilocaine 2.5% vs Placebo at LP site under propofol sedation	Indirect measures of pain: propofol dose, pt movement, HR changes	Lower propofol dose 4.0 vs 4.9/kg, less movement 8 vs 84%, lower Ave HR in topical lignocaine 2.5% / prilocaine 2.5% group	Effective adjunct to LP
Koscielniak-Nielsen et al 1998. Anaesthesia [10]	Prospective, Randomised, placebo-controlled n=180 adults	Topical lignocaine 2.5% / prilocaine 2.5% to back before LP vs placebo patches to Group 2 with additional lignocaine block and Group 3 placebo patch only	Visual analog scale in response to pain	Lower pain intensity in topical lignocaine 2.5% / prilocaine 2.5% group	
Sharma et al 1996. Reg Anesth. [11]	Randomized	Topical lignocaine 2.5% / prilocaine 2.5% vs local infiltration of lignocaine for spinal anaesthesia (Tubal ligation), n= 41	Pain on visual analog scale	Significantly lower pain score in topical lignocaine 2.5% / prilocaine 2.5% group compared to local infiltration with lignocaine	Application 30min before spinal provides good analgesia during needle insertion

3. Articles relevant to the safety

Reference	Type of trial	Intervention	Primary outcome	Results	Comments/ Recommendations
AN Tran, JY Koo, J Drugs Dermatol 2014 [12]	Systematic review: 1985-2013, Pubmed, English	12 studies (5 RCTs, 1 controlled trial without randomisation, 5 non uncontrolled trials, 1 medical record review).	Safety	**methHb in adults**: generally safe 1 case too big a dose 1 case too big a surface area No accumulation of metabolites with multiple repeat dosing. **LAST in adults:** 1 case	Caution in patients with hepatic/renal impairment in article. Avoid in patients taking methHb inducing agents and patients with G6PD deficiency.

Serious side effects include those of other local anaesthetics namely cardio and central nervous system toxicity (LAST – local anaesthetic systemic toxicity). In addition methehaemoglobinaemia is a possibility.

Summary

There is evidence that topical preparation of lignocaine 2.5% / prilocaine 2.5% can be beneficial in oncology patients requiring repeated invasive procedures. Topical preparation of lignocaine 2.5% / prilocaine 2.5% is a relatively safe agent, so long as dosage instructions are adhered to.

References

[1] ACTAVIS. EMLA Package Insert. 2015 [cited 2015 17 July]; Online Package Insert]. Available from: http://www.drugs.com/pro/emla.html

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[4] Hallen B, Carlsson P, Uppfeldt A. Clinical study of a lignocaine-prilocaine cream to relieve the pain of venepuncture. British journal of anaesthesia. 1985 Mar;57(3):326-8.

[5] Celik G, Ozbek O, Yilmaz M, Duman I, Ozbek S, Apiliogullari S. Vapocoolant spray vs lidocaine/prilocaine cream for reducing the pain of venipuncture in hemodialysis patients: a randomized, placebo-controlled, crossover study. International journal of medical sciences. 2011 2011;8(7):623-7.

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[7] Watson AR, Szymkiw P, Morgan AG. Topical anaesthesia for fistula cannulation in haemodialysis patients. Nephrol Dial Transplant. 1988;3(6):800-2.

[8] Nott MR, Peacock JL. Relief of injection pain in adults. EMLA cream for 5 minutes before venepuncture. Anaesthesia. 1990 Sep;45(9):772-4.

[9] Whitlow PG, Saboda K, Roe DJ, Bazzell S, Wilson C. Topical analgesia treats pain and decreases propofol use during lumbar punctures in a randomized pediatric leukemia trial. Pediatric blood & cancer. 2015 Jan;62(1):85-90.

[10] Koscielniak-Nielsen Z, Hesselbjerg L, Brushoj J, Jensen MB, Pedersen HS. EMLA patch for spinal puncture. A comparison of EMLA patch with lignocaine infiltration and placebo patch. Anaesthesia. 1998 Dec;53(12):1218-22.

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[12] Tran AN, Koo JY. Risk of systemic toxicity with topical lidocaine/prilocaine: a review. J Drugs Dermatol. 2014 Sep;13(9):1118-22.