

The Optimal Time for Applying 5% Lidocaine Medicated Plaster to Decrease Protective Sensation of Skin

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Background: Eutectic mixture of local anesthetics is commonly used to reduce pain during cutaneous interventions but it must be applied under an occlusive bandage. It can cause vasoconstriction, methemoglobinemia and skin wrinkling. Five percent lidocaine medicated plaster (5%LMP), which is indicated for neuropathic pain, may be an alternative topical anesthetic. However, there is no data about its relationship between time and level of decreasing protective sensation of skin.

Objective: To determine the optimal time for applying 5%LMP to decrease protective sensation of skin.

Materials and Methods: Twenty healthy adult volunteers were tested for baseline sensation at dorsum of hand by the Semmes-Weinstein monofilaments kit, then they were tested hourly for 8 hours after applied 5%LMP. Sensory levels were recorded as A-level to T-level which G-level means diminish protective sensation. The main result was

the onset time which defined as the time when G-level monofilament cannot be detected. The median time of the onset was analyzed.

Results: The volunteers were 10 for each sex and their mean age was 30.65 ± 5.9 years. All male volunteers were able to reach G-level, but females were 30% fail to reach the G-level within 8 hours. The median onset time was 5 hours (95%CI:2.809-7.191) but there was different between male and female ($P=0.000$); which were 3 hours (95%CI:1.482-4.518) and 7 hours (95%CI:4.934-9.006) respectively. No skin wrinkling or any complications were observed.

Conclusion: Applying 5%LMP to decrease protective sensation of skin takes at least 5 hours. This may take longer time in female.

Keywords: lidocaine, medicated plaster, onset, topical anesthesia

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Some cutaneous interventions such as venous puncture, intravenous cannulation and skin laser therapy can cause pain, so topical anesthetics may be used to reduce pain for improving patient's comfort and satisfaction.

One of the well-known formulas for intact skin is eutectic mixture of local anesthetics (EMLA) which is a mixture of 2.5% lidocaine base and 2.5% prilocaine base. It must be applied under an occlusive bandage for 45 to 60 minutes to obtain effective cutaneous anesthesia.¹ Previous studies found EMLA could cause significantly skin wrinkling and vasoconstriction which might interfere the cutaneous interventions.^{2,3} Although report of methemoglobinemia from prilocaine in this

preparation is rare but it is still in concern especially when use in children.^{1,4}

The 5% lidocaine medicated plaster (5%LMP) is also a formula for intact skin indicated for postherpetic neuropathic pain.⁵ The patch is an 10 x 14 cm adhesive plaster contains 700 mg of lidocaine. Each patch can be divided for small part of body and it is found to be safe when use up to 3 patches for 12 hours.^{6,7} The 5%LMP may be alternatively use prior to cutaneous interventions because it is an adhesive plaster which is easy to apply and it contains lesser liquid content than EMLA which may not cause skin wrinkling. It is interesting to study the optimal time of application which

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may facilitate cutaneous intervention. Our study aims to find the optimal time for applying 5%LMP to decrease protective sensation of skin.

Materials and Methods

This study was designed as longitudinal experimental research. It was approved by Ramathibodi Ethics Committee (ID 06-61-05) and registered in Thai clinical trial registry (TCTR20181004001). The study was conducted at the pain clinic, Ramathibodi Hospital, during November 1st, 2018 to August 31st, 2019.

The sample size was calculated using the exponential mean power analysis.⁸ This study had 80% power to detect the differences between the null hypothesis mean time to achieve decreasing protective sensation of skin of 3 hours and the alternative hypothesis mean time to achieve decreasing protective sensation of skin of 6 hours according to the pilot observation, using the two-sided test with 5% significance level. The sufficient number was 19 and the

final rounded-up number was 20.

Written informed consent was obtained from each volunteer. We recruited 20 healthy adult volunteers with the age more than 18 years old. Exclusion criteria are people with any one of these: 1) Abnormal sensation at the dorsum of the hand 2) Underlying diseases which cause neuropathy such as diabetes mellitus 3) Abnormal skin appearance such as scar, rash or edema 4) Known allergy to local anesthetic drug or it's preservative 5) Unable to communicate

Lignopad[®], Teikoku Seiyaku Co.,Ltd, Kagawa, Japan⁹ (Figure 1) was used in this study. It was divided into 6 pieces (10 x 14 cm to 5 x 4.67 cm) which were proper size for applying on the dorsum of the hand. Skin sensation was tested by the Semmes-Weinstein monofilaments¹⁰ (Figure 2) which is an aesthesiometer by using standardized set of nylon filaments (A-level to T-level filaments) that can provide the gradient in force which is necessary to determine level of cutaneous touch and interpret as table 1.

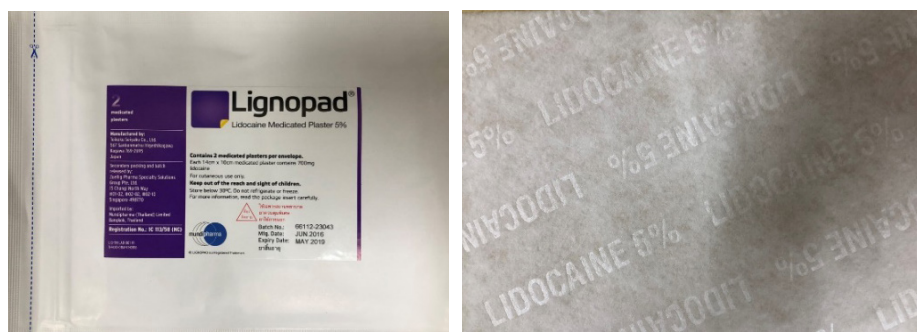


Figure 1 Lignopad[®], Teikoku Seiyaku Co.,Ltd, Kagawa, Japan



Figure 2 Semmes-Weinstein monofilaments

Table 1 Interpretation and relationship between nylon filaments in the Semmes-Weinstein monofilaments and forces

Color-code	Log force (rod markings)	Calculated force (grams)	Interpretation
Green	A 1.65	0.0045	Normal
	B 2.36	0.0230	
	C 2.44	0.0275	
	D 2.83	0.0677	
Blue	E 3.22	0.1660	Diminished light touch
	F 3.61	0.4082	
Purple	G 3.84	0.6958	Diminished protective sensation
	H 4.08	1.1940	
	I 4.17	1.4940	
Red	J 4.31	2.0520	Loss of protective sensation
	K 4.56	3.632	
	L 4.74	5.500	
	M 4.93	8.650	
	N 5.07	11.70	
	O 5.18	15.00	
	P 5.46	29.00	
	Q 5.88	75.00	
	R 6.10	127.0	
	S 6.45	281.5	
	T 6.65	447.0	

Each volunteer was tested for baseline sensation at dorsum of hand before applying 5%LMP. Cutaneous sensitivity was tested again hourly up to 8 hours.

During testing, the volunteers were closed their eyes and were instructed to give a verbal response, when they recognized that they were being touched by the particular filament. The filament was applied vertically above the skin of dorsum of the hand and slowly descend until the filament is bowed. This bow was maintained for approximately 1.5 seconds and removed in 1.5 seconds.

We defined the first level that can be detected as baseline sensation when the test was start from A-level filament, and the first time that G-level filament cannot be detected as the onset time.

Statistical analysis

SPSS 18 for Windows was used to analyze all data in this study. The demographic data were analyzed as mean $\pm$ SD and frequency (%). The primary outcome was analyzed as median onset time using Kaplan-Meier survival curve. The median onset times between each parameter were compared by log-rank test with a value of $P < 0.05$ was considered significant.

Results

Overall demographic data of 10 male and 10 female volunteers was shown in table 2. The median onset time was 5 hours (95%CI 2.8-7.2) (Figure 3). There was statistically significant difference when compared the median onset time in male and female volunteers which were 3 hours (95%CI 1.5-4.5) and 7 hours (95%CI 4.9-9.1) respectively with P -value = 0.000 (Figure 4).

After 8 hours of applying 5%LMP, we did not find any change of skin appearance and complications such as rash, erythema, skin wrinkling or edema in all of 20 volunteers.

Table 2 Demographic data

Characteristics	Results
Sex (M/F)	10/10
Male, n (%)	10 (50)
Female, n (%)	10 (50)
Age (years)	30.65 $\pm$ 5.9
Weight (kg)	63.65 $\pm$ 13.4
Height (cm)	165.5 $\pm$ 0.5
Body mass index (kg/m ²)	23.08 $\pm$ 3.6

Data report as mean $\pm$ SD

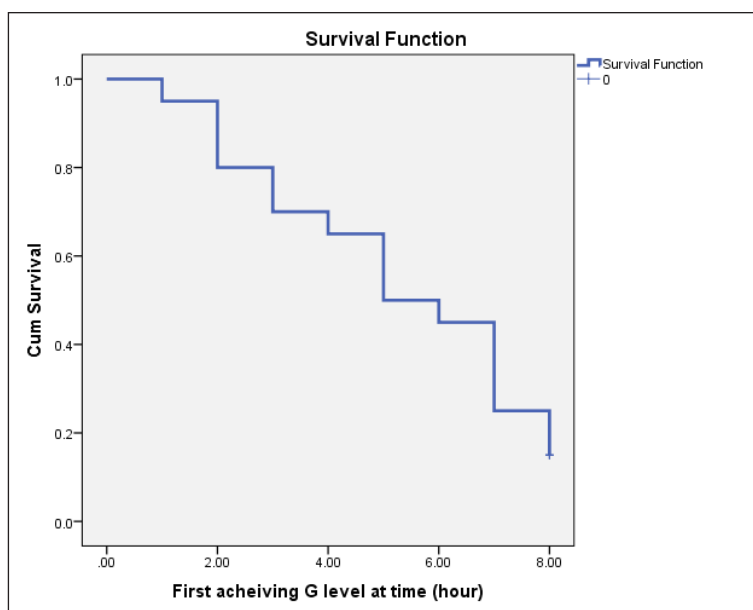


Figure 3 Kaplan-Meier survival curve for onset time of all volunteers after applying 5%LMP which defined as the first time with no detection of G-level of the Semmes-Weinstein monofilaments.

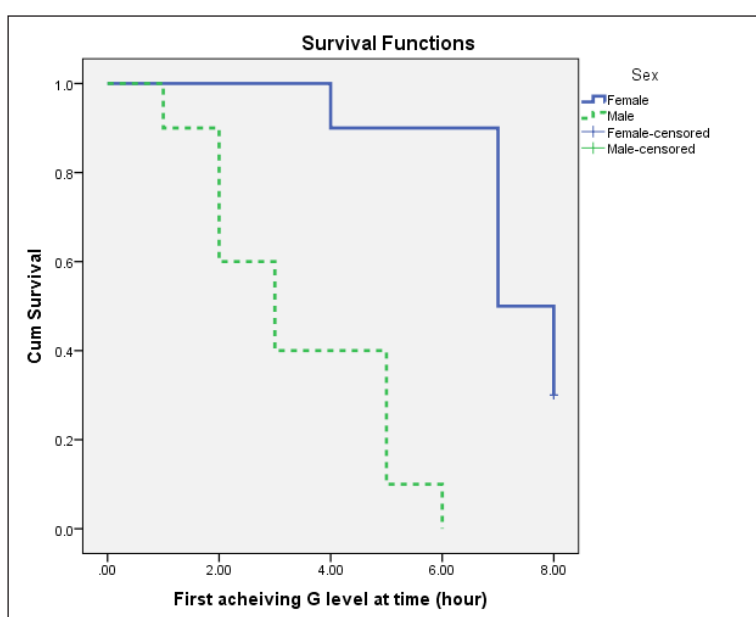


Figure 4 Kaplan-Meier survival curve for onset time after applying 5%LMP in female (solid line) and male (dash line). Log-rank test was used to compare the result between groups.

Discussion

The estimated optimal time for applying 5%LMP to decrease protective sensation of the skin is 5 hours which is longer than using EMLA, this might be because the 5%LMP is designed for chronic pain which does not need the fast onset. Female volunteers took longer time

in applying the 5%LMP to get same result when compare to male volunteers. It may be caused by female has lower pain threshold than male due to gonadal hormones and central nervous system.¹¹

Skin wrinkling was not found during this study, so this may determine that using the 5%LMP will not

increase difficulty for cutaneous intervention especially for intravenous cannulation. It might be less liquid component that caused less skin wrinkling or edema.

The 5%LMP is an adhesive plaster with no need of addition material which may increase cost-effectiveness. For example, one 5%LMP (200 baht) can be divided into 6-8 pieces for intravenous cannulation, so it would cost about 25-35 baht per one intervention. In the other hand, about 1 gm of EMLA cream for intravenous cannulation cost 26 baht and another 10 baht for an occlusive bandage so it would cost about 36 baht per one intervention. So, it is comparable cost-effectiveness with EMLA cream.

Our study shows that the optimal time for application of 5%LMP to decrease protective sensation of skin is at least 5-7 hours. So it may not be appropriate with the cutaneous interventions which have less time for the preparation. However, it may be benefit and suitable for the anesthesiologists or the ward nurses that they can apply it to the patients when they perform premedication in the evening or at night before surgery to prepare intravenous cannulation in the morning because they will have a lot of work to do in the morning.

Limitations in this study are the sample size was too small to represent overall population and we did not do real intervention (e.g. needle puncture) as practical which is recommended for future study. It will be more informative if we can compare with other topical local anesthetics.

Conclusion

Applying 5%LMP to decrease protective sensation of the skin takes at least 5 hours. This may take longer time in female. It can be alternative local anesthetic but it may not be appropriate with the cutaneous interventions which have less time for the preparation because of delayed onset of action.

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