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Comparative Study of the Effectiveness of EMLA Cream and Lidocaine Patch on Peripheral Intravenous Cannulation Pain in Patients Posted for Elective Surgeries

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ABSTRACT
Peripheral venous cannulation is a routine and mandatory procedure for hydration and intravenous drug administration of anaesthesia drugs in perioperative period. Present study was aimed to compare the effectiveness of EMLA cream and Lidocaine patch on peripheral intravenous cannulation pain in patients posted for elective surgeries. Present study was single-center, comparative study, conducted in Patients age group between 18-60 years, Both male and female patient. ASA grade I and II. On the day of elective surgery place patient into 2 groups as Group A (EMLA cream) and Group B (Lidocaine patch). Significant difference was seen in pain score just after cannulation, at 1 minute after cannulation between group A and B. (p value <.05) Mean±SD of pain score just after cannulation, at 1 minute after cannulation in group B was 2.38±0.66, 1.98±0.53 respectively which was significantly higher as compared to group A (1.59±0.57(p value<.0001), 1.18±0.38(p value<.0001)) respectively. Significant difference was seen in pain score by Visual Analogue Scale just after cannulation, at 1 minute after cannulation between group A and B. (p value<.05). Mean±SD of decrease in pain score by Visual Analogue Scale in group A was 0.79±0.69 which was significantly higher as compared to group B (0.29±0.46). (p value <.0001) Mean±SD of decrease in pain score by Verbal Rating Scale in group B was 0.95±1.02 which was significantly higher as compared to group A (0.61±0.75). (p value=0.018) EMLA cream is found to be more effective than lidocaine patch to reduce pain during peripheral cannulation for intravenous access.

INTRODUCTION

Peripheral venous cannulation is a routine and mandatory procedure for hydration and intravenous drug administration of anaesthesia drugs in perioperative period. For every patient undergoing surgery it is very important to secure safe and patent intravenous access, however this procedure is accompanied by pain. Many times, patient only remembers painful experience that occur during venepuncture, this seemingly trivial procedure sometimes assumes disproportionate magnitude and also may cause anxiety about further procedure which might deter patient from seeking medical care in future[1,2].

Pain during peripheral intravenous cannulation also results in hemodynamic alterations like increase in heart rate and blood pressure. The increase in heart rate and blood pressure leads to increase myocardial oxygen consumption and increase risk of myocardial infarction in patient at risk especially those having hypertension and heart diseases[3].

In cases with labile hemodynamics like hyperthyroidism and pheochromocytoma, hemodynamic response due to 18G wide bore cannulation pain perioperatively is not acceptable[4]. Thus attenuation of pain due to iv cannulation is crucial in perioperative period. Pain relief is a fundamental right of every patient. Present study was aimed to compare the effectiveness of EMLA cream and Lidocaine patch on peripheral intravenous cannulation pain in patients posted for elective surgeries

MATERIALS AND METHODS

Present study was single-center, comparative study, conducted in department of anaesthesiology, at XXX medical college and hospital, XXX, India. Study duration was of 3 years (June 2020-2023). Study was approved by institutional ethical committee.

Inclusion Criteria:

- Patients age group between 18-60 years, Both male and female patient. ASA grade I and II, willing to participate in present study.

Exclusion Criteria:

- Patients who refuse to participate.
- Patients having past history of arrhythmia
- Patients having local skin infection.
- Patients who took analgesics 24 hours before cannulation.
- Patients having vascular diseases.
- Patients having allergy or sensitivity to amide local anaesthetic and glycerine.
- Patient undergone >one attempt at cannulation.
- Patients having severe hepatic, renal, cardiac disease.
- Diabetic patients with peripheral neuropathy.
- Deranged coagulopathy.
- ASA grade III and IV.

Study was explained to participants in local language and written informed consent was taken. A routine pre operative assessment was done a day before surgery. The study protocol was explained to patient and they would be educated on the use of visual analog scale and verbal rating scale that would be used to assess the pain. Investigations done a day before surgery- CBC, LFT, RFT, PT-INR, Chest X-ray, ECG.

On the day of elective surgery place patient into 2 groups according to computer generated list.

Group A: EMLA cream was applied to the skin 60 minutes before peripheral intravenous cannulation and occlusive dressing done. Occlusive dressing was removed before entering patient into operation theater and looked for itching, burning, tingling and cold sensation.

Group B: Lidocaine patch was applied 30 minutes before peripheral intravenous cannulation in the pre op room. Lidocaine patch was removed before entering patient into operation theater Multi parameter monitor will be attached to patient to measure pulse rate, blood pressure, respiratory rate before, during and after 18G wide bore cannulation. After informing patient 18G wide bore cannula was inserted in proposed site. Pain score was taken for the site immediately after cannulation and one minute after cannulation by pain scoring scale. Four Point Pain Score will be used for objective evaluation by second assistant and subjective evaluation will be done by VAS Score and VRS Score.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS AND DISCUSSIONS

Distribution of age (years), gender, ASA grades were comparable between group A and B. Proportion of patients with hypertension was significantly higher in group A (26.25%) as compared to group B (13.75%). (p value=0.048). Distribution of other comorbidities was

comparable between group A and B. (Diabetes mellitus 6.25% vs 7.50% respectively (p value=0.755), Cardiac illness 3.75% vs 11.25% respectively (p value=0.131), Respiratory Illness 11.25% vs 5% respectively (p value=0.247)).

Table 1: General Characteristics

Age(years)	Group A(n = 80)	Group B(n = 80)	Total	P-value
18-30	29 (36.25%)	24 (30%)	53 (33.13%)	0.768†
31-40	40 (50%)	44 (55%)	84 (52.50%)	
41-50	7 (8.75%)	6 (7.50%)	13 (8.13%)	
51-60	4 (5%)	6 (7.50%)	10 (6.25%)	
Mean ± SD	33.5±9.09	34.59±9.16	34.04±9.11	0.452‡
Gender				
Male	41 (51.25%)	32 (40%)	73 (45.63%)	0.153†
Female	39 (48.75%)	48 (60%)	87 (54.38%)	
ASA grade				
1	52 (65%)	52 (65%)	104 (65%)	1†
2	28 (35%)	28 (35%)	56 (35%)	
Anthropometry				
Weight (kg)	65.71±15.1	63.65±15.29	64.68±15.19	0.392‡
Height (m)	1.64±0.1	1.63±0.11	1.63±0.1	0.688‡
Comorbidities				
Diabetes mellitus	5 (6.25%)	6 (7.50%)	11 (6.88%)	0.755†
Hypertension	21 (26.25%)	11 (13.75%)	32 (20%)	0.048†
Cardiac illness	3 (3.75%)	9 (11.25%)	12 (7.50%)	0.131*
Respiratory Illness	9 (11.25%)	4 (5%)	13 (8.13%)	0.247*

‡ Independent t test, † Chi square test

Proportion of patients with pain score just after cannulation, 1, 2 was significantly higher in group A as compared to group B. (1:-45% vs 10% respectively, 2:-51.25% vs 42.50% respectively). Proportion of patients with pain score just after cannulation: -3 was significantly lower in group A as compared to group B. (3: - 3.75% vs 47.50% respectively). (p value <0.0001)

Proportion of patients with pain score at 1 minute after cannulation: -1 was significantly higher in group A as compared to group B. (1:-82.50% vs 15% respectively). Proportion of patients with pain score at 1 minute after cannulation: -2, 3 was significantly lower in group A as compared to group B. (2: - 17.50% vs 72.50% respectively, 3: - 0% vs 12.50% respectively). (p value <0.0001)

Significant difference was seen in pain score just after cannulation, at 1 minute after cannulation between group A and B. (p value<.05) Mean±SD of pain score just after cannulation, at 1 minute after cannulation in group B was 2.38±0.66, 1.98±0.53 respectively which was significantly higher as compared to group A (1.59±0.57(p value<.0001), 1.18±0.38(p value<.0001)) respectively.

Table 2: Comparison of Pain Score (4-Point Scale) Just After Cannulation and 1 Minute After Cannulation.

Pain score	Group A (n = 80)	Group B (n = 80)	Total	P-value
Just after cannulation				
1	36 (45%)	8 (10%)	44 (27.50%)	<.0001†
2	41 (51.25%)	34 (42.50%)	75 (46.88%)	
3	3 (3.75%)	38 (47.50%)	41 (25.63%)	
Mean±SD	1.59±0.57	2.38±0.66	1.98±0.73	<.0001‡
1 minute after cannulation				
1	66 (82.50%)	12 (15%)	78 (48.75%)	<.0001†
2	14 (17.50%)	58 (72.50%)	72 (45%)	
3	0 (0%)	10 (12.50%)	10 (6.25%)	
Mean±SD	1.18±0.38	1.98±0.53	1.58±0.61	<.0001‡

‡ Independent t test, † Chi square test

Distribution of decrease in pain score was comparable between group A and B. (-1: - 0% vs 1.25% respectively, 0:- 58.75% vs 57.50% respectively, 1:-41.25% vs 41.25% respectively) (p value=1). Mean±SD of decrease in pain score in group A was 0.41±0.5 and in group B was 0.4±0.52 with no significant difference between them. (p value=0.876).

Table 3: Comparison of Decrease in Pain Score Between Group A and B.

Decrease in pain score	Group A(n = 80)	Group B(n = 80)	Total	P-value
-1	0 (0%)	1 (1.25%)	1 (0.63%)	1*
0	47 (58.75%)	46 (57.50%)	93 (58.13%)	
1	33 (41.25%)	33 (41.25%)	66 (41.25%)	
Mean±SD	0.41±0.5	0.4±0.52	0.41±0.51	0.876‡

‡ Independent t test, * Fisher's exact test

Proportion of patients with pain score by Visual Analogue Scale just after cannulation:-3 was significantly higher in group A as compared to group B. (3:-23.75% vs 0% respectively). Proportion of patients with pain score by Visual Analogue Scale just after cannulation: - 1, 2 was significantly lower in group A as compared to group B. (1:-32.50% vs 41.25% respectively, 2: - 43.75% vs 58.75% respectively). (p value <0.0001)

Proportion of patients with pain score by Visual Analogue Scale at 1 minute after cannulation: -1 was significantly higher in group A as compared to group B. (1:-87.50% vs 70% respectively). Proportion of patients with pain score by Visual Analogue Scale at 1 minute after cannulation: -2 was significantly lower in group A as compared to group B. (2:-12.50% vs 30% respectively). (p value=0.007).

Significant difference was seen in pain score by Visual Analogue Scale just after cannulation, at 1 minute after cannulation between group A and B. (p value <.05). Mean±SD of pain score by Visual Analogue Scale just after cannulation in group A was 1.91±0.75 which was significantly higher as compared to group B (1.59±0.5(p value=0.002)). Mean±SD of pain score by Visual Analogue Scale at 1 minute after cannulation in group B was 1.3±0.46 which was significantly higher as compared to group A (1.12±0.33(p value=0.007)).

Table 4: Comparison of Pain Score by Visual Analogue Scale Just After Cannulation and 1 Minute After Cannulation.

Pain score by Visual Analogue Scale	Group A(n = 80)	Group B(n = 80)	Total	P-value
Just after cannulation				
1	26 (32.50%)	33 (41.25%)	59 (36.88%)	<.0001†
2	35 (43.75%)	47 (58.75%)	82 (51.25%)	
3	19 (23.75%)	0 (0%)	19 (11.88%)	
Mean±SD	1.91±0.75	1.59±0.5	1.75±0.65	0.002‡
1 minute after cannulation				
1	70 (87.50%)	56 (70%)	126 (78.75%)	
	0.007†			
2	10 (12.50%)	24 (30%)	34 (21.25%)	
Mean±SD	1.12±0.33	1.3±0.46	1.21±0.41	0.007‡

‡ Independent t test, † Chi square test

Proportion of patients with decrease in pain score by Visual Analogue Scale: -1, 2 was significantly higher in group A as compared to group B. (1:-48.75% vs 28.75% respectively, 2:-15% vs 0% respectively). Proportion of

patients without decrease in pain score by Visual Analogue Scale was significantly lower in group A as compared to group B. (36.25% vs 71.25% respectively). (p value <0.0001). Mean±SD of decrease in pain score by Visual Analogue Scale in group A was 0.79±0.69 which was significantly higher as compared to group B (0.29±0.46). (p value <.0001).

Table 5: Comparison of Decrease in Pain Score by Visual Analogue Scale

Decrease in pain score by Visual Analogue Scale	Group A(n = 80)	Group B(n = 80)	Total	P-value
0	29 (36.25%)	57 (71.25%)	86 (53.75%)	<.0001†
1	39 (48.75%)	23 (28.75%)	62 (38.75%)	
2	12 (15%)	0 (0%)	12 (7.50%)	
Mean±SD	0.79±0.69	0.29±0.46	0.54±0.63	<.0001‡

‡ Independent t test, † Chi square test

Proportion of patients with pain score by Verbal Rating Scale just after cannulation: -1, 2 was significantly higher in group A as compared to group B. (1: - 46.25% vs 38.75% respectively, 2:-37.50% vs 26.25% respectively). Proportion of patients with pain score by Verbal Rating Scale just after cannulation: -3, 4 was significantly lower in group A as compared to group B. (3: -12.50% vs 13.75% respectively, 4:-3.75% vs 21.25% respectively). (p value=0.008) Mean±SD of pain score by Verbal Rating Scale just after cannulation in group B was 2.17±1.17 which was significantly higher as compared to group A (1.74±0.82(p value=0.007)).

Distribution of pain score by Verbal Rating Scale at 1 minute after cannulation was comparable between group A and B. (1:-87.50% vs 77.50% respectively, 2:-12.50% vs 22.50% respectively) (p value=0.096). No significant difference was seen in pain score by Verbal Rating Scale at 1 minute after cannulation (p value=0.097) between group A and B. Mean±SD of pain score by Verbal Rating Scale 1 minute after cannulation in group A was 1.12±0.33 and in group B was 1.23±0.42 with no significant difference between them.

Table 6: Comparison of Pain Score by Verbal Rating Scale Just After Cannulation and 1 Minute After Cannulation.

Pain score by Verbal Rating Scale	Group A(n = 80)	Group B(n = 80)	Total	P-value
Just after cannulation				
1	37 (46.25%)	31 (38.75%)	68 (42.50%)	0.008†
2	30 (37.50%)	21 (26.25%)	51 (31.88%)	
3	10 (12.50%)	11 (13.75%)	21 (13.13%)	
4	3 (3.75%)	17 (21.25%)	20 (12.50%)	
Mean±SD	1.74±0.82	2.17±1.17	1.96±1.03	0.007‡
1 minute after cannulation				
1	70 (87.50%)	62 (77.50%)	132 (82.50%)	0.096†
2	10 (12.50%)	18 (22.50%)	28 (17.50%)	
Mean±SD	1.12±0.33	1.23±0.42	1.18±0.38	0.097‡

‡ Independent t test, † Chi square test

Proportion of patients with decrease in pain score by Verbal Rating Scale: -0, 1 was significantly higher in group A as compared to group B. (0: - 55% vs 45% respectively, 1:-28.75% vs 23.75% respectively). Proportion of patients with decrease in pain score by Verbal Rating Scale: -2, 3 was significantly lower in group A as compared to group B. (2:-16.25% vs 22.50% respectively, 3:-0% vs 8.75% respectively). (p value=0.024)

Mean±SD of decrease in pain score by Verbal Rating Scale in group B was 0.95±1.02 which was significantly higher as compared to group A (0.61±0.75). (p value=0.018).

Table 7: Comparison of Decrease in Pain Score by Verbal Rating Scale Between Group A and B.

Decrease in pain score by Verbal Rating Scale	Group A(n= 80)	Group B(n = 80)	Total	P-value
0	44 (55%)	36 (45%)	80 (50%)	0.024*
1	23 (28.75%)	19 (23.75%)	42 (26.25%)	
2	13 (16.25%)	18 (22.50%)	31 (19.38%)	
3	0 (0%)	7 (8.75%)	7 (4.38%)	
Mean ± SD	0.61±0.75	0.95±1.02	0.78±0.91	0.018‡

‡ Independent t test, * Fisher's exact test

Many clinical procedures including arterial and venous punctures, percutaneous venous catheter insertion, lumbar puncture and dermatological procedures are associated with pain and consequent patient discomfort. IV cannulation procedure is one of the most common invasive methods that may cause pain, discomfort and anxiety in most of the patients. The pain and anxiety are more common when the peripheral veins are not easy to access and so the attempts to access the veins fail frequently.

There is evidence that failed IV cannulation may cause more pain and discomfort in patients. Venous puncture by wide bore cannula before induction of anaesthesia produces considerable pain. The pain of venous puncture is usually ameliorated by injection of local anaesthetics. However, local anaesthetic injection per se is painful, may causes intradermal turgor and can trigger local vasoconstriction, both of which reduce the puncture success rate, as demonstrated in a study done by K Ruetzler[5].

There are many interventions perform to sooth the pain and anxiety caused by intravenous cannulation like infiltration of local anaesthetics, topical anaesthesia in the form of cream or patch among them EMLA topical anaesthetic cream is widely notable. Topical analgesia is an attractive alternative to subcutaneous infiltration. Widely used topical preparation is eutectic mixture of 2.5% lidocaine and 2.5% prilocaine (EMLA). The lidocaine/tetracaine patch is one more formulation which is available.

In a study conducted by Tomomi Matsumoto[6] VAS scores for the EMLA cream hand were significantly lower than those for the lidocaine tape hand (4 [0-18] vs 17 [8-45], p=0.001, 95% CI -25 to-6) . VRS scores for the EMLA cream hand were also significantly lower than those for the lidocaine tape hand (2 [1–2] vs 2 [2–3], p=0.002, 95% CI - 0.8 to-0.2) The frequency of

local skin reactions was significantly higher in EMLA cream (EMLA 5/24, 21% vs lidocaine 0/24, 0%, p=0.022, relative risk 2.32, 95% CI 1.24-10.51). (93) These findings are not similar to our findings probably the veinflo gauge was the difference. We used 18 G cannula for the study. Our results also differ to the result of Tomomi Matsumoto *et al*. study for local reactions which were not found in our study.

In another study done by Herberger[7], found that the anaesthetic efficacy of 4% lidocaine cream and EMLA cream was comparable, the use of occlusive dressing over lidocaine had a faster onset of action than EMLA cream. Similarly, no adverse events were seen. The authors concluded that a topical preparation with 4% lidocaine is an effective and safe treatment option for superficial anaesthesia, with faster onset of action.

In study conducted by Selby and Bowles[8], concluded that the analgesic effect of lignocaine and ethyl chloride was better than that of EMLA cream applied for 5 min before venous cannulation. This is contrary to our observation with lidocaine and EMLA creams., the difference may be because we applied EMLA was applied 60 min before venepuncture in our study. Also, lidocaine group produced a greater number of failed cannulations, as it produced wheal, occasional hematoma that may obscure visibility of vein and subcutaneous injection of 1%lidocaine is per se painful. so we thought to use lidocaine patch instead of subcutaneous injection of 1% lidocaine. we used 18G cannula for the study for assessing the analgesic efficacy of EMLA cream and lidocaine patch by giving more painful stimulus through 18G wide bore cannula.

In study done by Oluwadun[9] observed minimal side effects on application of treatment creams. During cream application 1 patient in the EMLA group and 2 patients in the lidocaine group complained of burning. Tingling sensation was also reported by 1 patient in the lidocaine group. however, in our study we did not have similar experience with either EMLA cream or lidocaine patch.

In our study we used 5% lidocaine patch instead of 10% lignocaine cream to compare with the EMLA cream. As the penetrability of cream is >patch our outcome of the study are different. Mean heart rate between our study and Oluwadun[9] results are comparable but statistically insignificant just after cannulation. Similarly, a 1.5% decrease in heart rate in patients treated with lidocaine injection prior to cannulation was reported earlier as demonstrated in a study done by Langham[10] despite the difference in the route of administration and concentration of lidocaine in the two studies. The percentage change in mean heart rate at cannulation in group P (7.17%) is comparable with that in the placebo group (7.25%) in the latter study. However, the percentage increase in mean HR was sustained for 10 min in our study but for 3 min in another study done by Langham[10].

Miller[11] compared the analgesic effect of SC 1% lidocaine (0.3-0.5mL), 2.5 g EMLA cream and 1 mL iontocaine (a mixture of 2% lidocaine and 1:100,000 epinephrine) on pain at application of agent and during venous cannulation in adults scheduled for ambulatory surgery. A visual analog scale was used as the tool of measurement for pain. Results of the study showed that SC 1% locaine group experienced a higher pain score than either EMLA cream group or iontophoresis group, while group 2 experienced a higher pain score when the i.v. was started than either group 1 or group 3. Of the 3 methods tested, results seem to indicate that the Numby Stuff system using iontophoresis is the superior method for decreasing the pain associated with peripheral i.v. cannulation.

Several clinical studies reported mild side-effects in the use of the lidocaine/ tetracaine patch including mild erythema, oedema, blanching and burning sensations as demonstrated in a study done by Browne[12] and Yeon[13] however in our study we did not observe side effects, the only cutaneous complication they observed are mild erythema and the incidence was comparable in the lidocaine/tetracaine patch and placebo groups. The sensations reported by these patients subsided once the creams were removed.

Browne[12] reported mild pruritus following the use of amethocaine. Blanching of the skin after removal of treatment creams was observed in 1 patient in each group. A higher incidence had been reported earlier in a similar study., in the EMLA cream group, 3 patients (8.8%) had blanching of skin while 10 patients (29.8%) had erythema (16). EMLA cream is known to cause initial local vasoconstriction, leading to blanching; this is followed by vasodilatation, resulting in erythema and induration as demonstrated in a study done by Yeoh[13]. They reported no erythema and only 1 patient blanched, this we attributed to the dark skin of our studied population unlike other studies with light skinned patients. Kano[14] noticed local erythema in 8 out of 24 patients treated with lidocaine for venous cannulation pain. In our study we did not found any local reactions. This may require further additional clinical studies for safety of the drugs and procedure.

Anil Agarwal[15] observed that the incidence of venous cannulation pain was 100% in the control group, as compared to 37% and 48% of patients who experienced pain in the EMLA and diclofenac groups, respectively. So, it was concluded that transdermal diclofenac patch and EMLA both are equally effective in reducing venous cannulation pain, but signs of erythema, induration and edema are observed with the transdermal diclofenac patch. In our study we found that EMLA cream was effective for IV cannulation without any local side effects.

CONCLUSION

EMLA cream is found to be more effective than lidocaine patch to reduce pain during peripheral cannulation for intravenous access. EMLA cream causes less hemodynamic changes than lidocaine patch, neither EMLA nor lidocaine patch cause any local reactions during and after IV cannulation.

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