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# The clinical efficacy of EMLA cream for intravenous catheter placement in client owned dogs.

**Abstract**

*Objective*

Assessing the reaction of client owned dogs to

IV catheter placement after applying EMLA or placebo cream for either 30 or 60 minutes.

*Study design*

Prospective, randomised, blinded, placebo controlled, clinical trial.

*Animals*

Two hundred and two client owned dogs of various breeds.

*Methods*

With owner consent, dogs were randomly allocated to one of four treatment groups. Group 1 EMLA 60 minutes; Group 2 EMLA 30 minutes; Group 3 Placebo 60 minutes; Group 4 Placebo 30 minutes. After the cream was applied for the allocated time an IV catheter was placed and the behavioural reaction of the dog was scored. Reaction score was analysed using a Kruskall Wallis test followed by Mann Whitney tests of the multiple pairwise comparisons, with Bonferroni correction.

*Results*

A large number of dogs, even in the placebo groups, did not react to intravenous catheter placement. However, the Kruskall Wallis test showed there to be an overall difference between treatment groups (Chi sq = 11.029, df = 3, p = 0.012). The pairwise comparisons showed there to be a lower overall reaction score in the EMLA 60 group compared with the EMLA 30 group and the Placebo 60 group (adjusted p = 0.018 and adjusted p = 0.044, respectively).

*Conclusion and clinical relevance*

This study shows that EMLA cream applied for 60 minutes reduces the behavioural reaction of dogs to IV catheter placement and therefore this intervention can be advocated for routine use in veterinary medicine to enhance the welfare of dogs undergoing IV catheter placement.

**Keywords:** EMLA cream, dog, intravenous catheter, venepuncture

**Funding:**

## Introduction

Placement of an intravenous catheter in dogs is a very common procedure in contemporary veterinary medicine, but one which has been shown to be potentially aversive to the animal (Chebroux et al. 2015; Flecknell et al. 1990).

The use of EMLA cream, a eutectic mixture of the local anaesthetics lidocaine and prilocaine, is described in human medicine to desensitise the skin before venepuncture to make this procedure less aversive (Fetzer 2002; Rogers & Ostrow 2004). Flecknell et al (1990) showed that the use of EMLA cream reduced the aversiveness of intravenous catheter placement in laboratory dogs, cats and rabbits. Despite this study showing convincing evidence of improved welfare, its use has not become standard practice in veterinary medicine. One of the possible reasons why EMLA cream is not routinely used for IV catheter placement in veterinary medicine might be the manufacturer's recommendation of a 60 minutes application time before attempting venepuncture. In a clinical environment, a 60 minutes waiting period might be considered too long. A study in children (Hopkins et al. 1988) has shown that the application time can be shortened to 30 minutes. However, no data exist on the efficacy of EMLA cream after a 30 minutes application time in veterinary medicine. We feel it is worthwhile to study the efficacy of EMLA cream after a 30 minutes application time, as this shorter waiting period might make the routine use of EMLA cream before IV catheter placement more feasible in clinical veterinary practice. Also, due to patient, staff and environmental factors, the effect of EMLA might be less convincing or absent in a clinical setting compared with the laboratory study of Flecknell et al (1990). We therefore feel it is worthwhile to study the effect of EMLA in a clinical setting.

The aims of this study were to investigate the efficacy of EMLA cream in a busy clinical setting and to assess whether there would be a difference in efficacy when using either a 30 or 60 minutes application time. The objectives were to apply EMLA or a placebo

cream for either 30 or 60 minutes to client owned dogs scheduled for having an intravenous catheter placed and to score the reaction of the dog to catheter placement. The hypothesis was that, compared to placebo, EMLA cream would reduce the reaction of dogs to catheter placement and that shortening the waiting time to 30 minutes would be as effective as a waiting time of 60 minutes.

## Materials and methods

The study was designed as a randomised, prospective, blinded clinical trial andwas ethically approved by the institutional animal welfare and ethics review board under the number VIN/15/049.

*Subjects*

Two hundred and two (202) client owned dogs of mixed breeds were enrolled on the study after the owners signed for informed consent. All dogs enrolled, needed IV catheter placement for further treatment in our hospital. Dogs in which an IV catheter could not be placed without sedation because of their character were excluded. No other exclusion criteria were used. Dogs were randomly allocated to one of four experimental groups. Randomisation was done in blocks of 16, n=4 per experimental group, and achieved by drawing a pre-printed lot from an opaque envelope.

A specific power calculation has not been performed for this study, however, consideration for group size has been performed a priori.

*Procedure*

Once allocated to an experimental group, the skin over either the cephalic vein or saphenous vein was clipped and either EMLA cream (AstraZeneca, Luton, United Kingdom) or a Placebo (E45 cream, Reckitt Benckiser Healthcare, Slough, United Kingdom) was applied at

a dose of approximately 1.5 grams of cream per 10 $cm^2$ of skin, according to the manufacturer's instructions, and covered with an occlusive foil (kitchen cling film, B&M, Liverpool, United Kingdom). The creams were left on for either 30 or 60 minutes. Treatment for the different experimental groups was as follows: Group 1: After clipping, EMLA cream was applied and left on for 60 minutes before placing an IV catheter; Group 2: After clipping, EMLA cream was applied and left on for 30 minutes before placing an IV catheter; Group 3: After clipping, Placebo cream was applied and left on for 60 minutes before placing an IV catheter; Group 4: After clipping, EMLA cream was applied and left on for 30 minutes before placing an IV catheter..

After the designated time had elapsed, the skin over the vein was cleared of cream and prepped with chlorhexidine gluconate (ChloraPrep, BD, Basingstoke, United Kingdom). Subsequently an intravenous catheter (BD, Basingstoke, United Kingdom, 18 - 24 Gauge) was placed using a routine technique. Catheters were placed by members of staff (both veterinary nurses and veterinary surgeons) and students (both veterinary nursing and veterinary sciences students). Each dog was restrained by the primary investigator (), who was blinded to group allocation until the final statistical analysis.

*Data recording*

The primary outcome recorded was the reaction of the dog to first venepuncture using the scale as published by Flecknell et al (1990). Reaction 0: no reaction; Reaction 1: slight movement of limb, tensing of muscles; Reaction 2: Limb withdrawal, attempt to move away; Reaction 3: Marked attempts to escape, aggressive behaviour, vocalisation. The reaction was scored by the primary investigator.

Data recorded for each dog were breed, gender, age, weight, body condition score, and demeanour (1 = friendly, 2 = anxious, 3 = (fear) aggressive). Additional data recorded

were experience level of the catheter placer (novice, moderately experienced, experienced), outcome of placing a catheter at the prepped site (success, fail), and number of attempts and time needed to successfully place a catheter.

*Statistical analysis*

Continuous data of group demographics and experimental outcomes were analysed by one-way ANOVA, followed by a Tukey post-hoc test when appropriate. The residuals from parametric analyses were checked visually to ensure that they met the required assumptions of normality of error and homogeneity of variance. Categorical data on group demographics were analysed with a Chi-squared test. The primary outcome measure, reaction score, was analysed using a Kruskall Wallis test followed by Mann Whitney tests of the multiple pairwise comparisons, with p values adjusted using a Bonferroni correction. Statistical significance was considered when $p < 0.05$. The statistics package IBM SPSS Statistics v24 (IBM Corporation, New York) was used for the analysis.

**Results**

In total, 202 dogs representing 55 breeds were successfully enrolled, (EMLA60: n=50; EMLA30: n=51; Placebo 60: n=52; Placebo 30: n=49).

No differences between groups were found for age, weight, gender, body condition score, and demeanour (table 1).

A contingency table of treatment by reaction score is shown in table 2. The Kruskall Wallis test showed there to be an overall difference between treatment groups (Chi sq = 11.029, df = 3, p = 0.012). The pairwise comparisons showed there to be a lower overall reaction score in the EMLA 60 group compared with the EMLA 30 group and the Placebo 60

group (adjusted p = 0.018 and adjusted p = 0.044, respectively). None of the other pairwise comparisons were significant.

There was no effect of group allocation on the success rate to place an IV catheter at the prepped site or the total number of attempts needed. However, level of experience did have a significant effect on success rate (p=0.001), with novice placers having the highest failure rate (40.9%) compared to moderately experienced (5.8%) and experienced (13.9%). This was also reflected by the time needed to successfully place an IV catheter which was significantly longer (p<0.001) for the novice group (211.5 +/- 35.4 seconds), compared with the moderately experienced (56.5 +/- 11.5 seconds) and experienced (57.8 +/- 8.8 seconds) groups.

The level of experience of the catheter placer did not differ between groups, and had no effect on the reaction of the dog to first venepuncture.

**Discussion**

This study shows that EMLA cream applied for 60 minutes reduces the reaction of dogs to IV catheter placement. This finding is consistent with previous findings of Flecknell et al (1990). An interesting difference between the previous and present studies is that in the previous study by Flecknell et al (1990) 16.6 % of dogs undergoing IV catheterisation in the placebo group did not react to IV catheter placement. In contrast, in the present study 49.0% of dogs in group Placebo 30 and 61.2% of dogs in group placebo 60 did not react IV catheter placement. Several potential reasons can be put forward to explain this difference. First, Flecknell et al studied a population of laboratory beagles who were likely used to the surroundings and investigators carrying out the study. This study included dogs of different breeds and backgrounds, inherently introducing variations in behavioural reactions to catheter

158 placement *per se*. Second, in the present study the dogs were newly admitted to the hospital
159 and not familiar with the handlers. The latter may have resulted in a certain level of stress
160 which might have obscured (sometimes subtle) signs of reaction or could have induced a
161 temporary state of stress induced analgesia (Bodnar 1986) reducing the aversity of the
162 procedure. Thirdly, the behavioural scale used to assess the reaction of the dogs can be
163 considered subjective. As the two studies were carried out by different investigators this
164 could have introduced differences in outcome. Nevertheless, both studies show that, in a
165 laboratory and a busy clinical setting respectively, EMLA cream applied for 60 minutes prior
166 to IV catheter placement reduced the incidence and severity of an aversive reaction to this
167 procedure in dogs and thus can be advocated to enhance the welfare of canine patients.
168 Less reaction of dogs might improve ease of catheter placement, however, the data
169 from this study show that the success rate of IV catheter placement was not enhanced by the
170 application of EMLA cream. Conversely, success was not decreased, either. This implies that
171 the occasionally cited fear of vasoconstriction after application of EMLA cream, leading to
172 greater difficulty to place an IV catheter (Schreiber et al. 2013), is unjustified. Other
173 concerns that have been cited for the use of EMLA cream in the clinical setting are the
174 development of local anaesthetic toxicity and methaemoglobinaemia. Although not assessed
175 in this study, previous studies in man and cats have shown that these problems were not
176 encountered during clinical use of EMLA cream (Wagner et al. 2006; Robieux et al. 1990).
177 Additionally, in none of the dogs in the present study were signs of local anaesthetic toxicity
178 observed. We therefore conclude that EMLA cream appears to have no negative side effects
179 in its clinical use and that fears for such effects should be discarded as reasons to not use
180 EMLA cream in the clinical setting.
181 E45 cream was used as a placebo in this study. The data sheet of E45 cream states
182 under side effect that ‘Occasionally allergic reaction may occur’. This could make this cream

less suitable to use as a placebo. However, as we have not observed any form of allergic reaction to either of the creams in any dog during this study, and since E45 cream resembles EMLA cream in appearance and lacks the local anaesthetic effect, we feel it fulfilled the purpose of placebo well. Indeed, this cream has been used before as a placebo cream in human subjects without any reported problems (Speirs et al 2001).

A limitation of this study was that the level of experience of the catheter placers was based on a self-judgement. The levels of experience therefore could have been biased by the overall confidence level of the person asked. However, most people judging themselves as novice were found to be truly novice as they had placed catheters only once or twice before. Most of the moderately experienced people were end of year final year veterinary students, whereas the people who judged themselves as experienced were very confident final year students, nurses and anaesthetists. We therefore feel that the judgment of the level of experience, although potentially biased, was accurate.

Novice catheter placers needed more attempts to successfully place an IV catheter than moderately experienced and experienced ones. This might suggest that the use of EMLA is particularly useful when inexperienced people perform the procedure. However, as the level of experience of the catheter placer did not influence the reaction of the dog to first venepuncture it seems that the use of EMLA cream can be advocated for placers of all levels of experience.

A specific power calculation has not been performed for this study, however, consideration for group size has been performed a priori. In a controlled laboratory study with a uniform Beagle population, Flecknell et al (1990) demonstrated an effect of EMLA cream with a sample size of 12 per group. This sets a lower limit for sample size. The relatively innocuous consequences of the four treatments being applied allowed ready expansion of sample size. Given the context of the current study which introduced a wide

range of extraneous, uncontrolled error variation, that would be found in a teaching hospital, with a wide range of dog breeds being treated, sample size was maximised and constrained only by the number of suitable dogs that were seen within the time limits of the study.

In conclusion, this is the first clinical study on the use of EMLA cream in dogs, and it provides evidence that the routine use of EMLA cream in the clinical setting before placement of and IV catheter in dogs improves their welfare. However, as the cream only seems to be effective after being applied for 60 minutes, implementation only seems feasible for elective/non-emergency cases.

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255 Table 1. Demographic data of the dogs enrolled in the four different groups. BCS; body
256 condition score. Demeanour; 1 = friendly, 2 = anxious, 3 = (fear) aggressive. Experience
257 level of catheter placer; Nov = Novice, Mod = Moderately experienced, Exp = experienced
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| Group | EMLA 60 | EMLA 30 | Placebo 60 | Placebo 30 |
|---|---|---|---|---|
| Age (months) mean +/- stdev | 55.5 ± 43.1 | 57.6 ± 36.2 | 74.7 ± 41.7 | 67.4 ± 43.0 |
| Weight (kg) mean +/- stdev | 19.1 ± 15.4 | 15.9 ± 12.2 | 18.8 ± 11.4 | 22.7 ± 15.6 |
| Gender N | | | | |
| Male | 31 | 32 | 24 | 31 |
| Female | 19 | 19 | 28 | 18 |
| BCS (1 – 9) median (range) | 5 (4-8) | 5 (4-9) | 5 (4-8) | 5 (3-8) |
| Demeanour N | | | | |
| 1 | 46 | 43 | 43 | 42 |
| 2 | 4 | 8 | 9 | 7 |
| 3 | 0 | 0 | 0 | 0 |
| Experience level N | | | | |
| Nov | 4 | 7 | 5 | 6 |
| Mod | 12 | 8 | 17 | 14 |
| Exp | 34 | 36 | 30 | 29 |

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261 Table 2. Reaction of dogs to first venepuncture. Reaction 0: no reaction; Reaction 1: slight
262 movement of limb, tensing of muscles; Reaction 2: Limb withdrawal, attempt to move away;
263 Reaction 3: Marked attempts to escape, aggressive behaviour, vocalisation.
264

| | | | Group allocation | | | |
|---|---|---|---|---|---|---|
| | | | EMLA 60[a] | EMLA 30[b] | Placebo 60[b] | Placebo 30[a,b] |
| Reaction to first attempt | 0 | Count | 38 | 25 | 27 | 30 |
| | | % | 76.0% | 49.0% | 51.9% | 61.2% |
| | 1 | Count | 7 | 10 | 10 | 10 |
| | | % | 14.0% | 19.6% | 19.2% | 20.4% |
| | 2 | Count | 3 | 7 | 6 | 6 |
| | | % | 6.0% | 13.7% | 11.5% | 12.2% |
| | 3 | Count | 2 | 9 | 9 | 3 |
| | | % | 4.0% | 17.6% | 17.3% | 6.1% |
| Total | | Count | 50 | 51 | 52 | 49 |
| | | % | 100.0% | 100.0% | 100.0% | 100.0% |

265 Groups with different letters[(a or b)] are significantly different.