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- 1 **The clinical efficacy of EMLA cream for intravenous catheter placement in client**
- 2 **owned dogs.**
- 3

4 **Abstract**

5 *Objective*

6 Assessing the reaction of client owned dogs to  
7 IV catheter placement after applying EMLA or placebo cream for either 30 or 60 minutes.

8 *Study design*

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

10 *Animals*

11 Two hundred and two client owned dogs of various breeds.

12 *Methods*

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

19 *Results*

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

26 *Conclusion and clinical relevance*

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

30

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

32 **Funding:**

33

34 **Introduction**

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

38         The use of EMLA cream, a eutectic mixture of the local anaesthetics lidocaine and  
39 prilocaine, is described in human medicine to desensitise the skin before venepuncture to  
40 make this procedure less aversive (Fetzer 2002; Rogers & Ostrow 2004). Flecknell et al  
41 (1990) showed that the use of EMLA cream reduced the aversiveness of intravenous catheter  
42 placement in laboratory dogs, cats and rabbits. Despite this study showing convincing  
43 evidence of improved welfare, its use has not become standard practice in veterinary  
44 medicine. One of the possible reasons why EMLA cream is not routinely used for IV catheter  
45 placement in veterinary medicine might be the manufacturer's recommendation of a 60  
46 minutes application time before attempting venepuncture. In a clinical environment, a 60  
47 minutes waiting period might be considered too long. A study in children (Hopkins et al.  
48 1988) has shown that the application time can be shortened to 30 minutes. However, no data  
49 exist on the efficacy of EMLA cream after a 30 minutes application time in veterinary  
50 medicine. We feel it is worthwhile to study the efficacy of EMLA cream after a 30 minutes  
51 application time, as this shorter waiting period might make the routine use of EMLA cream  
52 before IV catheter placement more feasible in clinical veterinary practice. Also, due to  
53 patient, staff and environmental factors, the effect of EMLA might be less convincing or  
54 absent in a clinical setting compared with the laboratory study of Flecknell et al (1990). We  
55 therefore feel it is worthwhile to study the effect of EMLA in a clinical setting.

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

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

64

## 65 **Materials and methods**

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

### 69 *Subjects*

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

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

79

### 80 *Procedure*

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

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

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

100

#### 101 *Data recording*

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

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

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

112

### 113 *Statistical analysis*

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

123

### 124 **Results**

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

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

129 A contingency table of treatment by reaction score is shown in table 2. The Kruskal  
130 Wallis test showed there to be an overall difference between treatment groups (Chi sq =  
131 11.029, df = 3,  $p = 0.012$ ). The pairwise comparisons showed there to be a lower overall  
132 reaction score in the EMLA 60 group compared with the EMLA 30 group and the Placebo 60



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

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

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

145

146

## 147 **Discussion**

148 This study shows that EMLA cream applied for 60 minutes reduces the reaction of dogs to IV  
149 catheter placement. This finding is consistent with previous findings of Flecknell et al (1990).

150 An interesting difference between the previous and present studies is that in the previous  
151 study by Flecknell et al (1990) 16.6 % of dogs undergoing IV catheterisation in the placebo  
152 group did not react to IV catheter placement. In contrast, in the present study 49.0% of dogs  
153 in group Placebo 30 and 61.2% of dogs in group placebo 60 did not react IV catheter  
154 placement. Several potential reasons can be put forward to explain this difference. First,  
155 Flecknell et al studied a population of laboratory beagles who were likely used to the  
156 surroundings and investigators carrying out the study. This study included dogs of different  
157 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

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

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

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

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

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

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

216

217

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251 hospitalized cats. *J Feline Med Surg* 8, 141-144.

252

253

254

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  
 258

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

259

260

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	EMLA	Placebo	Placebo	
		60 <sup>a</sup>	30 <sup>b</sup>	60 <sup>b</sup>	30 <sup>a,b</sup>	
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 <sup>(a or b)</sup> are significantly different.