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Decrease in behaviors associated with pain during catheter placement using a topical anesthetic formulation in cats.☆

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ABSTRACT

In veterinary practice, peripheral catheter placement is very common. For some cats, this procedure can be painful and stressful. This study aimed to determine the effect of a topical anesthetic cream on pain reaction related to cephalic catheter placement in healthy, awake cats. 20 healthy cats, enrolled for ovariohysterectomy, were randomized to either a lidocaine 2.5%-prilocaine 2.5% cream or placebo cream group. In each group, the cream was applied for 30 minutes on a previously shaved skin overlying the cephalic vein and venipuncture was carried out using a 22-gauge catheter. The Cat Stress Score system was applied before venipuncture to ensure that the reaction observed was not associated with cat stress level. The behaviors associated with pain during venipuncture were also evaluated. All cats tolerated the application of the cream well. Cat Stress Score before venipuncture ranged from fully relaxed to very tense in both groups and no correlation was found between the behaviors associated with pain during venipuncture and cat stress level. 30 minutes of application time was effective in providing local anesthesia, with cats in the treatment group showing significantly fewer behaviors associated with pain than cats in the placebo group. The use of a topical anesthetic cream before peripheral catheter placement in non-emergency cases is feasible.

Introduction

Reducing patient stress is essential to achieve appropriate diagnosis and treatment, and encourage pet owners to visit veterinary clinics (Volk et al., 2011). Invasive procedures such as catheter placement are routinely carried out in veterinary hospitals, and cat behavior during this procedure is variable (Ashby, 2017). Sedation of the cat previous to venipuncture can be done, but not all patients are eligible for sedation (Lamont, 2008). Catheter placement can be painful and stressful, and the use of a topical anesthetic cream is recommended by the Feline-Friendly Nursing Care Guidelines (Carney et al., 2012). In human medicine, eutectic mixture of local anesthetics (EMLA), as the combination of lidocaine 2.5% and prilocaine 2.5% cream, has been proven to decrease pain associated with catheter placement in children (Chang et al., 1994; Hopkins et al., 2007). In cats, EMLA has also been evaluated for venipuncture and placement of jugular catheters in conscious cats (Flecknell et al., 1990; Wagner et al., 2006) and cephalic catheters placement in sedated cats (Oliveira et al., 2019). EMLA is not currently commercially available for veterinary purposes in Chile, but similar lidocaine 2.5%-prilocaine 2.5% cream formulation can be prepared in pharmacies which could help to achieve less painful experiences in feline patients. Also, most studies have used EMLA for 60 minutes before intravenous catheter application, which is impractical for clinical and hospital contexts. Thus, determining the shortest time of application may increase the use of topical anesthetic be-

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Table 1
Scores of behaviors associated with pain during venipuncture in the treatment and placebo groups.

Score	Group	
	Treatment (n,%)	Placebo (n, %)
0 = no reaction	8.0+/-0.0 (80%)	2.0+/-0.0 (20%)
1 = a slight movement of a limb, tensing of muscles	2.0+/-0.0 (20%)	4.0+/-0.0 (40%)
2 = limb withdrawal, attempt to move away	0.0+/-0.0 (0%)	2.0+/-0.0 (20%)
3 = marked attempts to escape, aggressive behavior, vocalization	0.0+/-0.0 (0%)	2.0+/-0.0 (20%)
Score mean+/-SD	0.2+/-0.4[a]	1.4+/-1.0[b]

[a] and [b] represent statistical differences of $P < 0.001$.

fore painful procedures. This study determined the effect of the application of a lidocaine 2.5%-prilocaine 2.5% cream formulation for 30 minutes before catheterization on behaviors associated with pain during cephalic catheter placement in healthy conscious cats.

Materials and methods

A prospective, randomized, blind, placebo-controlled, clinical trial was designed following the recommendation of PREPARE guideline (Smith et al., 2018). The study was carried out at the Small Animal Veterinary Medicine Teaching Hospital of Universidad de Las Americas, Santiago, Chile. 20 clinically healthy female cats enrolled for ovariohysterectomy (ranging from 6 months to 2 years old) were used. Informed consent of the owners was obtained before enrollment. A lidocaine 2.5%-prilocaine 2.5% cream and a placebo cream (containing only the excipients) were prepared in a local pharmacy subjected to national standards and regulations[1]. Cats were randomly assigned to either a lidocaine 2.5%-prilocaine 2.5% cream group (Treatment) or placebo cream group (Placebo). Once inside the hospital, and in absence of the owner, The Cat Stress Score (CSS) consisting of seven categories (ranging from fully relaxed to terrified) and described previously by (Kessler and Turner 1997) was used by 3 members of the research team to evaluate whether stress levels before venipuncture were related to the behavior associated with pain during catheter placement. 1 gram (ca. 1 g) of cream was applied on shaved skin (50 mm x 20 mm, 1000 mm^2) overlying the cephalic vein (1g/10 cm^2 surface area) using gloves. The application area was covered using an occlusive dressing (plastic film held by an elastic bandage) for 30 minutes. Then, the dressing was removed, and the remaining cream was wiped using a 70% isopropyl alcohol solution and clean paper towel. Venipuncture was carried out using a 22-gauge catheter and catheters were secured using conventional dressing techniques. All catheters were placed by one experienced veterinary surgeon and cats were covered and carefully handled using a towel by one member of the research team. Sedation was not used before or during catheter placement.

Behaviors associated with pain during venipuncture were evaluated by three observers: 1) the veterinary surgeon placing the catheter, 2) one person holding the cat, and 3) an additional observer, using a previously described scoring system (Flecknell et al., 1990), which can be seen in (Table 1). Each observer recorded the score independently and inter-observer differences were evaluated post-hoc. Additionally, videos were recorded during the procedure for each cat using a mobile phone for behavioral analysis, if necessary. Any clinically relevant change in the skin at the site of application was evaluated and recorded immediately after cream removal and classified as erythema, swelling, blanching or pruritus. Any sign of toxicity of treatment such as vomiting, diarrhea, tremors, cyanosis, dyspnea or tachycardia were continually assessed visually for 8 h following cream application. All veterinary surgeons and staff participating were blinded for the experimental groups. Descriptive statistics (mean and standard deviations) were carried out for all results of CSS and pain behaviors. Statistical differences between the CSS and behaviors associated with pain during venipuncture in experimental groups were assessed using the Kruskal-Wallis test and correlations were explored using the Spearman test. Kruskal-Wallis test was used to determine inter-observer differences. Data were analyzed with R software (R Development Core Team, 2014) and a p value <0.05 was considered to be statistically significant.

[1] The cream is commercially available in most countries but not in Chile, thus the need for special preparation in this study.

Table 2
Cat stress score in the treatment and placebo groups previous to venipuncture.

Score	Group	
	Treatment (n,%)	Placebo (n, %)
1 = fully relaxed	0.6+/-1.1 (7%)	1.0+/-0.0 (10%)
2 = weakley relaxed	3.0+/-1.7 (30%)	3.0+/-1.7 (30%)
3 = weakly tense	3.0+/-1.7 (30%)	3.6+/-2.3 (36%)
4 = very tense	2.6+/-0.5 (26%)	1.6+/-1.1 (17%)
5 = fearful, stiff	0.6+/-0.5 (7%)	0.6+/-0.5 (7%)
6 = very fearful	0.0+/-0.0 (0%)	0.0+/-0.0 (0%)
7 = terrified	0.0+/-0.0 (0%)	0.0+/-0.0 (0%)
Score mean+/- SD	2.9+/-1.0	2.8+/-1.0

Results

The group treated with lidocaine 2.5%-prilocaine 2.5% cream formulation showed significantly fewer behaviors associated with pain to cephalic catheter placement than the placebo group (0.2 vs. 1.4, $X^2 = 24.1$, $P < 0.001$, Table 1). 80 per cent of cats in the treatment group showed no reaction (score 0) and the remaining 20% showed only a mild reaction (score 1) with a slight movement of the limb and/or tensing of muscles. In the placebo group, 80% of cats had a score different from 0, including vocalization and marked attempts to escape. Cats of both groups scored between fully relaxed to very tense before venipuncture in CSS and no statistical differences were found ($X^2 = 0.37$, $P = 0.53$, Table 2). In the treatment group, only 25% of cats that showed no reaction to catheter placement were fully relaxed before venipuncture. Very tense cats in the placebo group had pain reaction score 0, 1 or 2 during catheter placement, whereas very tense cats in the treatment group had a score 0. No correlation was detected between CSS and behaviors associated with pain ($S = 34444$, $P = 0.74$). Inter-observer variation was not detected for CSS ($X^2 = 1.05$, $P = 0.59$) and behaviors associated to pain during venipuncture ($X^2 = 0.0$, $P = 1$). No video was used for behavioral analysis.

All cats tolerated the application of the cream and occlusive dressing well with no secondary skin or clinical signs of toxicity.

Discussion

In this study, there was an effective improvement in scores of behaviors associated with pain using a lidocaine 2.5%-prilocaine 2.5% cream formulation for 30 minutes before catheter placement. This result is in contrast to those obtained by (van Oostrom and Knowles 2018) who did not find differences in pain behaviors using an EMLA preparation for 30 minutes before catheterization in dogs. This might be explained by skin thickness differences between species. Dogs have much thicker skin than cats (0.5 to 5.0 mm in dogs vs. 0.4 to 2.0 mm in cats, as described by (Affolter and Moore 1994) which suggests that a shorter time (30 minutes) is needed in cats to have the desired effect. This is further supported by a study performed in children (skin thickness 1.58 mm) using EMLA that reached analgesia at 30 minutes (Hopkins et al., 2007). Previous studies in cats (Gibbon et al., 2003; Wagner et al., 2006) have shown similar results but only when applying EMLA for 60 minutes instead of 30 minutes as in our study. In a recent study in cats treated with EMLA, no pain reaction was observed after 20 min of application (Oliveira et al., 2019) but all cats were sedated before venipuncture and a 24-gauge catheter was used, while we used a 22-gauge which might have affected pain behaviors scores.

Most cats in the treatment group showed no reaction to venipuncture but 25% of cats showed tensing of muscle and slight movement of the limb. This result is similar to those reported by Flecknell et al. (1990) where cats treated with EMLA showed a significantly lower reaction to venipuncture, and reaction scores were 0 and 1. Also, (Wagner et al., 2006) found lower levels of struggling, but not lower levels of aggression or vocalization, using EMLA before jugular catheter placement.

Stress level determined by CSS did not affect the behaviors related to pain by venipuncture, similar to a previous study (Kessler and Turner, 1997). For example very tense cats in the treatment group showed no reaction while very tense cats in the placebo group showed tensing of muscles, a slight movement of the limb, limb withdrawal or attempt to move away. Two cats in placebo group showed no reaction to venipuncture what could be due to freeze response that cats can display when facing a threat. These results suggest that the CSS is not a good predictor of how cats will behave during venipuncture, independently of any previous treatment to calm them.

Finally, no secondary skin signs of lesions were observed which is similar to previous studies using EMLA (Flecknell et al., 1990; Wagner et al., 2006). Although lidocaine/prilocaine and methemoglobin serum concentrations were not evaluated, no clinical systemic adverse signs were observed (vomiting, diarrhea, tremors, cyanosis, dyspnea or tachycardia) within 8 hours after the cream was applied, which is in agreement with previous studies (Gibbon et al., 2003; Wagner et al., 2006). Altogether, these results suggest that the application of lidocaine 2.5%-prilocaine 2.5% as skin ointments are safe at the doses used in this study and reported in others.

Conclusions

The behavioral pain response related to intravenous catheterization can be decreased by the application of a lidocaine 2.5%-prilocaine 2.5% cream formulation 30 minutes before venipuncture and these are not influenced by previous cat stress level. Adding this procedure during peripheral catheter placement in non-emergency cases seems to be safe and could contribute to cat-friendly care while improving welfare in feline patients. Further studies may focus on shorter or different application times and investigation of other topical local anesthetics.

Ethical approval

This work involved the use of owned non-experimental animals in addition to internationally recognized high standards ('best practice') of veterinary clinical care for the individual patient and PREPARE guidelines. The study was approved by the Ethical Committee of Universidad de Las Americas (number CEC_PI_2019044).

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Conflict of Interest

The authors declare no conflict of interest.

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