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SHORT REPORT

Inefficacy of Dilute Epinephrine in Preventing Feline Scrotal Hematomas: Results From a Randomized Control Trial

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Abstract

***Introduction*:** The authors previously investigated the use of epinephrine at 1:400,000 dilution to prevent scrotal hematoma but found no significant reduction in hematomas. We hypothesized that higher concentrations of epinephrine would reduce the incidence of hematomas.
***Methods*:** Male cats trapped for Midwestern University College of Veterinary Medicine's Trap-Neuter-Return program were assigned to one of three treatment groups in this randomized control trial: LRS control (A), 1:40,000 epinephrine (B), or 1:120,000 epinephrine (C). Each patient received 0.2 mL of treatment as a topical wash within the scrotum. Veterinarians blinded to the treatment group assessed for the presence and severity of hematoma at three stages.
***Results*:** 398 cats were enrolled into groups A (n = 136), B (n = 133), and C (n = 129). Number of hematomas occurring in each group were 15 (11%, 95% confidence interval [CI]: 6–18%), 12 (9%, 95% CI: 5–15%), and 8 (6%, 95% CI: 3–12%), respectively. There was no difference in the incidence of scrotal hematoma (P = 0.397) or scrotal hematoma requiring treatment (P = 1.0). Weight was the only variable associated with the risk of hematoma (odds ratio [OR]: 7.3; 95% CI: 3.9–13.9; P < 0.0001).
***Conclusion*:** Despite its vasoconstrictive effects, dilute epinephrine as a topical wash was not effective in preventing feline scrotal hematomas.

Keywords: *feline medicine*; *TNR*; *trap-neuter-return*; *scrotal hematoma*; *epinephrine*; *community cats*; *preventative medicine*

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Scrotal hematomas are the most common postsurgical complication in the immediate postoperative period for cats in veterinary general practice[1] and are particularly problematic in high quality, high volume spay-neuter settings because of the potential to disrupt clinic operations.[2] Ice packs and manual mechanical pressure are effective treatments, but inconvenient and time consuming.[2] Epinephrine induces vasoconstriction, but is not commonly utilized for hemostasis because of concerns regarding tissue necrosis.[3–7] Although tissue necrosis is documented at 1:10,000 dilution of epinephrine, this effect is not supported in systematic reviews on the use of epinephrine for hemostasis.[8–10] This study follows up on previous work from our group that suggested dilute epinephrine (1:400,000) reduced the incidence of scrotal hematoma by extending the range of concentrations evaluated up to 1:40,000.[2]

Methods

Intact male free-roaming cats, excluding cryptorchids, presented for neuter at Midwestern University College of Veterinary Medicine's Trap Neuter Return (TNR) events were enrolled between June 2022 to April 2023. Patients were assigned through block randomization (via randomization.com) to one of the three experimental conditions: lactated Ringer's solution (LRS, control), 1:40,000 epinephrine (high dose) in LRS, or 1:120,000 epinephrine (low dose) in LRS. Visually identical solutions, labeled A, B, and C, were prepared by one author (J.W.N.). All others involved in the trial, including faculty and adjunct veterinarians supervising at TNR events, were blinded to the experimental condition, and treatments were distributed to student surgeons for administration. Experimental conditions were unblinded following data analysis.

Age was estimated based on dentition, and surgery time was defined as from the time of the first incision to autoligation of the last testicle. Student surgeons performed castration as previously described[11] and infused 0.10 mL of the assigned wash to each scrotal sac after the removal of the testicle, for a total of 0.20 mL, using a 1 cc tuberculin syringe without attached needle. Surgery duration

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and order of testicle removal were recorded. Veterinarians evaluated the cats for the presence of hematomas at three distinct stages: immediate (on the table following castration), return to trap, and immediately prior to discharge. Scrotal hematoma was defined as frank blood issuing from either incision, frank blood on the newspaper lining the traps, and/or noticeable swelling or bruising of the perineum. Scrotal hematoma requiring treatment was defined as scrotal hematoma that had evidence of ongoing bleeding.

Age, weight, and surgery duration were assessed with Kruskal-Wallis tests to ensure groups were not different at baseline. Normality was determined using tests of skewness and kurtosis. Fisher's exact tests were used to determine differences in hematoma rates across groups, the stages at which they occurred, and whether they required treatment. Logistic regression clustered on day was used to assess relationships between treatment, age, weight (as binary variable of less than 3 kg or greater or equal to 3 kg), surgery duration, student year, initial testicle removed (left or right), and hematoma occurrence. Models were validated using deviance goodness-of-fit. Two-sided tests of proportion were used to compare proportions. Significance was set at $P < 0.05$. Statistical analyses were performed using Stata (Version 18). The sample size for the two-sided tests of proportion was determined using the proportion of hematomas in the control group of the original study, 0.16, as the first proportion and 0.04 (a reduction of 75%) as the second. Using an alpha 0.05 and power of 0.9 resulted in 130 cats required per arm.

Results

Over 14 clinics, 398 cats were enrolled, with 136 controls, 133 high doses, and 129 low doses. One cat was excluded from low dose for being cryptorchid, and three cats were mistakenly enrolled in control rather than low dose. Median age was 18 months (interquartile range [IQR]: 4–36), median weight was 2.9 kg (IQR: 1.8–4.0), median surgery duration was 5 min (IQR: 3–8), with no differences between groups ($P = 0.130$, $P = 0.089$, and $P = 0.854$, respectively) (Table 1). Students performed most surgeries (356/396, 90%), with veterinarians performing the remainder. Surgeon year was unidentifiable for two patients.

A total of 35 scrotal hematomas occurred for an overall rate of 9% (95% CI: 6–12%): 15 in control (12%, 95% CI: 6–17%), 12 in high-dose (9%, 95% CI: 5–15%), and eight in low-dose (6%, 95% CI: 3–12%) conditions. No differences were apparent in the occurrence of hematomas ($P = 0.397$) or hematomas requiring treatment ($P = 1.0$) between experimental conditions. Six (17%) of the 35 scrotal hematomas required treatment: three in the control group, two in high dose epinephrine group, and one in low-dose epinephrine group. All treatments consisted of placing a clip to provide pressure, except one that involved suture ligation of the subcutaneous tissue. Five (14%) hematomas were diagnosed on the surgical table (95% CI: 5–33%), 18 in recovery (51%; 95% CI: 30–81%), and 12 (34%; 95% CI: 18–60%) at discharge. There were no differences in the stages at which hematomas occurred ($P = 0.315$). Of the 25 hematomas with side recorded, 9 (36%) were left, 12 (48%) were right, and 4 (16%) were bilateral, with no difference between left and right ($P = 0.364$). Starting side was not associated with hematoma side ($P = 0.412$).

In univariable logistic regression, only weight (OR: 7.3; 95% CI: 3.9–13.9; $P < 0.0001$) and age (OR: 1.03; 95% CI: 1.02–1.04; $P < 0.0001$) were significantly associated with hematoma. Students were not more likely to induce hematoma than veterinarians ($P = 0.655$). Only age and weight were candidates for a multivariable model, and age was not significant when combined with weight ($P = 0.079$). The median epinephrine dose for all cats was 1.2 mcg/kg, with 1.7 mcg/kg for the high-dose group and 0.6 mcg/kg for the low-dose group. There was no difference in hematoma risk by dose of epinephrine after controlling for weight ($P = 0.785$).

Discussion

Neither concentration of epinephrine was more effective in preventing scrotal hematomas than the LRS control, and therefore we do not recommend using dilute epinephrine as a preventative due to its lack of efficacy. The LRS control represents an improvement over the "no treatment" control used previously,[2] as blood-tinged leakage from the scrotum of epinephrine-treated cats could be misinterpreted as a hematoma and biasing towards the null. The overall hematoma rate of 9% (95% CI: 6–12%) reported here is congruent with that of 13% (95% CI: 9–18%) reported previously. The positive association between patient weight and hematoma risk is congruent to prior report although the odds ratios cannot be compared directly.[2] Age was not significant in a multivariable model with weight, which may be due to age being only an estimate and, in cats, collinear with weight.

Table 1. Descriptive statistics of patients across treatment groups (significance set at $P < 0.05$)

Wash group (Epinephrine concentration)	A (LRS control)	B (1:40,000)	C (1:120,000)	*P*
Median age (months)	24 (IQR: 5–36)	12 (IQR: 4–36)	12 (IQR: 4–24)	0.130
Median weight (kgs)	3.2 (IQR: 2.0–4.1)	2.9 (IQR: 1.8–3.9)	2.6 (IQR: 1.6–3.9)	0.089
Median surgery duration (min)	5 (IQR: 3–7)	5 (IQR: 3–8)	6 (IQR: 4–8)	0.854

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The lack of difference between students and veterinarians is congruent with prior literature.[12] While the hematoma rate on the surgery table was lower in this study (14% compared to 33%), the CIs largely overlapped (5–33% compared to 17–58%). Unlike the previous study, surgical duration was not associated with risk of hematomas requiring treatment. Hematoma occurrence did not differ between starting sides, and hematoma side was not associated with the starting side. Precise locations of hemorrhage (subcutaneous vessels, damage to either the testicular artery or vein proximal to the knot, or loss of the knot) were not determined. In the author's experience, lost knots result in abdominal rather than scrotal bleeding, and the measures that are successfully employed to control scrotal hematoma, ice packs and pressure, suggest that the source of bleeding for this population is likely to be subcutaneous. The sample size was calculated using values from a previous study that also enrolled cats of all weights,[2] but the percent of cats greater than 3 kg in this study (48%) was less than the prior study (71%), which may have resulted in this study being underpowered. Instead of 130 cats per arm, 178 cats would have been required to prove a decrease of 75% using the proportion of scrotal hematoma for this study's control group. For greater efficiency, future studies of feline scrotal hematoma may wish to limit enrollment to cats over 3 kg due to the low risk of scrotal hematoma below that weight.

Conclusion

Epinephrine washes of concentrations equal or less than 1:40,000 are ineffective for preventing scrotal hematoma. However, because cats 3 kg and heavier were found to be more prone to developing hematoma, they should be monitored more closely during recovery in TNR and HQHVSN settings.

Authors' contributions

Emma Vitello: conceptualization, data analysis, writing; Sara Sheffer: conceptualization, data collection, writing; Jeffery Norris: conceptualization, data analysis, treatment formulation, writing; Rachael Kreisler: conceptualization, data analysis, writing

Conflict of interest and funding

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