Intracanalicular injection of *N*-acetylcysteine as adjunctive treatment for sialoceles in dogs: 25 cases (2000–2017)

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OBJECTIVE

To describe intracanalicular injection of 10% *N*-acetylcysteine (IINAC) as adjunctive treatment for sialoceles in dogs.

ANIMALS

25 client-owned dogs.

PROCEDURES

Hard copy medical records at 2 veterinary ophthalmology practices were searched to identify dogs that underwent IINAC for treatment of sialoceles from January 2000 to December 2017. Signalment, affected salivary gland, clinical signs, duration of signs, other treatments administered, diagnostic tests performed, anesthetic approach, *N*-acetylcysteine volume administered, complications, follow-up time, and recurrence of sialoceles were recorded. Descriptive statistics were reported.

RESULTS

Boxers and mixed-breed dogs were most commonly represented. Subjectively decreased globe retropulsion and conjunctival or periorbital swelling (23/25 [92%] dogs each) were the most common clinical signs, with no vision deficits in any patient. The zygomatic gland was mainly affected (23/25 [92%] dogs), followed by parotid and mandibular glands (1 [4%] dog each). The condition was unilateral in 22 (88%) dogs. Ultrasonography (19/25 [76%] dogs), MRI (14 [56%]), fine-needle aspiration (20 [80%]), and biopsy (4 [16%]) were performed; however, the condition was deemed idiopathic in 22 (88%) dogs. Most IINACs were performed with local anesthesia (median volume, 5 mL/gland; range, 1.5 to 9 mL). No complications were identified. Other treatments included antimicrobials and anti-inflammatories. Mean follow-up time was 18.8 months. All recurrences (5/23 [22%] dogs) were controlled with medical management.

CONCLUSIONS AND CLINICAL RELEVANCE

Results suggested noninvasive IINAC may be a useful adjunctive treatment for sialoceles in dogs. The procedure was easily and safely performed with local anesthesia (or general anesthesia with concurrent diagnostic imaging) in these dogs. (*J Am Vet Med Assoc* 2020;257:826–832)

Disorders of the salivary glands are considered rare in dogs and cats, with a reported overall incidence of < 0.3%.[1] In dogs, recognized diseases affecting the major salivary glands (parotid, mandibular, sublingual, and zygomatic) include neoplasia, sialocele, sialadenitis, sialadenosis, and sialolithiasis.[2] Sialocele, also known as salivary mucocele, is the most common condition of the salivary glands in dogs, most often involving the sublingual gland. The condition consists of collections of saliva within subcutaneous tissue lined by inflammatory connective tissue, and these saliva-filled cavities are not considered true cysts because they do not have a secretory lining. The accumulation of saliva results from disruption of a salivary gland or its duct.

ABBREVIATIONS

IINAC	Intracanalicular injection of 10% *N*-acetylcysteine
NAC	*N*-acetylcysteine

The etiopathogenesis of sialocele formation in dogs is often unclear,[1,3–6] although sialadenitis,[7–9] sialolithiasis,[10] foreign body,[11] trauma,[12,13] dirofilariasis,[14] and neoplasia[9] have been listed as possible causes. In addition, sialocele development has been described as a postoperative complication[15–19] or in combination with a segmental maxillary malformation.[20]

Depending on the salivary gland affected, sialoceles are classified as cervical, pharyngeal, sublingual, or zygomatic, with an affected zygomatic gland being the most likely to induce ocular signs.[2] Sialoceles are often painless swellings that have a relatively rapid onset and fluctuate in size. The presence and type of clinical signs can vary, depending on the location of the affected gland. In cervical sialoceles, the collection of retained saliva is in the upper neck region, under the jaw, or in the intermandibular region, but rarely causes respiratory distress. Conversely, the fluid in pharyngeal sialoceles accumulates almost entirely in the pharynx,

creating a high risk of airway obstruction. A sublingual sialocele, also known as a ranula, involves saliva accumulation in tissues at the base of the mouth along the tongue, causing dysphagia or respiratory distress in severe cases. Clinical signs observed in dogs with zygomatic sialoceles can mimic the signs of retrobulbar disease owing to the location of the gland along the ventrolateral aspect of the orbit. Clinically, an early zygomatic sialocele causes a painless soft tissue swelling ventral to the globe, which is usually well tolerated and might go unnoticed. In more chronic stages, a sialocele in this location can induce exophthalmos, protrusion of the nictitating membrane, and signs of pain on either opening the mouth or palpation of the orbital region.

Historically, sialoceles in veterinary patients have been successfully managed by surgical excision of the lesion and associated gland (sialadenectomy), marsupialization, and ductal ligation.[2] More recently, adjunctive treatments with radiation therapy[17,21] or ultrasound-guided injections of sclerosing agents[5] have also been described. However, most of these procedures involve partial or complete gland removal or progressive gland atrophy, potentially leading to persistent xerostomia. Thus, new treatments aiming to preserve the integrity and functionality of the salivary tissue should be considered for sialoceles.

N-acetylcysteine, a cysteine prodrug and glutathione precursor, has been used mainly as a mucolytic and antioxidant agent.[22] Thus, the expected effect when locally applied to a sialocele would be disruption of thick salivary secretions, generally by altering the degree of cross-linking or the interactions between molecules, which could contribute to sialocele resolution in combination with anti-inflammatory and antimicrobial treatment. Although the use of NAC for the treatment of zygomatic sialoceles in dogs has been reported sporadically in international veterinary ophthalmology meetings,[a,b] to the authors' knowledge, no retrospective or prospective studies have been published on its efficacy for the treatment of this condition in dogs. Therefore, the purpose of the retrospective study reported here was to determine the clinical outcomes of dogs that underwent intracanalicular injection of NAC as adjunctive treatment for sialoceles.

Materials and Methods

Case selection criteria

Hard copy medical records were searched to identify dogs that underwent an intracanalicular injection of a salivary gland duct with NAC (ie, IINAC) for the treatment of sialoceles at the Veterinary Teaching Hospital of the Autonomous University of Barcelona and the Animal Eye Practice of Berlin from January 1, 2000, to December 31, 2017. All dogs that underwent the procedure during this period and had complete records related to NAC treatment (gland or glands affected, amount of NAC administered, concurrent treatments, and response to treatment) were eligible for study inclusion.

Medical records review

Data collected from each record included breed, age (in years), sex, affected salivary gland, proposed cause of the sialocele, clinical signs, duration of signs (in days), treatments prior to referral (if applicable), diagnostic techniques, volume of NAC injected (absolute volume and volume on a per–body weight basis), number of IINACs, need for sedation or general anesthesia, complications after IINAC, administration of other topical and systemic treatments, follow-up time (in days), outcome, and treatments for sialocele recurrence.

Procedures

All dogs underwent a complete bilateral ophthalmic examination by a veterinary ophthalmologist (certified by the European College of Veterinary Ophthalmologists as a specialist in veterinary ophthalmology) or a veterinary ophthalmology resident-in-training, including examination from a distance, neuro-ophthalmic evaluation (menace response, dazzle reflex, and pupillary light reflex), Schirmer tear test 1, periorbital palpation and globe retropulsion, slit-lamp biomicroscopy, rebound or applanation tonometry, indirect ophthalmoscopy, and application of fluorescein to the ocular surface.

For all dogs, the major papilla of the affected salivary gland was identified in the oral mucosa for cannulation and retrograde IINAC. The zygomatic gland papilla was located at the caudal aspect of the last maxillary molar tooth, about 1 cm caudal to the parotid gland papilla, which was at the level of the maxillary fourth premolar tooth **(Figure 1)**; the man-

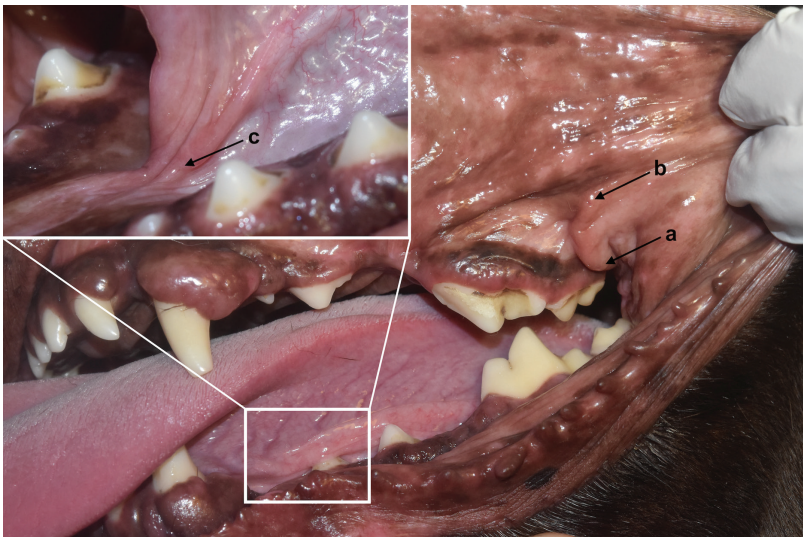

Figure 1—Photographs depicting the anatomic locations of papillae for the left zygomatic (a), parotid (b), and mandibular (inset; c) salivary glands in a 6-year-old spayed female Beagle.

dibular salivary papilla was identified at the sublingual caruncle lateral to the lingual frenulum, and the sublingual papilla was located just caudal to the mandibular duct.[23] After identifying the papilla of the affected gland, the adjacent oral mucosa was routinely disinfected with povidone-iodine solution[c,d] diluted in 1:50 sterile saline (0.9% NaCl) solution. Patients were gently physically restrained in lateral recumbency, and a topical anesthetic (0.5% proxymetacaine hydrochloride solution)[e] was applied with a soaked cotton tip applicator that was rolled over the area of the oral papilla with gentle pressure for 60 to 90 seconds. A single intracanalicular injection of commercially available injectable 10% NAC solution[f,g] was applied directly by retrograde infusion through the papilla of the affected gland via a 22- or 25-gauge lacrimal cannula or IV catheter. The NAC was slowly injected after the catheter was gently inserted into the papilla. Owing to a lack of published data about the NAC volume to apply, a continuous application was delivered in a retrograde manner until reflux from the duct was observed at the papilla **(Figure 2)**. All IINACs were performed by a veterinary ophthalmologist or resident-in-training. The IINAC was completed with the patient under sedation or general anesthesia only if the dog was deemed aggressive or difficult to handle or when diagnostic imaging techniques that required sedation or anesthesia were used.

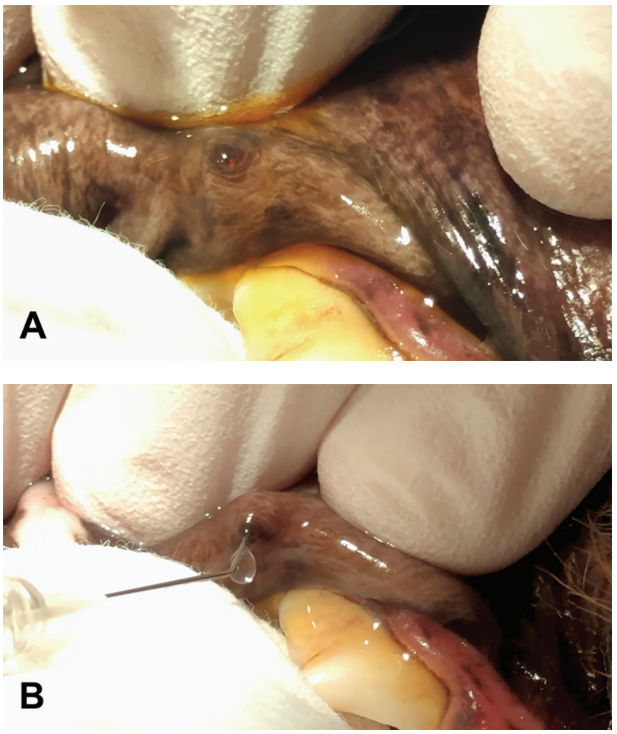

Figure 2—Photographs obtained during IINAC for a 1-year-old male Beagle with a right zygomatic salivary gland sialocele that was deemed idiopathic. A—Location of the major papilla at the caudal aspect of the last right maxillary molar tooth. B—The NAC was slowly infused through a 22-gauge lacrimal cannula until mild reflux was observed.

All patients were discharged from the hospital with orally administered anti-inflammatory drugs (either NSAIDs or corticosteroids), antimicrobials, or both at the clinician's discretion. For patients with concurrent ocular disease, topical antimicrobials, anti-inflammatory medications, cycloplegic agents, artificial tears, and ocular hypotensive drugs were also prescribed as deemed necessary by the clinician responsible for the case.

Outcome was assessed at the last follow-up visit and classified as successful when sialocele signs were not observed after the topical or orally administered treatments were discontinued. Recurrence of sialoceles, the number of recurrences, and the type of treatment used for patients with recurrence were recorded if applicable.

Statistical analysis

Descriptive statistics were calculated with a commercial software package.[h] Quantitative variables were reported as mean ± SD or as median and range for normally or nonnormally distributed data, respectively (as assessed by the Kolmogorov-Smirnov test). Qualitative or categorical variables were summarized as the number and percentage of affected dogs.

Results

Twenty-five dogs met the inclusion criteria; 14 (56%) dogs were males (2 neutered) and 11 (44%) were females (5 spayed). The mean ± SD age of the dogs was 7.1 ± 3.8 years and mean ± SD body weight was 20.6 ± 10.8 kg (45.3 ± 23.8 lb) at the time of IINAC. In addition to mixed-breed dogs, 16 breeds were represented. Boxers and mixed-breed dogs were most commonly represented (3/25 [12%] each).

The most common clinical findings were summarized **(Table 1)**. No vision deficits were detected

Table 1—Common clinical findings at presentation for 25 dogs that underwent treatment for sialoceles, including IINAC, between January 1, 2000, and December 31, 2017.

Clinical finding	No. (%) of dogs
Subjectively decreased globe retropulsion	23 (92%)
Conjunctival or periorbital swelling (or both)	23 (92%)
Protrusion of oral mucosa caudal to the last maxillary molar tooth	21 (84%)
Signs of pain on opening the mouth	18 (72%)
Exophthalmia	18 (72%)
Protrusion of a mass beneath the conjunctiva in the inferior temporal or nasal conjunctival fornix	18 (72%)
Protrusion of the nictitating membrane	16 (64%)
Signs of pain on palpation over the globe	14 (56%)
Deviation of the visual axis (mainly exotropia)	6 (24%)
Folliculitis	2 (8%)
Prolapse of the nictitating membrane gland	1 (4%)
Eversion of the nictitating membrane cartilage	1 (4%)
Keratoconjunctivitis sicca	1 (4%)
Corneal fibrosis	1 (4%)
Enophthalmia	1 (4%)
Corneal ulceration	1 (4%)
Ocular hypertension (intraocular pressure ≥ 35 mm Hg)*	1 (4%)

*Measurement by rebound or applanation tonometry.

in any patient. The median duration of clinical signs prior to referral was 7 days (range, 0 to 304 days). Seven dogs had not received previous medical treatments. Seven dogs were being treated with systemic anti-inflammatory drugs and antimicrobials, and 2 dogs were receiving gastroprotectants (omeprazole). Three dogs were receiving topical NSAIDs, corticosteroids, and broad-spectrum antimicrobials alone or in combination for concurrent ocular diseases. Treatment information prior to referral was not available for 11 dogs. No dogs had shown clinical improvement with medical treatment prior to the referral. An exploratory orbitotomy had been performed twice in 1 dog without achieving a final diagnosis.

The zygomatic gland was the most commonly affected salivary gland (23/25 [92%] dogs; **Figure 3**), followed by parotid and mandibular glands (1 [4%] dog each). A unilateral sialocele was found in 22 (88%) dogs (right-sided in 13 and left-sided in 9). Ultrasonography (19 [76%] dogs) and MRI (14 [56%] dogs) were the most common imaging techniques used, whereas radiography and CT were performed less frequently (1 [4%] dog each). Fine-needle aspiration with or without ultrasound guidance was performed for 20 (80%) dogs, and incisional biopsy was performed for 4 (16%) dogs.

Despite the diagnostic protocols, sialoceles were considered idiopathic in 22 of 25 (88%) dogs. A cause was elucidated in 3 (12%) dogs: a 1-year-old female Weimaraner had a diagnosis of rhabdomyosarcoma involving the right zygomatic gland, a 2-year-old male Pug had sialadenitis of unknown origin in the right zygomatic gland, and a 10-year-old spayed female mixed-breed dog had bilateral zygomatic gland sialadenitis secondary to a dental procedure. Bacterial culture was performed for a sample from a 1-year-old neutered male mixed-breed dog with an idiopathic zygomatic gland sialocele, and *Corynebacterium* spp were isolated.

No complications attributable to IINAC were identified during or after the procedure in any patient, regardless of the volume used. The median absolute volume of NAC delivered was 5 mL/gland (range, 1.5 to 9 mL), and the median volume on a per–body weight basis was 0.2 mL/kg (0.09 mL/lb; range, 0.1 to 1.2 mL/kg [0.05 to 0.55 mL/lb]). Although most applications were completed with topical anesthesia for dogs under gentle physical restraint (16/25 [64%]), 9 (36%) dogs had IINAC performed during the sedation or general anesthesia that was induced for diagnostic imaging.

A modified lateral orbitotomy by zygomatic arch resection[24] was performed 1 week after IINAC in the dog with rhabdomyosarcoma. After IINAC, medical treatment was administered in all patients and consisted mainly of orally administered anti-inflammatory drugs, antimicrobials, and analgesics, alone or in combination **(Table 2)**. Dexamethasone sodium phosphate (n = 2), ketorolac tromethamine (2), gramicidin-neomycin-polymyxin B (10), heterologous serum (1), cyclopentolate hydrochloride (1), tobramycin-dexamethasone (2), tobramycin-diclofenac (1), dorzolamide-timolol (1), dexpanthenol (1), sodium hyaluronate (1), and carbomer (7) ophthalmic solutions were topically applied at a range of frequencies, depending on the nature and severity of concurrent ocular clinical signs.

Mean ± SD follow-up time from the initial visit to the last recheck examination was 18.8 ± 15.8 months (n = 23 dogs). One dog was lost to follow-up, and the dog with rhabdomyosarcoma was euthanized 2 weeks after surgery because of the severity of the or-

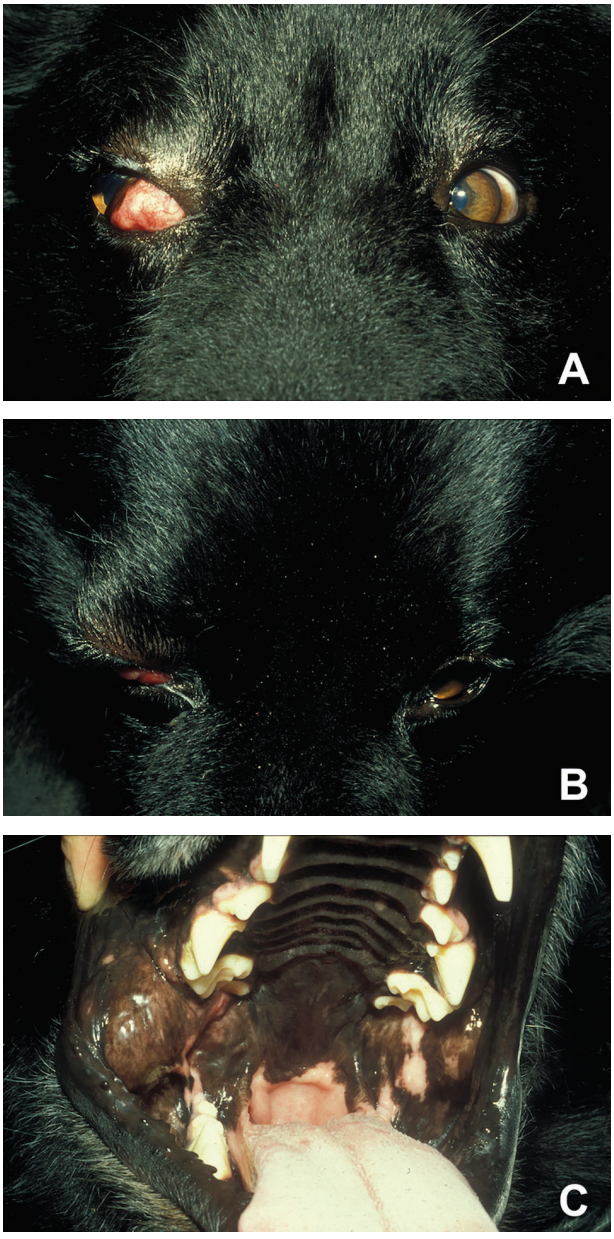

Figure 3—Photographs of a dog with a right-sided idiopathic zygomatic sialocele. A—The nictitating membrane of the right eye is protruding. B—Exophthalmia is evident. C—The oral mucosa caudal to the last right maxillary molar tooth is protruding.

Table 2—Orally administered treatments following IINAC for the 25 dogs in Table 1.

Drug	Dose (mg/kg)	Dosing interval (h)	Duration (d)	No. (%) of dogs
Carprofen	5	24	3–21	13 (52%)
Prednisone	0.5–1	12–24	10–27	7 (28%)
Robenacoxib	1	24	3–4	2 (8%)
Meloxicam	0.1	24	14	1 (4%)
Enrofloxacin	5	24	3–21	14 (56%)
Cephalexin	25	12	7–16	5 (20%)
Amoxicillin–clavulanic acid	12.5–20	12	10–32	5 (20%)
Tramadol hydrochloride	3	12	30	1 (4%)

To convert mg/kg to mg/lb, divide by 2.2.

bital disease. Grossly detectable sialoceles resolved in all 23 dogs; owing to the retrospective nature of the study and inconsistency in the timing of follow-up evaluations, time to resolution was not assessed. Sialoceles recurred prior to the last follow-up for 5 of 23 (22%) dogs with a mean ± SD time to recurrence of 3.7 ± 2.8 months; however, recurrences were successfully controlled with medical treatment in all patients (by administration of the same orally administered medications that were prescribed after IINAC but extended over longer periods). No additional IINAC infusions were performed in any patient. The median NAC volume per gland used in patients with and without recurrence was 5 mL (0.2 mL/kg; range, 0.2 to 0.5 mL/kg) and 5 mL (0.2 mL/kg; range, 0.1 to 1.2 mL/kg), respectively.

Discussion

In veterinary medicine, sialadenectomy has been historically considered the treatment of choice for sialoceles[2]; however, there is currently no consensus regarding the best treatment for this condition in dogs. To the authors' knowledge, reports on the clinical outcome of IINAC for the treatment of sialoceles in this species are scarce. Results of the retrospective study reported here supported that IINAC may be a useful adjunctive treatment for sialoceles that had not previously responded to orally administered medications.

Sialoceles are more frequently diagnosed in human beings than in dogs, and several nonsurgical treatment modalities are considered for treatment, depending on the salivary gland affected. Sclerotherapy with different substances such as fibrin glue, OK-432, and bleomycin[25]; pingyangmycin[26]; and absolute ethanol[27] had good outcomes in clinical cases refractory to medical treatment. Furthermore, systemic treatment with g-linolenic acid,[28] transdermal application of scopolamine,[29] and intralesional injection of corticosteroids[30] and botulinum toxins type A and B[31] have also been postulated as treatments for the management of sialoceles. Other techniques, including cryosurgery with liquid nitrogen,[32] treatment with various types of lasers (including neodymium:yttrium-aluminum-garnet [commonly termed Nd:YAG][33]; CO_2[34]; erbium[35]; diode[36]; erbium, chromium-doped yttrium, scandium, gallium, and garnet [described as Er,Cr:YSGG][36]; and potassium titanyl phosphate [also termed KTP][36]), and microwave ablation,[37] have been described for treatment of oral mucoceles. Although sialadenectomy is still the most frequently used surgical technique, several minimally invasive approaches such as percutaneous needle aspiration,[38] surgical creation of controlled internal fistulas,[39] placement of intraductal cannulas,[40] peroral drainage,[41] and micromarsupialization of the affected salivary gland[42] have recently been developed, mainly for parotid gland sialoceles, to avoid gland excision.

Surgical excision of the affected salivary gland and surrounding tissue is the most commonly recommended method to resolve this condition in dogs; however, alternative treatments have also been described. Intralesional injections of sclerosing agents such as polidocanol[5] have been successfully used for orbital mucocele treatment in this species. In addition, radiation therapy (total dose of 36 Gy in 9-Gy fractions) has been used to control a zygomatic sialocele observed as a postoperative complication following caudal hemimaxillectomy in a dog.[17] Unfortunately, the expected effect was insufficient, and sialadenectomy was necessary to excise the remaining functional salivary tissue.[17] However, authors of a more recent study[21] found that radiation with a minimum total dose of 16 or 20 Gy in 4-Gy fractions was useful for the treatment of recurrent cervical sialoceles refractory to surgical management in 11 dogs. Finally, various minor surgical interventions such as drainage by fine-needle aspiration (paracentesis), drainage caudal to the last ipsilateral maxillary molar tooth, and marsupialization have been reported in combination with supportive care and systemic anti-inflammatory treatments with variable results.[7,11,43,44]

N-acetylcysteine is an *N*-acetyl derivative of the endogenous amino acid L-cysteine, which is a direct precursor to glutathione synthesis; therefore, this is a known substitute for the deficiency of this enzyme. *N*-acetylcysteine also has anti-inflammatory and antioxidant properties, although its mechanisms of action are poorly understood.[22,45] In addition, for the past several decades, certain mucolytic activity has also been attributed to this agent, suggesting that disruption of the salivary gel can be expected when NAC is locally administered into the salivary duct. Injectable 10% to 20% NAC is commercially available

in Europe and as an FDA-approved human drug in the United States, so it can be used in dogs in an extralabel manner when appropriate conditions are met. In 2004, Allgoewer et al[a] described the successful resolution of 10 clinical cases of zygomatic gland adenitis with and without cystic inclusions in dogs through a combination of medical treatment and retrograde flushing of the zygomatic salivary duct with NAC. It was postulated that this procedure facilitated the excretion of the viscous saliva obstructing the duct and that systemic treatment with NSAIDs and broad-spectrum antimicrobials addressed the associated adenitis. Almost a decade later (in 2012), Delgado[b] described the resolution of a zygomatic gland sialocele in a dog by use of NAC in combination with drainage caudal to the ipsilateral last maxillary molar tooth. Consequently, both authors recommended flushing of an affected salivary gland duct with NAC to potentially avoid surgical excision of the sialocele and associated gland.

The volume of NAC applied in the study reported here was variable and did not necessarily correspond to dogs' body weight. In fact, the volumes used were higher than the amounts recommended for contrast medium in sialography of dogs (0.5 to 1 mL/10 kg [0.23 to 0.45 mL/10 lb] of body weight).[46] This variation could be associated with differences between the volume of apparently normal salivary glands versus those with sialoceles, but also with the anatomic site at which the obstruction or blockage was located, considering that obstructions closer to or within the gland would allow a greater volume to be delivered. Further work is warranted to determine whether there is an optimal range of NAC volumes depending on variables such as body weight and the type and severity of the sialocele. In the present study, in addition to the mucolytic action of NAC, canalicular dilation induced mechanically by the injection could have made excretion of viscous saliva easier. In fact, lavages with isotonic saline (0.9% NaCl) solution under hydrostatic pressure have been described to cause dilation of the duct, thus facilitating the removal of debris in human patients.[47] Owing to the retrospective nature of the study reported here and the lack of a control group, it was not possible to establish the role that dilation of the duct (vs the action of NAC) had in the resolution of clinical cases of sialocele, and this was likely attributable to a combined effect of both factors.

The recurrence rate found following the IINAC procedure in the present study was proportionally high (5/23 [22%]), compared with results reported for dogs following other treatments (2/50 [4%] to 2/14 [14.3%]),[44,48] but all relapses were successfully controlled with medical management, and no patients required additional IINAC. This fact could be explained by a combined effect of the IINAC with the described systemic medical treatments. In a recent study[21] of 11 dogs that had sialoceles treated by radiation therapy, a complete and partial response to treatment was reported for 6 and 5 dogs, respectively. Three dogs had progression of the disease, but it was controlled with additional doses of radiation. However, this procedure was performed for recurrent sialoceles refractory to surgical management, but not as a first therapeutic approach; therefore, caution should be taken when comparing the results with those in the present study. In the authors' opinion, IINAC could be advantageous over surgical excision or radiotherapy, as it is simple to perform, well tolerated by patients, and less invasive and has not been associated with complications.

Because the study reported here was retrospective, it lacked a control group managed exclusively with medical treatments or with a combination of medical treatment and flushing with saline solution. However, an appropriate control group would have been difficult to establish because sialadenectomy remains as the gold standard for the treatment of sialoceles in dogs, and medical therapy is mostly insufficient to resolve the condition. In addition, owing to the various clinical presentations, there was considerable variation in diagnostic and treatment approaches for each case, which limited our ability to draw direct comparisons between cases with regard to final diagnoses and treatment outcomes.

Our results supported that IINAC is a noninvasive and potentially effective adjunctive treatment for some sialoceles in dogs, and it can be easily performed with local anesthesia in cooperative dogs. This conservative medical management could have a role as a first therapeutic approach to sialoceles in this species, potentially reducing the need for surgical intervention. Prospective and randomized studies are recommended to understand the specific mode of action of NAC in the treatment of canine sialoceles as well as to better elucidate the safety, efficacy, and most appropriate volume range of IINAC for this purpose.

Acknowledgments

No third-party funding or support was received in connection with this study or the writing or publication of the manuscript. The authors declare that there were no conflicts of interest.

Presented in abstract form at the Annual Scientific Meeting of the European College of Veterinary Ophthalmologists, Florence, Italy, May 2018.

Footnotes

a. Allgoewer I, Jurina K, Stockhaus C. Canine zygomatic adenitis (abstr). *Vet Ophthalmol* 2004;7:E1.
b. Delgado E. Canine mucocele of the zygomatic gland (abstr). *Vet Ophthalmol* 2012;15:E9.
c. Betaisodona Lösung, Mundipharma GmbH, Limburg, Germany.
d. Braunol, B Braun VetCare SA, Barcelona, Spain.
e. Proparakain-POS, Ursapharm Arzneimittel GmbH, Saarbrücken, Germany.
f. NAC-ratiopharm 100 mg/mL injection Lsg, Ampullen, Ratiopharm GmbH, Ulm, Germany.
g. Flumil 100 mg/mL solución inyectable, Zambon Pharma SAU, Barcelona, Spain.
h. SPSS, version 22.0, IBM, Chicago, Ill.

References

1. Spangler WL, Culbertson MR. Salivary gland disease in dogs and cats: 245 cases (1985–1988). *J Am Vet Med Assoc* 1991;198:465–469.
2. Ritter MJ, Stanley BJ. Salivary glands. In: Tobias KM, Johnston SA, eds. *Veterinary surgery: small animal*. St Louis: Elsevier Saunders, 2012;1439–1447.
3. Bellenger CR, Simpson DJ. Canine sialocoeles—60 clinical cases. *J Small Anim Pract* 1992;33:376–380.
4. Atkins RM, Hecht S, Westermeyer HD, et al. What Is Your Diagnosis? A zygomatic salivary gland mucocele. *J Am Vet Med Assoc* 2010;237:1375–1376.
5. Stuckey JA, Miller WW, Almond GT. Use of a sclerosing agent (1% polidocanol) to treat an orbital mucocele in a dog. *Vet Ophthalmol* 2012;15:188–193.
6. McDonald JE, Knollinger AM, Dees DD. Ventral transpalpebral anterior orbitotomy: surgical description and report of 3 cases. *Vet Ophthalmol* 2016;19:81–89.
7. McGill S, Lester N, McLachlan A, et al. Concurrent sialocoele and necrotising sialadenitis in a dog. *J Small Anim Pract* 2009;50:151–156.
8. Cannon MS, Paglia D, Zwingenberger AL, et al. Clinical and diagnostic imaging findings in dogs with zygomatic sialadenitis: 11 cases (1990–2009). *J Am Vet Med Assoc* 2011;239:1211–1218.
9. Boland L, Gomes E, Payen G, et al. Zygomatic salivary gland diseases in the dog: three cases diagnosed by MRI. *J Am Anim Hosp Assoc* 2013;49:333–337.
10. Lee N, Choi M, Keh S, et al. Zygomatic sialolithiasis diagnosed with computed tomography in a dog. *J Vet Med Sci* 2014;76:1389–1391.
11. Philp HS, Rhodes M, Parry A, et al. Canine zygomatic salivary mucocoele following suspected oropharyngeal penetrating stick injury. *Vet Rec* 2012;171:402.
12. Knecht CD, Slusher R, Guibor EC. Zygomatic salivary cyst in a dog. *J Am Vet Med Assoc* 1969;155:625–626.
13. Schmidt GM, Betts CW. Zygomatic salivary mucoceles in the dog. *J Am Vet Med Assoc* 1978;172:940–942.
14. Henry CJ. Salivary mucocele associated with dirofilariasis in a dog. *J Am Vet Med Assoc* 1992;200:1965–1966.
15. Termote S. Parotid salivary duct mucocoele and sialolithiasis following parotid duct transposition. *J Small Anim Pract* 2003;44:21–23.
16. Guinan J, Willis AM, Cullen CL, et al. Postenucleation orbital sialocele in a dog associated with prior parotid duct transposition. *Vet Ophthalmol* 2007;10:386–389.
17. Clarke BS, L'Eplattenier HF. Zygomatic salivary mucocoele as a postoperative complication following caudal hemimaxillectomy in a dog. *J Small Anim Pract* 2010;51:495–498.
18. Adams P, Halfacree ZJ, Lamb CR, et al. Zygomatic salivary mucocoele in a Lhasa Apso following maxillary tooth extraction. *Vet Rec* 2011;168:458.
19. Young WM, Betbeze CM, Fisher SC, et al. Enucleation or exenteration in two dogs with previous parotid duct transposition: parotid duct ligation versus reverse parotid duct transposition. *Vet Ophthalmol* 2018;21:413–418.
20. Cirla A, Rondena M, Bertolini G, et al. Exophthalmos associated to orbital zygomatic mucocele and complex maxillary malformation in a puppy. *Open Vet J* 2017;7:229–234.
21. Poirier VJ, Mayer-Stankeová S, Buchholz J, et al. Efficacy of radiation therapy for the treatment of sialocele in dogs. *J Vet Intern Med* 2018;32:107–110.
22. Rushworth GF, Megson IL. Existing and potential therapeutic uses for *N*-acetylcysteine: the need for conversion to intracellular glutathione for antioxidant benefits. *Pharmacol Ther* 2014;141:150–159.
23. Evans HE. The salivary glands. In: Evans HE, ed. *Miller's anatomy of the dog*. 3rd ed. Philadelphia: WB Saunders Co, 1993;415–419.
24. Slatter DH, Abdelbaki Y. Lateral orbitotomy by zygomatic arch resection in the dog. *J Am Vet Med Assoc* 1979;175:1179–1182.
25. Chen WL, Zhang LP, Huang ZQ, et al. Percutaneous sclerotherapy of sialoceles after parotidectomy with fibrin glue, OK-432, and bleomycin. *Br J Oral Maxillofac Surg* 2013;51:786–788.
26. Cai Y, Wang R, Yang SF, et al. Sclerotherapy for the mucoceles of the anterior lingual salivary glands with pingyangmycin. *Oral Dis* 2014;20:473–476.
27. Zhang J, Wang C. The application of absolute ethanol in the treatment of mucocele of the glands of Blandin–Nuhn. *J Craniofac Surg* 2016;27:e641–e642.
28. McCaul JA, Lamey PJ. Multiple oral mucoceles treated with gamma-linolenic acid: report of a case. *Br J Oral Maxillofac Surg* 1994;32:392–393.
29. Lapid O, Kreiger Y, Sagi A. Transdermal scopolamine use for post-rhytidectomy sialocele. *Aesthetic Plast Surg* 2004;28:24–28.
30. Sinha R, Sarkar S, Khaitan T, et al. Nonsurgical management of oral mucocele by intralesional corticosteroid therapy. *Int J Dent* 2016;2016:2896748.
31. Lovato A, Restivo DA, Ottaviano G, et al. Botulinum toxin therapy: functional silencing of salivary disorders [Terapia con tossina botulinica: silenziamento funzionale dei disordini salivari]. *Acta Otorhinolaryngol Ital* 2017;37:168–171.
32. Moraes PC, Teixeira RG, Thomaz LA, et al. Liquid nitrogen cryosurgery for treatment of mucoceles in children. *Pediatr Dent* 2012;34:159–161.
33. Jinbu Y, Tsukinoki K, Kusama M, et al. Recurrent multiple superficial mucocele on the palate: histopathology and laser vaporization. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003;95:193–197.
34. Kopp WK, St-Hilaire H. Mucosal preservation in the treatment of mucocele with CO_2 laser. *J Oral Maxillofac Surg* 2004;62:1559–1561.
35. Boj JR, Poirier C, Espasa E, et al. Lower lip mucocele treated with an erbium laser. *Pediatr Dent* 2009;31:249–252.
36. Romeo U, Palaia G, Tenore G, et al. Excision of oral mucocele by different wavelength lasers. *Indian J Dent Res* 2013;24:211–215.
37. Feng H, Wang S, Liu Y, et al. Microwave ablation: a novel treatment for the mucoceles of anterior lingual salivary glands. *J Oral Maxillofac Surg* 2017;75:530–535.
38. Araujo MR, Centurion BS, Albuquerque DF, et al. Management of a parotid sialocele in a young patient: case report and literature review. *J Appl Oral Sci* 2010;18:432–436.
39. Gahir D, Clifford N, Yousefpour A, et al. A novel method of managing persistent parotid sialocele. *Br J Oral Maxillofac Surg* 2011;49:491–492.
40. Lisan Q, Raynal M, Pons Y, et al. Catheterization of post-traumatic parotid duct sialocele. *Eur Ann Otorhinolaryngol Head Neck Dis* 2014;131:317–318.
41. Asha'ari ZA, Razali MS, Leman WI, et al. A simple, safe, and effective surgical technique for the treatment of post-traumatic parotid sialocoele. *Malays J Med Sci* 2014;21:72–74.
42. Giraddi GB, Saifi AM. Micro-marsupialization versus surgical excision for the treatment of mucoceles. *Ann Maxillofac Surg* 2016;6:204–209.
43. Spreull JS, Head KW. Cervical salivary cysts in the dog. *J Small Anim Pract* 1967;8:17–35.
44. Benjamino KP, Birchard SJ, Niles JD, et al. Pharyngeal mucoceles in dogs: 14 cases. *J Am Anim Hosp Assoc* 2012;48:31–35.
45. Elbini Dhouib I, Jallouli M, Annabi A, et al. A minireview on *N*-acetylcysteine: an old drug with new approaches. *Life Sci* 2016;151:359–363.
46. Harvey CE. Sialography in the dog. *Vet Radiol Ultrasound* 1969;10:18–27.
47. Nahlieli O, Schacham R, Schlesinger M, et al. Juvenile recurrent parotitis: a new method of diagnosis and treatment. *Pediatrics* 2004;114:9–12.
48. Glen JB. Canine salivary mucocoeles. Results of sialographic examination and surgical treatment of fifty cases. *J Small Anim Pract* 1972;13:515–526.