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Original article

Integrated basic lung and heart ultrasound with X-ray (TUSX) for the diagnosis of asthma, chronic bronchitis and laryngeal paralysis, and treatment with inhaled fluticasone using home-made mask in dogs and cats

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Abstract

Basic lung and heart ultrasound examination combined with chest X-ray (TUSX) is currently considered to be very useful for differentiation of asthma, chronic bronchitis and laryngeal paralysis from other diseases with dyspnea/coughing. Among 252 client-owned animals with persistent dyspnea/cough/noisy breathing, in 197 of them: pulmonary edema, pneumonia, lung cancer, free pleural fluid, pneumothorax, lung contusion or heart disease were diagnosed. The remaining 55 animals (42 dogs and 13 cats) were diagnosed with asthma (in 13 cats), chronic bronchitis (in 37 dogs) and laryngeal paralysis (in 5 dogs) using TUSX. These animals were qualified for inhaled fluticasone treatment using 3 types of spacers – two commercial and a home-made mask. 36 animals (65.5%) completed the trial. In 26 of them (72.2%) the owners observed complete, long lasting relief of the symptoms, and the owners of 7 animals (19.5%) declared a considerable clinical improvement, regardless of the type of spacer used. The owners of 3 animals (8.3%) did not see any improvement. The proposed diagnostic and therapeutic management improved long-term clinical status of the vast majority (91.7%) of animals. Therefore, it seems justified to include the TUSX diagnostic protocol in daily veterinary practice and to encourage owners to prepare home-made face masks for inhaled fluticasone treatment.

Key words: cats, dogs, glucocorticosteroids, echocardiography, thorax ultrasonography

Introduction

Lung ultrasonography (LUS) is a versatile diagnostic approach for quick detection of most important acute respiratory diseases. Furthermore, basic echocardiography added to LUS, called as thoracic ultrasonography (TUS), resulted in a significant improvement of initial diagnosis when compared to standard methods and it is widely use in human medicine with well documented high accuracy (Labovitz et al. 2010, Bataille et al. 2014, Shah et al. 2016). It has also been shown that TUS has much better diagnostic accuracy than X-ray and auscultation (Lichtenstein et al. 2004, Tasci et al. 2016). Many basic heart and lung sonographic protocols under various names were proposed both in human and veterinary medicine. They differ from each other mainly in the site of probe application (different schemes), and the scope of the test which is often related to a particular policy of hospital departments. For lung sonography these are mainly: Veterinary Bedside lung ultrasound exam (Vet Blue), Thoracic Focused Assessment with Sonography for Trauma (TFAST) (Boysen and Lisciandro 2013), Point-Of-Care Ultrasonography (POCUS) (Ward et al. 2018, Nakao et al. 2020) or bedside chest ultrasound (Hew and Tay 2016). For heart examination it is focused echocardiography, Focused Intensive Care Echo (Hall et al. 2017, Ward et al. 2018), focus assessed transthoracic echocardiography (FATE) (Lucina et al. 2017), focused cardiac ultrasound (Loughran et al. 2019). They enable a preliminary diagnosis usually within a few minutes (Szaluś-Jordanow et al. 2021). Basic ultrasound heart examination in emergency situations includes only two-dimensional and M-mode echocardiography (Tse et al. 2013). In basic LUS pleural line, gliding signs (also known as sliding signs), as well as A and B lines should be evaluated (Lichtenstein 2015, Lisciandro 2021). Dyspnea and/or chronic cough are common symptoms in humans and animals. Computer tomography (CT) is regarded as the most useful for the diagnosis of most lung diseases although it has some important limitations (Bekgoz et al. 2019) such as a high cost of the examination and, in the veterinary medicine, the need of anesthesia. As TUS is free from these shortcomings it may be a much less expensive, quicker and safer alternative. The usefulness of TUS in diagnosing of pneumonia, pulmonary edema, neoplasm and pleural effusion is well documented in human and veterinary medicine (Lichtenstein 2007, Lisciandro 2021, Łobaczewski et al. 2021). The diagnostic value of these techniques is also confirmed but to a lesser extent for diagnosing of asthma, chronic bronchitis or laryngeal paralysis. The accuracy of diagnosis made by ultrasound lung examination is estimated at 90% in patients with dyspnea. This medical procedure proto-

col is known as the “decision tree of the BLUE protocol” and is also used in veterinary medicine (Lichtenstein 2017, Lisciandro 2021) (Table 1). Disadvantage of LUS is that it is usually unable to detect lesions that are located deep in the lung lobe. Therefore, we aimed in this study to use an integrated diagnostic tool (TUSX) composed of simplified lung and heart sonography (TUS) supplemented with chest X-ray examination to recognize the above-mentioned conditions and apply treatment with inhaled glucocorticoids.

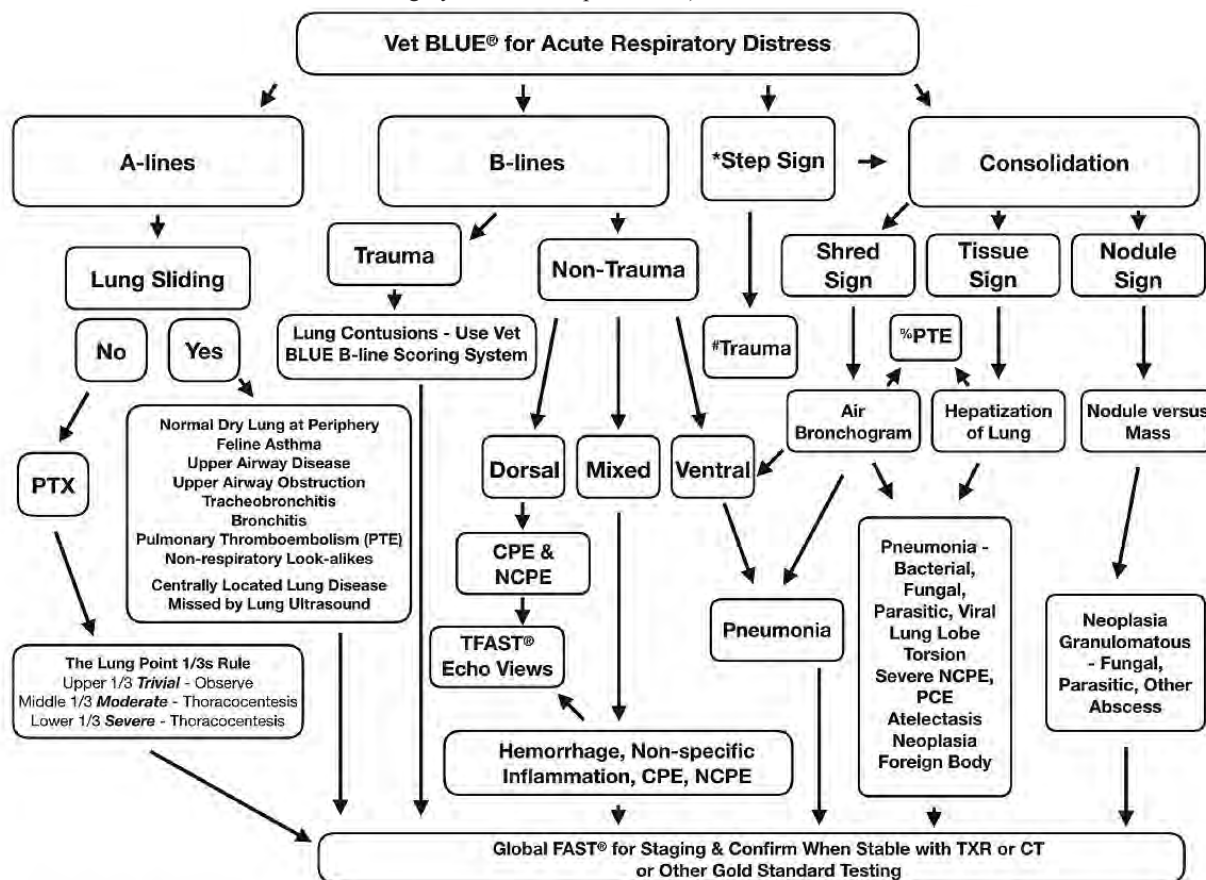
A common applied treatment of asthma, chronic bronchitis and laryngeal paralysis are still injectable or oral corticosteroids. However, such medication may cause serious side effects (Canonne et al. 2016). For these reasons, inhaled corticosteroids have been developed. They are very effective in inhibiting inflammatory processes in the respiratory mucosa at considerably lower risk of generalized adverse effects as doses used are thousands times lower than during the systemic treatment (Padrid 2006). However, commercial spacers are expensive. Therefore, in our study we also compared the usefulness of home-made face masks with commercially available ones in dogs and cats as it has already been done in human medicine.

Materials and Methods

Animal examination

In total 252 client-owned patients including 151 dogs and 101 cats with dyspnea and/or persistent cough and/or noisy breathing indicative of laryngeal paralysis were enrolled in this study. In each patient a clinical interview, full clinical examination, basic echocardiography, LUS and X-ray of the chest in two projections were performed. Basic echocardiography included right parasternal long and short axis projection. The projections were aimed at obtaining measurements of the left atrium, aorta, left and right ventricles and the thickness of the left ventricular walls as well as detecting pericardial effusion or heart tumors if present. LUS followed the Vet BLUE protocol. All transducers were positioned transverse to the ribs in order to visualize the “gator sign” (the pleural line and two ribs). Four regions were examined on each thoracic side (caudodorsal, perihilar, middle, and cranial) with one scan for each region. A-lines with a lung gliding were defined as normal aerated lung. Interstitial-alveolar edema was recognized by the presence of B-lines. Additional ultrasound lesions were described according to Ward et al. (2019) following the descriptions used in human medicine like the shred, tissue-like or nodule sign (Lisciandro et al. 2014, 2017, Ward et al. 2018). A certified veterinarian with 12-year experience in basic echocardiography and

Table 1. Vet Blue algorithm for acute respiratory distress in dogs and cats (from Point-of-Care Ultrasound Techniques for the Small Animal Practitioner used with dr Gregory's Lisciandro permission).



*Step sign is a deviation from the linear expectation of the PPI and the "lung line."

*In trauma the step sign's rule-out list includes thoracic wall injury (intercostal tear, rib fracture(s), subcostal hematoma/mass), pleural space disease (diaphragmatic hernia, mass, heart enlargement), and pulmonary consolidation (shred sign, tissue sign, nodule sign, wedge sign).

*Pulmonary thromboembolism (PTE) is supported by triangulated shred sign or tissue sign-like findings in the Perihilar and Caudodorsal lung regions (Lisciandro 2013, unpublished data).

PTE, pulmonary thromboembolism; PTX, pneumothorax; CPE, cardiogenic pulmonary edema; NCPE, noncardiogenic pulmonary edema; TXR, thoracic radiography; CT, computed tomography. Source: Courtesy of Dr Gregory Lisciandro, Hill Country Veterinary Specialists and FASTVet.com, Spicewood, TX.

10-year experience in LUS performed the examination. For LUS the linear or convex probe held horizontally was applied to the chest in 4 sites on each side. For heart examination a convex or phased array probe was used. From each application of the probe a short video-clip was recorded for re-evaluation by a board-certified specialist. A routine thoracic radiographic examination including 2 projections was performed. The heart and lung ultrasound examinations were performed in standing position. Hair was parted without clipping and alcohol and coupling gel were used. Two ultrasound devices were used: Mindray M7 with a 4-2s MHz phased array and a L12-4s MHz linear probe, and GE Healthcare with a 12-6 MHz linear probe and a 10-6 MHz convex array. All settings and scanning methods were identical for all patients.

Eligibility criteria for the fluticasone-treatment study were as follows:

- history of dyspnea and/or persistent cough or

noisy breathing (indicating of laryngeal paralysis) for over 2 months;

- correct echocardiographic examination including measurements of the left atrium, aorta, left and right ventricles, the thickness of the left ventricular walls. All values were compared with echocardiographic reference values with correlation with body weight. Additionally, for purebred dogs, a comparison was made with reference values for a given breed (Boon 2011). The study included patients with all parameters within the reference values, with no pericardial fluid, no heart tumors or other abnormalities;
- correct chest ultrasound including the "gator sign" lung gliding and the A-line. All patients with pleural effusion, tissue-like sign indicating lung consolidation, the B-line, nodules or any other abnormalities were excluded from the study;
- unremarkable chest x-ray including normal lung



Fig. 1. Oxygen mask produced by the company Grande Finale.

patterns and radiological anatomy. Patients with alveolar, bronchial, vascular, interstitial including nodular or diffuse lung pattern or with any other abnormalities with anatomy were excluded from the study;

- lack of owner's consent for additional diagnostics under anesthesia, such as respiratory tract endoscopy or computed tomography;
- no treatment with oral or injected corticosteroids in previous 8 weeks.

Treatment

Patients enrolled in the study were treated with fluticasone propionate (Flixotide®; GlaxoSmithKline, UK) administered via inhalation. This inhaled steroid was chosen due to its well-evidenced therapeutic effect in animals and the fact that it is a drug whose absorption from the oral cavity is negligible. According to various

studies only 1-1.5% of whole dose of fluticasone is absorbed in the oral cavity. It is because of fact, that fluticasone is a large molecule and acts topically with the airway mucosa (Brutsche et al. 2000, Falcoz et al. 2000, Church et al. 2008, Allen et al. 2013). The initial dose varied from 50 to 250 µg twice daily, and was later modified based on clinical response, if necessary. This treatment was continued as a monotherapy for three months. The drug was administered through three types of spacer devices: AeroDawg® Canine Aerosol Chamber for dogs and AeroCat Feline Aerosol Chamber (Trudell Animal Health, Canada), oxygen masks (Grande Finale, Poland) (Fig. 1) and a home-made mask (Fig. 2 and 3). The owners were instructed how to prepare a home-made mask using the top of a 250, 330, 500 or 1000 ml plastic bottle, depending on the size of the animal's muzzle. On the first visit the owners were instructed how to place the mask over the animal's face/head and administer the appropriate dose of the



Fig. 2. Home-made mask.

drug. Using the AeroDawg or AeroCat masks the animal had to breathe five to ten times (Bexfield et al. 2006). In case of Grande Finale or home-made masks the inhalation lasted one minute.

The first re-check was performed via phone or e-mail after 5 days of treatment. The owners were asked to assess the response to therapy on the 4-point scale: no improvement, mild improvement, considerable improvement and resolution of clinical signs (clinical remission). Moreover, the owners were asked to provide feedback on how the animal tolerated the drug delivery system. In the case of clinical remission the owners were advised to taper the dose by 50% or reduce the administration frequency to once a day. If clinical remission sustained further reduction of administration frequency to once per two days was recommended. Otherwise, the initial dose was restored. The final recheck was performed after 3 months of the treatment.

Statistical analysis

Numerical variables were summarized using the median, interquartile range (IQR) and range and compared between groups with the Mann-Whitney U test. Categorical variables were presented with frequency

and percentage in the group and compared between groups using the Fisher's exact test. Ninety five percent confidence intervals (CI 95%) for proportions were calculated using the Wilson score method. All tests were two-sided and the significance level (α) was set at 0.05. Statistical analysis was performed in TIBCO Statistica 13.3 (TIBCO Software Inc., Palo Alto, CA).

Results

Of 252 patients 55 (21.8%) met the eligibility criteria and were initially enrolled in the fluticasone treatment study. The remaining 197 animals were excluded from the study based on any abnormalities in X-ray, lung or heart examination, since one or more of the following conditions had been detected: enlarged heart chambers, fluid in the pericardial sac, heart tumor, B-lines, shred, tissue-like or nodule sign, abnormal radiological anatomy or lung patterns indicating: pulmonary edema, pneumonia, lung cancer, free pleural fluid, pneumothorax, lung contusion or heart disease.

The study population included 42 dogs (18 males) and 13 cats (8 males). Age of the patients ranged from 2 to 16 years and dogs were significantly older than cats



Fig. 3. Inhalation of fluconazole through a homemade mask.

– median (IQR) of 12 (10 to 13) years vs. 8 (8 to 11) years, respectively ($p=0.010$). Eighteen of 42 dogs (42.9%) were cross-breeds. Of remaining 24 pedigree dogs, 10 were Yorkshire terriers. Body weight of dogs ranged from 2 to 45 kg with the median (IQR) of 7 (4 to 11) kg. Only 7 dogs (16.7%) weighed more than 15 kg – 2 Labrador retrievers, a Golden retriever, a German shepherd, a Collie shepherd, a Staffordshire terrier, and a cross-breed. All cats were of domestic shorthair breed and weighed between 3 and 7 kg (median of 5 kg).

Thirty seven dogs were diagnosed with chronic

bronchitis and 5 were suspected of laryngeal paralysis (2 Labrador retrievers, a Golden retriever, a German shepherd, and a cross-breed weighing 12 kg). All cats were diagnosed with asthma.

Of 55 animals enrolled in the fluticasone treatment study 15 (27.3%; 12 dogs and 3 cats) gave up participation due to the expected problems with administration of the drug. This reduced the study population to 40 individuals – 30 dogs and 10 cats – in which an attempt to administer fluticasone was made. In four dogs (10%) aggressive behavior precluded administration of fluti-

Table 2. Demographic and clinical characteristics of 40 animals enrolled in the fluticasone treatment study presented as n (%) or median (IQR).

Characteristic	Improvement after 5 days			Aggressive behavior
	Complete	Considerable	None	
Dogs (n=30)				
	n=18	n=6	n=2	n=4
Sex				
Males (n=15)	7 (46.7)	6 (40.0)	1 (6.7)	1 (6.7)
Females (n=15)	11 (73.3)	0	1 (6.7)	3 (20.0)
Age (years)	12 (10-13)	12 (12-13)	10, 10	12 (12-13)
Body weight (kg)	8 (4-12)	35 (18-36)	3, 4	3.5 (2.5-4)
Breed				
Cross-breed	9 (75.0)	0	2 (16.7)	1 (8.3)
Pedigree	9 (50.0)	6 (33.3)	0	3 (16.7)
Breeds	Yorkshire terrier (n=4) Shih-tzu (n=1) Pekingese (n=1) Miniature pinscher (n=1) Spitz (n=1) Collie (n=1)	Labrador retriever (n=2) Golden retriever (n=1) German shepherd (n=1) Staffordshire terrier (n=1) Yorkshire terrier (n=1)	-	Yorkshire terrier (n=2) Miniature pinscher (n=1)
Diagnosis				
Chronic bronchitis	17 (68.0)	2 (8.0)	2 (8.0)	4 (16.0)
Laryngeal paralysis	1 (20.0)	4 (80.0)	0	0
Type of mask				
AeroDawg	3 (60.0)	1 (20.0)	0	1 (20.0)
Grande finale	4 (100)	0	0	0
Home-made	11 (52.4)	5 (23.8)	2 (9.5)	3 (14.3)
Cats (n=10)				
	n=8	n=1	n=1	n=0
Sex				
Males	6 (100)	0	0	-
Females	2 (50.0)	1 (25.0)	1 (25.0)	-
Age	9 (8-11)	6	11	-
Body weight (kg)	5 (4-6)	7	3.5	
Type of mask				
AeroCat	1 (33.3)	1 (33.3)	1 (33.3)	
Grande finale	1 (100)	0	0	
Home-made	6 (100)	0	0	

casone and these dogs were removed from the study. In no cat such behavior was observed.

A commercial mask was used in 13 individuals (32.5%): Aerosol chamber in 8 animals (20.0%; 5 dogs and 3 cats), and Grande finale in 5 animals (12.5%; 4 dogs and 1 cat). A home-made mask was used in 27 individuals (67.5%; 21 dogs and 6 cats). Three dogs with home-made masks and 1 dog with an aerosol chamber showed aggressive behavior.

In the first re-check after 5 days of treatment the

improvement was observed in 33 of 36 individuals (91.7%; CI 95%: 78.2%, 97.1%) – 24 dogs (80% of 30 dogs that entered the study and 92.3% of 26 dogs that tolerated the treatment) and 9 cats (90.0% of 10 cats that entered the study). The improvement was complete (clinical remission) in 18 dogs (75.0%) and 8 cats (88.9%), and considerable in 6 dogs (25.0%) and 1 cat (10.0%). There was no significant difference in the proportion of animals in which improvement was observed between dogs and cats ($p=0.999$), males and females

($p=0.574$), types of mask used ($p=0.677$), or diagnoses ($p=0.767$). The degree of improvement was not significantly associated with the type of mask ($p=0.386$). However, in dogs it was significantly linked to the body weight ($p=0.016$) – dogs with clinical remission were significantly lighter than dogs with considerable improvement, and to the diagnosis ($p=0.007$) – clinical remission was observed in 17 of 19 dogs (89.5%) with chronic bronchitis and only in 1 of 5 dogs (20%) with laryngeal paralysis. Detailed characteristics of 40 animals which entered the study are presented in Table 2.

In 6 patients (3 dogs and 3 cats) the frequency of application was reduced after the first re-check to once a day and in 3 others (2 dogs and 1 cat) to every other day. In the second re-check after 3 months the improvement changed from considerable to complete in 2 more patients (1 dog and 1 cat).

Discussion

In recent years, the usefulness of ultrasound for lung examination has been proven both in human and veterinary medicine (Lisciandro et al. 2014, Hew and Tay 2016, Shah et al. 2016, Lichtenstein 2017, Lisciandro et al. 2017, Bekgoz et al. 2019, Nakao et al. 2020, Lisciandro 2021). LUS is particularly effective to confirm asthma and COPD, pneumonia or pulmonary oedema, and tends to be a beneficial alternative to other imaging approaches like X-ray or CT in patients with respiratory problems in critical care unit (Staub et al. 2019, Lisciandro 2021). During LUS in patients with chronic bronchitis, asthma or upper respiratory tract obstruction artifacts typical for normal lungs are visualized, such as gliding sign and A-lines. B lines or subpleural consolidation are not visible (Lichtenstein 2017, Bekgoz et al. 2019). Therefore, LUS is very helpful to distinguish COPD or asthma from other diseases causing dyspnea or cough mainly based on the exclusion of other diseases (Staub et al. 2019) which we considered in our study. As these symptoms may result also from cardiological conditions, it is advisable to perform also an ultrasound examination of the heart, for which a device equipped with a convex probe is sufficient. In humans, the above tests combined have 89% sensitivity and 97% specificity in detecting chronic bronchitis, asthma or upper respiratory tract obstructions (Lichtenstein 2017). It is known that CT is considered as a golden diagnostic standard. However, even in human medicine in highly scored publications the respiratory abnormalities diagnosis [including pneumonia, acute heart failure, chronic obstructive pulmonary disease (COPD) and asthma] is based on history, clinical examination and laboratory results only. Out of 25 publications on causes of dyspnea

in humans, which were included in a meta-analysis, only 3 used CT for diagnosis and 2 subsequent CT or X-ray (Hew and Tay 2016). In the remaining 20 reports clinical improvement after treatment was considered as confirmation of the initial diagnosis. This is because patient-reported outcome is one of the main indicators of the treatment efficacy, since the main objective of medical care is to increase patient well-being (Hew and Tay 2016). Therefore, in our study owner-reported outcome was the basis for assessment of the efficacy of the therapy of the disease, where the diagnosis was made based on TUSX.

Among 36 patients that entered our study with clinical symptoms and correct lung and heart ultrasound examination and X-ray, 26 (72.2 %) of the owners observed complete, long lasting relief of the symptoms, and 7 (19.4%) declared a significant reduction of respiratory distress (coughing was sporadic and short enough, and the owners did not consider switching from inhalation therapy to systemic administration of steroids). These observations are consistent with earlier reports that fluticasone inhalations in dogs and cats used as monotherapy is an effective treatment. It is also worth emphasizing that the poorer improvement in dogs was correlated with body weight. Significantly greater body weight was observed in dogs with laryngeal paralysis. This chronic disease has general weaker drug treatment effects than chronic bronchitis or asthma due to large mechanical component of its pathophysiology.

It has been demonstrated that full therapeutic effect could be observed after 1-2 weeks of fluticasone application (Padrid 2006). Our previous unpublished experience suggested that significant clinical effect was visible earlier. Therefore, we decided to carry out the first health check after 5 days of the treatment. It revealed that in over 90% of our patients clinical signs had resolved completely or mostly. Thus, it seems reasonable to propagate this diagnostic and therapeutic approach among first-contact veterinarians. However, the response was not always satisfactory, as 5 of 33 patients (15.2%) needed 2-3 times additional short (1-3 days) systemic steroid therapies (dexamethasone or prednisolone) due to exacerbation of the symptoms during 3 months of observation. Furthermore, 3 animals (8.3%) did not respond at all to fluticasone treatment. A false diagnosis could be the reason, but it seems improbable, as in all 3 of them oral prednisolone application eliminated the clinical signs completely. It cannot be excluded the fluticasone was given incorrectly to these 3 patients as compared to human study (Rodriguez et al. 2008, Schor et al. 2017). Unfortunately, besides showing videos no further training was conducted for these owners, which should be consi-

dered in similar situations in future to avoid the treatment failure. It is also noteworthy that in 2 of 5 dogs with laryngeal paralysis, systemic steroid treatment had been performed before entering our study, and no reduction of coughing and wheezing had been achieved, but in all of them inhalation of fluticasone significantly improved the clinical state.

Even though most patients responded very well to fluticasone therapy, an unexpectedly large group of owners did not take up inhalation treatment, despite their initial acceptance to join the study. In fact, much more owners did not start inhalation treatment due to concerns about problems with drug administration (15/55 caretakers), compared to the group of owners who had difficulties with cooperation of their animals (4/40 patients).

The most known commercially available spacers are AeroDawg© Canine Aerosol Chamber for dogs and AeroCat Feline Aerosol Chamber for cats. However, their prices are relatively high, and considering that fluticasone is more expensive than prednisolone, the cost may be a reason of rejection of the inhalation therapy by the owners as in human medicine in low income countries (Rodriguez et al. 2008, Schor et al. 2017). Indeed, due to financial reasons, only 8 owners decided to use commercial spacers. Another type of mask (Grande Finale) is five times cheaper compared to the aforementioned commercial equipment. However, some owners were uncertain whether such masks would be effective, and others were afraid that their animals would not accept a full-head mask. Therefore, only 5 owners decided to use this equipment. As a result, most of the owners in our study decided to use a mask made by themselves. In treatment of asthma and COPD in humans it has been demonstrated that a modified top of a 500 ml plastic bottle can effectively replace a metered dose inhaler for both children of all ages and adults. Clinical studies have shown that such home-made spacers are as effective as a commercially available equipment (Rodriguez et al. 2008, Schor et al. 2017). Our study shows that home-made masks prepared according to instructions of veterinarians are able to provide therapeutic effects comparable to commercial equipment.

It is also worth emphasizing that the number of veterinarians performing basic ultrasound of lungs and heart gradually increases. In both human and veterinary medicine these techniques can be trained during short courses, and the accuracy of the diagnoses after such training is high even in beginners with no previous experience with diagnostic imaging. After 6-hour training of cine-loop of the heart ultrasound in dogs, pleural effusion was correctly identified by 90% of participants, pericardial effusion by 95% and atrial enlargement

by 86% (Tse et al. 2013). Similar results were observed in the human medicine. After half an hour training of lung ultrasound in humans with dyspnea novices identified sonographic B-lines with similar accuracy as expert sonographers (Chiem et al. 2015). This shows that the TUSX protocol we propose can be widely used after proper training.

Conclusions

The proposed diagnostic and therapeutic management resulted in a return to good clinical status in the vast majority of dogs and cats suffering from non-infectious chronic coughing/dyspnea (chronic bronchitis, asthma and laryngeal paralysis). Therefore, it seems justified to include the TUSX diagnostic protocol in daily veterinary practice, and to encourage owners to prepare home-made face masks for inhaled fluticasone treatment of these conditions.

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