PAPER

Primary care veterinary usage of systemic glucocorticoids in cats and dogs in three UK practices

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Objectives: To describe systemic glucocorticoid usage in cats and dogs by three primary care veterinary practices in England and to ascertain risk factors for clinical use. To evaluate consistency of prescribing patterns across clinics. To validate a merged database of primary veterinary clinical data as a functional tool for clinical epidemiological research.

Methods: A merged database was established from clinical data on 31,273 cat and dog consultations with pharmacotherapy from three veterinary practices in England. Descriptive statistics described systemic glucocorticoid drug use in cats and dogs while mixed-effects logistic regression modelling evaluated risk factors. Individual clinic usage was compared.

Results: Overall, 1877 (16·68%) cat consultations and 2913 (14·55%) dog consultations resulted in systemic glucocorticoid therapy. Cats received higher parenteral ($P<0·0001$) and oral ($P<0·0001$) dose levels than dogs. Pathophysiological indication, age, skin condition, sex and clinic attended were significant risk factors for glucocorticoid prescription. Clinics varied widely in their odds of systemic glucocorticoid usage ($P<0·0001$).

Clinical Significance: An evidence base for systemic glucocorticoid prescribing by primary care small animal practices in England is provided. Clinic attended was a significant risk factor, indicating wide variation in prescribing patterns between clinics. A merged primary care veterinary clinical database was effective for epidemiological research.

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INTRODUCTION

Glucocorticoids are among the most widely used (and misused) class of drugs in veterinary medicine; yet, there is little information on prescribing patterns in general practice (Ferguson and others 2009). Glucocorticoids are potent anti-inflammatory and immunosuppressive agents and the majority of therapeutic applications for these agents fall into these classifications (Ferguson and others 2009). Glucocorticoids are also indicated to treat deficiency states, neoplasia and as antishock agents (Rang and others 2007). Because of the presence of glucocorticoid receptors in almost all cells, both the desired and undesired effects of glucocorticoid therapy are manifold, making the need for prudent use particularly important (Behrend and Kemppainen 1997).

Hill and others (2006) showed that systemic glucocorticoids were prescribed in 162 of 795 (20%) skin cases in primary care practice. However, prescribing data for general small animal caseloads is lacking. Increasing computerisation within small animal veterinary practice (94% of UK practices use a computerised system for client details (Robinson and Hooker 2006)) means that collaborative research projects can now capture and analyse primary care clinical data.

The primary objectives of this study were to describe prescribing practices and ascertain risk factors for systemic glucocorticoid

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use in cats and dogs by three primary care veterinary practices in England and to explore prescribing level variation between clinics. A secondary objective was to validate a merged database of primary veterinary electronic patient records for epidemiological research.

MATERIALS AND METHODS

Participants and procedure

This study was a retrospective analysis of all clinical records from three small animal veterinary practices in England participating between January 01, 2007 and December 31, 2009 within the pilot phase for the VetCompass Animal Surveillance project (VetCompass 2011). Practice selection was a convenience sample using RxWorks practice management system (PMS) (RxWorks 2011) and willingness to participate. Participating practices assigned consultations with summary diagnoses from the VeNom Code list of veterinary-specific terms (The VeNom Coding Group 2011). PMS data fields captured included unique clinic, animal and consultation numbers, consultation date, veterinarian initials, species, breed, sex, neutering status, birth-date, weight, clinical notes, summary diagnosis and treatment. Systemic glucocorticoids were defined as glucocorticoid products administered either parenterally or orally. Consultations were defined as same-day "episodes of care" involving a cat or dog by a single veterinarian resulting in pharmacotherapy. Ethics approval was granted by the Royal Veterinary College Ethics & Welfare Committee.

Data analysis

An integrated query extracted clinical data from individual PMS's (Upjohn and others 2008) for checking and cleaning in a spreadsheet (Microsoft Office Excel 2007, Microsoft Corp.). Non-veterinarian, non-cat/non-dog and non-pharmacotherapeutic observations were removed. Breed type was assigned by the owner or veterinary practice based on phenotype and categorised as "Breed status" (purebreed or crossbreed) and "Breed status" (purebreed, dominant cross or crossbreed). Cat breeds were further categorised by cat-type (shorthaired or longhaired) (TICA 2010) and dog breeds by dog-size based on height at the shoulder (small: <23 cm, medium: 23 to 46 cm, large: 47 to 61 cm, giant: >62 cm) (American Kennel Club 2011, The Kennel Club 2011a,b). Crossbreeds were the referent for analysis. "Age" was categorised into life stages (<1 year, 1 to 6·99 years, 7 to 11·99 years and >12 years). "Month" and "Season" variables were generated (spring: March to May, summer: June to August, autumn: September to November, winter: December to February).

Assigned summary diagnoses were categorised as skin disease and also by pathophysiological indication for systemic glucocorticoid treatment: physiological (glucocorticoid deficiency), inflammatory (not including hypersensitivity conditions), hypersensitivity, immunosuppressive, neoplastic, shock/spinal trauma, no apparent indication.

Treatment data were searched for systemic glucocorticoid branded and generic names (NOAH 2010). Active ingredient doses were calculated for parenteral by injection (mg/kg bodyweight) and oral (daily mg/kg bodyweight) treatments based on recorded bodyweights. Initial dose was used where oral dose changed over time. Oral and parenteral dosages were categorised as low or high based on average recommended dosages (Table 1) (Ramsey 2007, NOAH 2010) Parenteral formulations were categorised as short-acting (duration <5 days): dexamethasone sodium phosphate (Colvasone, Norbrook; Dexadreson, Intervet UK Ltd; Duphacort Q, Fort Dodge Animal Health), methylprednisolone sodium succinate (Solu-Medrone V; Pfizer Limited), dexamethasone isonicotinate (Voren; Boehringer Ingelheim Limited) or long-acting (duration >5 days): dexamethasone phenylpropionate/dexamethasone sodium phosphate combination (Dexafort; Intervet UK Ltd), methylprednisolone acetate (Depo-Medrone V; Pfizer Limited) (Table 1) (NOAH 2010).

Statistical analysis used Stata Version 11 (Stata Corp.) and was separated by cats and dogs. Prevalence of glucocorticoid usage was evaluated by standard methods (Kirkwood and Sterne 2003). Inter-species usage levels were compared using the Mann-Whitney U test. Risk factor analysis used mixed-effects logistic regression with animal ID as a random effect to account for clustering of consultations within animals. Statistical significance was set at the 5% level or where an a priori interest dictated inclusion.

Table 1. Parenteral and oral glucocorticoid dose-level cut-points used to categorise dosages as low or high and summary statistics for the cat and dog dosages used in three UK small animal practices

Glucocorticoid name	Cats				Dogs			
	Cut-point	No. Obs	Med	Range	Cut-point	No. Obs	Med	Range
Parenteral mg/kg								
Methylprednisolone acetate	2·00	343	4·62	1·93 to 10·81	1·00	14	1·38	0·26 to 5·03
Dexamethasone sodium phosphate	0·15	301	0·20	0·05 to 3·5	0·10	511	0·10	0·08 to 0·96
Dexamethasone phenylpropionate and Dexamethasone sodium phosphate	0·15	411	0·35	0·12 to 1·78	0·15	88	0·21	0·04 to 0·48
Methylprednisolone sodium succinate	30·00	0	N/A	N/A	30·00	2	11·64	4·06 to 19·23
Dexamethasone isonicotinate	1·0	4	0·27	0·18 to 0·3	1·0	4	0·30	0·22 to 0·41
Oral mg/kg daily								
Fludrocortisone	0·02	0	N/A	N/A	0·02	2	0·02	0·01 to 0·02
Methylprednisolone	1·00	7	0·39	0·27 to 1·07	0·35	115	0·33	0·05 to 1·13
Prednisolone/Cincophen*	N/A	0	N/A	N/A	0·62	12	0·11	0·05 to 0·15
Prednisolone	1·10	120	0·78	0·08 to 3·70	0·50	407	0·53	0·01 to 5·00

No. Obs Number of observations, Med Median dosage, N/A Not applicable
*Prednisolone dose only

RESULTS

Three practices contributed 31,273 consultations with pharmacotherapy [11,254 (35·99%) cat and 20,019 (64·01%) dog]. Two practices were single-centre [4880 (15·60%) and 7735 (24·73%) consultations] while the third comprised five clinics [18,658 (59·66%) consultations]. The 24 veterinarians contributed from 5 to 3798 consultations each (median: 647). Overall, 4790 (15·32%) of consultations resulted in systemic glucocorticoid pharmacotherapy; 2878 (9·20%) parenteral only, 1675 (5·36%) oral only and 237 (0·76%) both parenteral and oral (Table 2).

Frequency and mode of glucocorticoid treatment in cats and dogs

Comparing the species, cats had 1·18 [95% confidence interval (CI) 1·10 to 1·25, P<0·0001] times the odds of systemic glucocorticoid pharmacotherapy and 8·85 (95% CI 7·38 to 10·60, P<0·0001) times the odds of parenteral therapy than dogs. Parenteral dose levels were significantly higher for cats than dogs for methylprednisolone acetate (Depo-Medrone V; Pfizer Limited) (median cat 4·62 mg/kg *versus* median dog 1·38 mg/kg, P<0·0001) and dexamethasone sodium phosphate (Colvasone; Norbrook; Dexadreson, Intervet UK Ltd; Duphacort Q, Fort Dodge Animal Health) (median cat 0·20 mg/kg *versus* median dog 0·10 mg/kg, P<0·0001). Cat oral daily dose levels significantly exceeded dogs for prednisolone (median cat 0·78 mg/kg/daily *versus* median dog 0·53 mg/kg/daily, P<0·0001) (Table 1). Cats were significantly more likely to have lower oral dosing frequencies than dogs (once-daily or less: cat 77·88% *versus* dog 57·12%, P=0·0002) (Table 2).

Table 2. Glucocorticoid usage statistics for cat and dog consultations that include systemic glucocorticoid pharmacotherapy

	Cat*		Dog*	
	Frequency	Percent (%)	Frequency	Percent (%)
Mode of administration				
Only parenteral glucocorticoid	1651	87·96	1227	42·12
Only oral glucocorticoid	196	10·44	1479	50·77
Both parenteral and oral glucocorticoid	30	1·60	207	7·11
Parenteral formulation used				
Short-acting	475	28·26	1053	73·43
Long-acting	1206	71·74	381	26·57
Oral glucocorticoid active ingredient				
Fludrocortisone	0	0	8	0·47
Methylprednisolone	23	10·18	390	23·13
Prednisolone and cinchophen tablets	0	0	47	2·79
Prednisolone	203	89·82	1241	73·61
Oral glucocorticoid dose schedule†				
Once weekly	8	3·54	19	1·13
Once every 4 days	2	0·88	0	0
Twice weekly	0	0	1	0·06
Every third day	7	3·10	14	0·83
Three times weekly	4	1·77	6	0·36
Every other day	42	18·58	188	11·15
Four times weekly	0	0	1	0·06
Daily	113	50·00	734	43·53
Twice-daily	50	22·12	721	42·76
Three times daily	0	0	2	0·12
Parenteral dose level based on recommended species doses†				
Low	90	8·50	181	29·24
High	969	91·50	438	70·76
Oral dose level based on recommended species doses†				
Low	86	67·72	261	48·69
High	41	32·28	275	51·31

*A total of 1877 (16·68%) cat and 2913 (14·55%) dog consultations resulted in treatment with or dispensation of systemic glucocorticoids
†Where an oral prescription specified a dose changing with time, the initial dose was used
†Dosage cut-points for dose-level categories are given in Table 1

For cat consultations, 1877 (16·68%) employed systemic glucocorticoids with 1651 (87·96%) of these employing only parenteral therapy. The majority of parenteral formulations (71·74%) were long-acting. For cat oral glucocorticoid dose regimens, 50·00% were once-daily while 22·12% were twice-daily. Dosages were "high" for 91·50% of cat parenteral doses and 32·28% of cat oral treatments (Table 2).

Among dogs, 2913 (14·55%) of consultations employed systemic glucocorticoids with 1227 (42·12%) of these including only parenteral therapy. Of dog parenteral treatments, 26·57% were long-acting formulations. Prednisolone (73·61%) and methylprednisolone (Medrone V Tablets; Pfizer Ltd) (23·13%) were the most common oral preparations. Once-daily and twice-daily oral dose regimens covered 43·53 and 42·76% of oral doses, respectively. Dose-levels were "high" for 70·76% of dog parenteral treatments and 51·31% of dog oral treatments (Table 2).

Risk factors for glucocorticoid treatment in cats

Five predictors were retained in the final cat multivariable model (Table 3): "Pathophysiological indication", "Age", "Skin", "Sex" and "Clinic".

Compared with inflammatory conditions, consultations for neoplastic conditions had 4·28 (95% CI 2·93 to 6·24, P<0·0001) times the odds of receiving systemic glucocorticoids while consultations with no record of an apparent glucocorticoid indication had 0·39 times the odds (95% CI 0·31 to 0·49, P<0·0001). Cats 1 to 7 years old had 3·41 times the odds of receiving a systemic glucocorticoid (95% CI 2·00 to 5·81, P<0·0001) than cats under one year old, while 7 to 12 year-old cats had 6·37 times the odds (95% CI 3·69 to 10·98, P<0·0001).

Male cats had 0·72 (95% CI 0·57 to 0·90, P=0·0011) times the odds of treatment compared with female cats. Consultations at Clinic C5 had 2·66 (95% CI 1·62 to 4·40, P<0·0001) the odds compared with Clinic A. Prescribing levels within the multi-centre practice clinics (C1-C5) appeared more uniform than in comparison with the two single practices (A and B).

Risk factors for glucocorticoid treatment in dogs

The final dog multivariable model retained five risk factors (Table 4): "Pathophysiological indication", "Age", "Skin", "Sex" and "Clinic". Consultations with no record of an apparent glucocorticoid indication had 0·54 (95% CI 0·46 to 0·66, P<0·0001) times the odds of receiving systemic glucocorticoids compared with inflammatory conditions. Dogs 7 to 12 years old had 1·55 times the

Table 3. Final mixed-effects model for risk factors associated with systemic glucocorticoid therapy for CAT consultations

Risk factor	Odds ratio	95% CI	P-value
Pathophysiological indication			
Anti-inflammatory (not including hypersensitivity conditions)	1·00	Reference	<0·0001
Hypersensitivity	61·65	38·62 to 98·44	
Immunosuppressive	13·65	7·64 to 24·39	
Neoplastic	4·28	2·93 to 6·24	
Shock/spinal trauma	4·16	1·74 to 9·98	
No apparent indication for glucocorticoid	0·39	0·31 to 0·49	
Age			
<1 year	1·00	Reference	<0·0001
1 to 6·99 years	3·41	2·00 to 5·81	
7 to 11·99 years	6·37	3·69 to 10·98	
12 years and older	9·17	5·36 to 15·68	
Skin			
No skin condition diagnosed	1·00	Reference	<0·0001
Skin condition diagnosed	3·64	2·75 to 4·80	
Sex			
Female	1·00	Reference	0·0011
Male	0·72	0·57 to 0·90	
Clinic			
A	1·00	Reference	0·0027
B	2·76	1·77 to 4·31	
C1	1·51	0·63 to 3·61	
C2	1·63	1·05 to 2·53	
C3	1·91	1·27 to 2·87	
C4	1·30	0·85 to 1·99	
C5	2·66	1·62 to 4·40	
Random effect			
Animal ID	—	1·94 to 3·10	

Table 4. Final mixed-effects model for risk factors associated with systemic glucocorticoid therapy for DOG consultations

Risk factor	Odds ratio	95% Confidence interval	P-value
Pathophysiological indication			
Anti-inflammatory (not including hypersensitivity conditions)	1·00	Reference	<0·0001
Physiological	78·92	13·72 to 453·89	
Hypersensitivity	6·91	5·52 to 8·64	
Immunosuppressive	3·88	2·60 to 5·79	
Neoplastic	1·08	0·78 to 1·49	
Shock/spinal trauma	3·58	2·01 to 6·38	
No apparent indication for glucocorticoid	0·54	0·46 to 0·66	
Age category			
<1 year	1·00	Reference	<0·0001
1 to 6·99 years	1·26	0·98 to 1·63	
7 to 11·99 years	1·55	1·18 to 2·03	
12 years and older	2·07	1·52 to 2·83	
Sex			
Female	1·00	Reference	0·0650
Male	1·16	0·99 to 1·35	
Skin			
No skin condition diagnosed	1·00	Reference	<0·0001
Skin condition diagnosed	6·75	5·81 to 7·85	
Clinic			
A	1·00	Reference	<0·0001
B	1·27	1·01 to 1·61	
C1	0·74	0·44 to 1·25	
C2	0·45	0·34 to 0·61	
C3	0·61	0·48 to 0·78	
C4	0·49	0·37 to 0·65	
C5	0·75	0·55 to 1·02	
Random effect			
Animal ID	—	1·53 to 2·17	

odds of receiving a systemic glucocorticoid (95% CI 1·18 to 2·03, P<0·0001) than dogs under 1 year old while dogs over 12 years old had 2·07 times the odds (95% CI 1·52 to 2·83, P<0·0001). Diagnosis of a skin condition increased the odds of receiving glucocorticoid therapy 6·75 (95% CI 5·81 to 7·85, P<0·0001) times. Male dogs had 1·16 (95% CI 0·99 to 1·35, P=0·0650) times the odds of treatment compared with female dogs. Dog consultations at Clinic C2 had 0·45 (95% CI 0·34 to 0·61, P<0·0001) times the odds of glucocorticoid therapy compared with Clinic A.

DISCUSSION

Overall, systemic glucocorticoid prescribing was common (15·32% of consultations) in accordance with the importance of glucocorticoid therapy (Ferguson and others 2009) but lower than the 20% recorded by Hill and others (2006) for skin conditions. Although statistically significantly different, the clinical significance of the prescribing frequency variation between cats (16·68%) and dogs (14·55%) would appear limited. Glucorticoid-treated cats were significantly more likely to receive parenteral format treatment than dogs, possibly because pill administration is difficult for many owners (Norsworthy 2006). Behrend (1997) recommended avoidance of repository glucocorticoid therapy for dogs but this study found that 26·57% of dog parenteral treatments employed long-acting formulations.

Both parenteral and oral glucocorticoid dosages were higher for cats than dogs, in agreement with general recommendations (Ramsey 2007, NOAH 2010) and reflecting more frequent side effects in the dog than the cat (Lowe and others 2008). A systematic review of oral glucocorticoid therapy for canine atopic dermatitis reported adverse drug events in 10 to 81% of dogs treated (Olivry and others 2010), while glucocorticoid treatment is typically well tolerated by cats (Lowe and others 2008). Veterinarians were more likely to use high dose levels for parenteral than for oral doses. This may result from the relatively high drug concentrations and small volumes of parenteral preparations or perceived reduced side effects from single parenteral doses in comparison with repeated oral dosing regimens. Although glucocorticoid recommended doses vary greatly between specific conditions, this study used general cut-points to provide an overall description of dosing regimens. No attempt was made to evaluate the appropriateness of dosages for the underlying conditions.

Risk factor analysis for systemic glucocorticoid administration was carried out separately for cats and dogs because of differences in pharmacodynamics (Lowe and others 2008), pragmatic

approach to drug administration (Norsworthy 2006) and veterinary perception of drug-safety differences between the species (Sturgess 2002).

Pathophysiological indication was highly predictive for both species, as would be expected from the widespread use and varied clinical indications for glucocorticoids (Sturgess 2002). Cats with neoplastic conditions had over four times the odds of glucocorticoid therapy compared with inflammatory conditions. Glucocorticoids at anti-inflammatory dose levels provide palliative management of certain neoplasms, whereas even higher doses may also have a direct antineoplastic effect on tumours such as lymphoma (LeCouteur 2007). There was a surprisingly high level of glucocorticoid use in conditions where an apparent indication for glucocorticoid use was not recorded for both cats and dogs. Glucocorticoids can induce non-specific reduction of clinical symptoms but Sturgess (2002) advises that corticosteroids should be reserved for specific purposes.

Skin disease increased treatment odds threefold in cats and sixfold in dogs, likely reflecting a perceived underlying inflammatory component to many skin conditions as well as demands by owners for rapid relief of clinical signs (pruritus, erythema) (Olivry and Mueller 2003).

Advancing age was a significant predictor for both cats and dogs. Reduced glucocorticoid therapy for kittens and puppies reflects good practice; glucocorticoids suppress growth hormone and somatostatin-mediated osteoblast function (Sturgess 2002). Increasing occurrence of conditions with a glucocorticoid therapy indication as animals age could explain this age-related trend; a study on Swedish dogs showed that 10-year-old dogs had twice the odds of inflammatory conditions and 14 times the odds of neoplastic conditions as 2-year-old dogs (Bonnett and Egenvall 2010). The finding that male cats had lower odds of glucocorticoid treatment while male dogs had higher odds is difficult to explain biologically. "Clinic identity" was a significant risk factor for both cats and dogs. Clinics comprising an overall practice group were more comparable in prescribing patterns than the stand-alone clinics, possibly demonstrating shared prescribing determinants within the multi-centre practice. These findings suggest that systemic glucocorticoid prescribing practices are determined less by overall veterinary medical diktat and more by practice protocol, clinical experience and personal opinion. Formal evidence-based guidance on the therapeutic use of systemic glucocorticoids in clinical practice may improve clinical outcomes whilst minimising drug-related side effects.

Several limitations are worth noting. The study included only consultations with pharmacotherapy to allow a robust "consultation" definition and will therefore over-estimate overall glucocorticoid prescribing levels. Coprescribing of alternative anti-inflammatory/immunosuppressive agents or topical glucocorticoid products was not examined. Veterinarians recorded the most important diagnoses pertaining to each specific visit but may not have recorded underlying comorbid conditions which could have contributed to the recorded high level of usage for cases without an apparent clinical indication. Practice selection was a convenience sample, potentially introducing selection bias and limiting generalisation of the results.

The study validated a "proof of concept" that primary veterinary practice clinical data can be successfully merged to create an effective research database. Although over 30,000 cat and dog consultations were included, an increased number of participating practices will be required to robustly generalise results.

CONCLUSIONS

This study described prescribing practices and evaluated risk factors for systemic glucocorticoid pharmacotherapy in a large cohort of UK cats and dogs attending three practices and validated the role of electronic patient records for research. Systemic glucocorticoid therapy is common. Pathophysiological indication, advancing age, sex, skin conditions and clinic attended were significant risk factors for systemic glucocorticoid therapy for both species. Further studies to explore the wide variations in prescribing behaviour across practices could help optimise prescribing and identify factors affecting drug use itself and also drug use patterns that fall outside recommended prescribing behaviour.

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Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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