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Owner compliance in canine epilepsy

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Abstract

Background: Poor medication compliance by human epilepsy patients is one of the leading causes of treatment failure and increased seizure frequency. The aim of this cross-sectional study was to analyse owner compliance in pharmacological treatment of canine idiopathic epilepsy and to identify factors associated with poor compliance.

Methods: The number of antiseizure drug tablets was recorded to determine if the patient received sufficient tablets to cover the time period between prescriptions and to assess compliant prescription cycles. Additionally, compliance was assessed by an online survey of owners.

Results: For the prescription monitoring data from 94 cases from three small animal practices in the United Kingdom revealed an overall median compliance of 56%. Thirty-three per cent of owners were ≥80% compliant, while 21% were 100% compliant. During a non-compliant prescription cycle, a patient missed a median of 6 days (0.11-519 days) of treatment. Patients on polytherapy had higher compliance rates than on monotherapy ($p = 0.031$). The survey (229 respondents from online canine epilepsy groups) showed that low daily dosing was associated with better compliance ($p = 0.049$).

Conclusion: Owner compliance was subpar in this study and could represent a significant issue in epilepsy management, which needs to be considered by veterinary surgeons when treating canine epilepsy.

INTRODUCTION

A plethora of antiseizure drugs (ASDs) have been tested in the search for a more efficacious and tolerable canine epilepsy treatment.[1–4] The percentage of dogs reported to be treated successfully for canine epilepsy (defined by achieving seizure cessation -also known as remission) ranges from 6–85%,[1] with randomised controlled prospective studies reporting the highest remission rate (85%).[5] This wide range in reported outcomes can in part be explained by the variable design of ASD efficacy studies. However, in prospective trials owners are aware that their caregiving is being observed and documented, which can result in a more consistent adherence to medication regimen. This observer effect, also known as the Hawthorne effect, should be considered when evaluating clinical studies.[6] There is a limited choice of ASDs available for canine epilepsy, and excellent compliance by owners is essential to ensure that therapy can be as effective as possible and to reduce the risk of drug resistance. Nearly 40% of dogs with epilepsy are euthanised due to poor seizure control.[7,8]

Compliance is defined as how closely a patient follows their prescriber's recommendations.[9] In human medicine, the term 'compliance', which is characterised by 'obedience', is nowadays less frequently used than the term 'adherence', both describing different perspectives of the same phenomenon but with latter focusing more on maintaining patient's independence, autonomy and free will to adhere or not to adhere to a given medical protocol. The term 'adherence' reflects independence in decision making for once own health issues.[10–12] In veterinary medicine, the term 'adherence' cannot be applied easily. The owners of the diseased pet are not the individuals suffering from the disease directly, but do provide the treatment and are the carer of the sick animal. Due to the semantic discrepancy and the intermediary role of owners, the term 'compliance' was used in this study.

Compliance has been identified as one of the main factors of inadequate seizure control in human medicine.[13–15] Good medication compliance is crucial to successfully managing epilepsy to ensure that plasma drug concentrations reach steady state and are

within the drug's therapeutic range. With ASDs such as phenobarbital, a steady state in the therapeutic range can be relatively easily achieved. Phenobarbital has a 24-hour half-life in dogs and will require five half-lives for the ASD to reach a steady state in 97% of patients.[16] However, drugs with a shorter half-life such as levetiracetam (around three to four hours in dogs[17]) can drop below a therapeutic level despite dosing every eight hours. Due to the short half-life and duration of the dosing interval, the concentration will decrease over 75% during this eight-hour period so inconsistent dosing, either missed or delayed doses, leads to suboptimal drug concentrations and can quickly result in breakthrough seizures.[18]

There have been several studies in the veterinary literature on medication compliance[19–21] but none on compliance with ASDs for canine epilepsy. However, numerous studies have been conducted in human patients. Two recent reviews found compliance to be approximately 60%.[22,23] Several studies have highlighted that human patients with poor medication compliance are more likely to experience a higher seizure frequency than patients with good compliance.[15,24] Cramer et al assessed 661 respondents in a postal survey and found that 45% of patients who missed a dose of their ASDs had seizures shortly after, emphasising the importance of good compliance for reducing seizure frequency.[25] This also highlights how fine the balance of maintaining therapeutic drug concentrations in patients with epilepsy is.

Unfortunately, poor compliance makes it difficult to distinguish between true drug-resistant epilepsy and pseudo-refractory epilepsy without honest discussion with the owner. Cramer et al reported that only 32% of human patients reported missed doses to their physician.[25] Kutlu et al identified that poor compliance was the reason for a pseudo-refractory condition in 40% of the human epilepsy patients presenting with presumed refractory epilepsy.[26] Following intervention to help improve compliance, the patients in this study were seizure free for at least 1 year.

Similarly, pseudo-refractory epilepsy could lead to unnecessary stress to canine patients with a heightened risk of breakthrough seizures, more frequent veterinary visits and increased strain on the owner due to poor seizure control. It could also lead to a needless change in medication with stronger drugs, polytherapy and/or higher dose given. This comes at an increased financial cost to the owner and a higher incidence of side effects such as ataxia and sedation.[27–29] It was recently demonstrated that polytherapy with ASDs in dogs leads to reduced trainability indicating a negative effect on cognitive functions,[30] a phenomenon also demonstrated in humans.[31]

In people with epilepsy, the reasons for poor compliance have been associated with financial constraints, socio-cultural issues, a negative patient-physician relationship, apparent side effects of the medication and poor understanding by the patient of the condition and treatment. All of these factors could also influence owners of dogs with epilepsy.[22–24,32–34] Several human studies about different medical conditions have found that compliance decreases with monotherapy and increases doses per day so fewer daily doses are preferable.[35–40] High daily dosing also reduces medication compliance in veterinary medicine.[20,41] Unfortunately, multiple daily dosing might be unavoidable with ASDs such as levetiracetam which requires an eight-hour dosing schedule due to its short (3- to 4-hour) half-life.[17] Hovinga et al found that 72% of human patients with poor seizure control had alterations made to their therapeutic plan to try to improve compliance.[24]

As this area has not been previously studied in canine epilepsy patients, the aim of this study was to assess ASD compliance in a population of dogs with idiopathic epilepsy and to identify risk factors associated with poor owner compliance.

MATERIAL AND METHODS

Prescription analysis

Two data collection methods were used to provide objective and subjective data to assess compliance. The first method involved analysing prescriptions of dogs diagnosed with idiopathic epilepsy from patient case records from several practices in the United Kingdom. For the case records to be included, the patients had to meet three criteria. They had to have:

(i) Tier I diagnosis of idiopathic epilepsy according to the criteria of the International Veterinary Epilepsy Task Force (IVETF),[42]
(ii) Three or more recorded prescriptions, indicating long-term ASD use, and
(iii) No evidence of requesting written prescriptions to collect medications elsewhere.

Prescriptions from a time period of 2 years or since the patient first received ASD medications if the time period was less than 2 years were reviewed. Compliance was calculated by recording the time interval (days) between ASD medication prescription refills, the number tablets dispensed at each prescription and calculating the number of tablets required for that time interval if compliance was 100%, that is no tablets were missed. If there appeared to be an insufficient supply of tablets during a time interval between prescription refills, previous prescriptions were assessed to see if the owner would have had sufficient tablets at home to cover the missed doses. A prescription was deemed non-compliant if the number of tablets required between prescriptions was greater than the number of tablets supplied by at least 0.5 tablets. Compliance was calculated as a percentage of compliant prescription cycles out of the total number of prescription cycles.

TABLE 1 Key questions extracted from the online survey. The survey was loosely based on the study of Hovinga et al with the majority of the questions being newly created[22]

Focusing on	Questions (extract)
Clinical signs of epilepsy	'Approximately how many seizures has your dog experienced in the past 3 months?'
Medication	'How many times a day do you give these (antiseizure) medications?'
	'How many tablets/capsules of each medication does your dog receive per day?'
Response to medication	'Has the antiseizure medication reduced the number of seizures your pet has?'
	'Are you satisfied with your pet's medication and control of their epilepsy?'
Compliance	'Has your pet ever missed a dose of their antiseizure medication?'
	'How many doses has your pet missed in the past 3 months/since the start of their epilepsy treatment?'
Veterinary help and education	'Apart from prescription collections, how often do you visit your vets to discuss your pet's progress and epilepsy medications?'
	'When your pet was first diagnosed with epilepsy, how well did your veterinarian explain the purpose of the medications your pet would be taking?'

Compliance survey

The second method to assess compliance was via an online survey hosted on SurveyMonkey (www.surveymonkey.co.uk). Owners of epileptic dogs were recruited via advertisements to canine epilepsy groups on social media. Data were collected between July and October 2016. Owners were eligible to be included in the study if patients met the following criteria:

(i) Tier I diagnosis of idiopathic epilepsy according to the IVETF,[42] and
(ii) Receiving ASDs for treatment of seizures.

The survey consisted of 49 questions focusing on several aspects of epilepsy some of which are listed in Table 1. The survey was loosely based on the study of Hovinga et al with the majority of the questions being newly created.[24] Owners were considered fully compliant if they never missed a dose since the start of epilepsy treatment of their pet.

Ethics approval

Consent was gained via a statement in the opening page detailing the storage and use of their data in accordance with the United Kingdom's General Data Protection Regulation (GDPR). The study was approved by the local ethics committee (approval number RVC Animal Welfare and Ethics Committee 2016-U15), and the methods were carried out in accordance with the approved guidelines.

Statistical analysis

The data were analysed with GraphPad Prism (GraphPad Software Inc., San Diego, CA). Mann-Whitney U-tests were used to compare compliant and non-compliant groups in terms of potential risk factors in the prescription and survey data. All tests were two-sided, and a p-value of <0.05 was deemed significant. Data are presented as mean ± standard deviation (SD), or median (range), where appropriate.

RESULTS

Prescription analysis

Ninety-four cases of canine epilepsy from three first opinion, small animal practices in the United Kingdom were included in the study. Fifty-three per centof the dogs were male with a median age of 83 months (range 12–216 months). One patient did not have an age listed. Eighty-four percent of the cases were uninsured. The median number of prescriptions per patient was 12 (range 3–24). The median number of non-compliant prescriptions per patient was five (range 0–18). The median time period between prescription collections was 32 days (range 1–529 days). The median number of tablets per prescription was 60 (range 4–1404). The number of tablets that should have been used per prescription cycle if compliance was 100% was 80 (range 2–1539).

Overall median compliance was 56% (range 0–100%). The percentage of cases with a compliance rate of 80% or greater was 33%. Only 21% of owners were 100% compliant. For non-compliant prescription cycles, the median number of days the patient did not receive treatment for was 6 days (range 0.11-519 days), and they missed a median of 13 tablets (range 0.5-711). Patients receiving one ASD (monotherapy) were found to have a lower compliance rate than patients receiving either more than one ASD (polytherapy) or another medication for concurrent disease ($p = 0.031$). There was no significant association found between compliance and the total number of tablets a patient received per day ($p = 0.61$), and compliance of the uninsured and insured population was not found to be significantly different ($p = 0.98$) (Table 2).

Compliance survey

There were 269 respondents to the survey. Forty responses were incomplete and therefore excluded from the study resulting in 229 analysable responses.

TABLE 2 Associations between potential compliance risk factors and actual compliance in the prescription data

Compliance factors	Response	Median compliance percentage (range)	p-Value
Number of medications	One medication (n = 70)	50% (0–100)	0.031
	Two or more medications (n = 24)	75% (0–100)	
Total number of tablets per	One or less tablets (n = 14)	64.8% (0–100)	0.61
Day	1.5 or more tablets (n = 80)	56.4% (0–100)	
Insurance	Insured (n = 15)	70% (0–100)	0.98
	Not insured (n = 79)	55.6% (0–100)	

TABLE 3 Associations between potential compliance risk factors and actual compliance in the survey data

Survey question	Compliant-median (range)	Non-compliant-median (range)	p-value
Number of doses per day (n = 229)	2 (0–4)	2 (1–4)	0.049
Seizure frequency over past 3 months (n = 228)	3 (0–75)	2.5 (0–24)	0.46
Total number of tablets per day (n = 229)	4 (0–14)	4.5 (1–16)	0.39
Number of vets involved in patient's therapy plan (n = 219)	2 (1–5)	2 (1–5)	0.85
Frequency of patient visits at their vet to discuss epilepsy (n = 205)	6 months (0–12 months)	6 months (0–12 months)	0.77
Survey questions	**Response**	**Median number of doses missed (range)**	**p-value**
Seizure reduction (n = 203)	Over 50% reduction in seizures (n = 139)	0 (0–21)	0.74
	Less than 50% reduction in seizures (n = 64)	0 (0–21)	
Number of medications in protocol (n = 229)	Receiving one ASD (n = 94)	0 (0–21)	0.53
	Receiving more than one ASD (n = 135)	0 (0–21)	
Veterinary explanation to owner about epilepsy and medications (n = 229)	≤50% (n = 80)	0 (0–12)	0.12
	>50% satisfied (n = 149)	0 (0–12)	

The majority of respondents were female (94%), aged between 40 and 69 years old (72%), with 52% of responses from the United Kingdom and 36% from the USA. The patients had a median age of 62 months (6-511). The median time since starting treatment was 20 months (0–156 months). The majority of the patients were male (68%), neutered (81%) and uninsured (67%). Fifty-nine per cent of patients received more than one ASD (polytherapy).

Fifty-six per cent of owners reported that they were 100% compliant. All participants reported compliance of over 80%. Owner-reported compliance decreased with an increased number of doses per day ($p = 0.049$). There was no significant relationship found between owner-reported compliance and seizure frequency ($p = 0.46$), polytherapy ($p = 0.53$), the total number of tablets per day ($p = 0.39$) or percentage reduction in seizures since starting treatment ($p = 0.74$). There was no significant association found between owner-reported compliance and how frequently the patient visited the veterinarian ($p = 0.77$), how many different vets have been involved in the patient's management ($p = 0.85$) or how well the owner felt his or her veterinarian had explained their pet's condition and medication ($p = 0.12$) (Table 3). Almost one quarter (23%) of respondents had altered their pet's therapy protocol since ASD treatment started without speaking to their veterinarian.

DISCUSSION

This is the first study to explore medication compliance in canine epilepsy patients and has identified strikingly low levels of ASD compliance from their human carers. The overall median compliance assessed by prescription analysis was 56%, with only one out of three owners having a more than 80% compliance rate. Just one in five owners was found to be fully compliant with their dog's prescribed ASD regimen. Malek et al recognised that a compliance rate below 80% impacts the success of therapy in human epilepsy patients, so these statistics are alarming.[22] Poor compliance can result in lowered plasma drug concentration levels and reduce the effectiveness of the ASD, leading to breakthrough seizures and pseudo-refractory epilepsy.[26,43]

Chronic diseases such as epilepsy, in which treatment is usually conducted in a lifelong and symptomatic manner, and in which clinical signs may be absent over a long period of time, are prone to non-compliance.[29] The mean number of days a patient in a non-compliant prescription cycle did not receive treatment was 6 days, and the median number of tablets missed per cycle was 13 tablets. It is impossible to tell at which stage of the prescription cycle patients missed doses or whether the missed doses were either isolated or grouped together. It is also impossible to tell whether the tablets were given at appropriate time intervals. A recently conducted meta-analysis of 13 studies in human paediatric epilepsy using objective assessment methods (e.g. serum drug levels, dried blood spot, pill count, electronic monitoring) revealed an overall compliance rate of 58%.[44] This comparable compliance rate to our study may be an example of the commonality between veterinary and paediatric epileptology as both groups of patients have no or limited abilities to communicate and comprehend their situation and are reliant on responsible persons ('carers') who assume the main part of communication with the doctor, administer the medications and, therefore, bear the main responsibility for good medication compliance. However, one important difference in human paediatric medicine versus veterinary medicine is that extent of a patient's independence and comprehension for their medical conditions and doctor's recommendations increases with age in children. Therefore, compliance assessment and interpretation are likely more complex due to temporally variable and partially unsteady factors related to economic, educational social, and interpersonal characteristics in parents, children and adolescents. Management of owner compliance by veterinarians is likely to be simpler, but from the results of this study clearly has room for improvement.

In our study there was a significant association found between compliance and polytherapy, indicating that compliance increases when patients receive multiple ASDs as part of their management plan. This relationship has been documented in previous studies of ASDs in human patients. It has surmised that this link is seen in patients with poorly controlled epilepsy, as they will be receiving various ASDs and are more likely to adhere to their protocol. This could be due to their appreciation of the importance of ASDs and their effects to help improve their own quality of life.[38] However, a few studies have noted a negative association between compliance and ASD polytherapy[45,46] arguing that polytherapy may lead to more severe side effects, to dissatisfaction with the treatment regime and, finally, to decreased compliance.[47,48] However, those factors might play a lesser role in veterinary medicine as the spectrum of different ASDs used during polytherapy and, consequently, of the resulting side effects is relatively narrow. Even though polytherapy in canine epilepsy was reported to exert increased cognitive impairments compared to monotherapy[30] and that the ASDs side effects, sedation and ataxia, affect the quality of life of owners significantly,[49] it is possible that the severity of side effects in animals cannot always be perceived adequately by owners nor vets. This could be a factor why polytherapy does not reduce owner compliance.

The survey data revealed that non-compliance increases with multiple daily dosing, which has been also documented in human medicine[35–37,39,40] and in other diseases in veterinary medicine as well.[20,41] Multiple dosing schedules demand a rigid schedule from owners, which may be more inconvenient and may impinge upon their lifestyle. In addition, frequent administrations of oral medication to animals may be a demanding and frustrating challenge to the owner, especially if the patient is reluctant to swallow the medication and if medication is not able to be given with food.[29] Furthermore, it may seem 'excusable' to the owner to omit one or two doses of an ASD in a high-frequency dosing schedule, as clinical signs are not necessarily immediately obvious compared to other pathological conditions. In low-frequency dosing schedules, however, maintenance of appropriate therapeutic coverage is more prone to enhanced variability in serum drug concentration due to higher dosages over longer time periods. Consequently, the potentially higher risk of breakthrough seizures due to a single omitted dose in low-frequency dosing schedules may have a greater impact on seizure control than occasional missed doses in a high-frequency schedule.[50] These observations demonstrate how important clear communication is between the owner and the veterinarian for successful canine epilepsy management.

There was no significant relationship between seizure frequency and compliance in the survey data in contrast to the significant negative association that has been reported in human epileptic patients.[15,24] There could be numerous and varied causes for this lack of negative association which were not further explored in this study. One cause could be that owners with dogs who frequently seizure aim to adhere to their protocol as closely as possible to prevent further seizures from occurring. A higher seizure frequency could lead to an increased sensibility of the owners in terms of solicitude and responsibility for guaranteeing an adequate quality of life in pets. Another possibility for the lack of association could be due to the survey population in this study. The respondents are members of canine epilepsy groups who can discuss their concerns with other owners and have increased knowledge of the importance of ASDs, increasing the likelihood of strict adherence to their dog's protocol.

The collection of compliance data via an online, owner-reported survey format is a potential limitation of the second part of this study. These data are potentially limited by recall errors. The survey featured questions such as total missed doses since the start of ASD treatment and the seizure frequency over the last 3 months, and it may be difficult for owners to recall the exact number of missed doses and seizures, especially as the median time since treatment

began was 20 months. In addition, responses are liable to social desirability bias, the tendency of some respondents to report an answer in a way they deem to be more socially acceptable than would be their 'true' answer.[51] This may exacerbate existing issues with owner estimation of compliance and may contribute to veterinarians not recognising intermittent underdosing as a factor in poor seizure control. Adams et al reported that compliance is often over-estimated by up to 27% by owner self-report.[52] In our study, the compliance rate reported by owners in the survey was higher than calculated by analysis of prescriptions, with a 67% difference in the >80% compliance rate. Overestimation in self-reported compliance has been documented in other veterinary studies. In one study, 71% of owners treating dogs claimed perfect compliance (both dose count and dose time), while electronic monitoring revealed that only 32% of owners were 100% compliant.[19] Adams and colleagues reported similar result with 74% compliance reported by owner self-reports versus 25% from electronic monitoring data.[41] In contrast, only 56% of owners in our study claimed 100% compliance. It is noteworthy that, in contrast to our experimental setup, those studies explored acute short-term antimicrobial treatments. Variable factors like chronicity, quality and clinical manifestations of different diseases with their associated treatments could influence compliance rate and honesty of owner reports. In addition, the quality of relationship between veterinarian and client is likely to change over the time course of the co-management of a chronic disease such as epilepsy, which may influence owner honesty regarding their compliance.

There are a variety of subjective and objective methods available to assess compliance including client self-report, pill counts, electronic pill bottle monitoring and physician estimate of compliance.[29] In addition to electronic and self-reporting data, Barter et al and Adams et al used pill count methods (10% vs 80% of perfect compliance, respectively) which we applied similarly by analysing prescription cycles (21% of perfect compliance).[19,41] The variability across studies concerning this objective data set could be explained by methodological differences. Such differences in clinical study design make it very difficult to compare data and to assess compliance. Electronic monitoring of opening and closing pill containers represents the benchmark of compliance assessment so far.[53] However, it is very expensive and not free from susceptibilities, since it cannot be guaranteed that patients received the right dosage at the right time.[29] Current methods for compliance assessment have different advantages and disadvantages and are not suited to measure true compliance. Nevertheless, they provide good approximate values. In this study we used a combined approach of collecting and assessing subjective and objective data. Farrukh et al and Anghel et al highlighted the importance of combining subjective and objective assessment tools in order to obtain more realistic estimates about actual levels of compliance and more information about compliance-related issues.[23,53]

Compliance not only refers to missed doses but also if owners actively alter their pet's protocol without speaking to their veterinarian. It is hard to identify if an owner has altered or lowered their pet's dose when checking prescriptions, which could result in owners not collecting prescriptions on time. This was a relatively common finding in this survey, with 23% of owners admitting to altering their pet's medication regimes, and potentially more who were unwilling to report this honestly. Problems with veterinarian-client communication have been reported in other areas of epilepsy management. In a recent study of the use of dietary supplements to manage canine epilepsy, less than one fifth of owners consulted their vet on the use of supplements.[54] In a study of focal seizures in canine epilepsy, owners reported they were less likely to report focal seizures to their vets than generalised seizures.[55] As such, veterinarians may not get a full picture of the efficacy of the treatment they prescribe. Promoting better veterinarian-client communication in canine epilepsy management more widely should be a priority in veterinary medicine.

CONCLUSION

This is the first study to assess owner compliance in veterinary epileptology. With an overall compliance rate of just 56%, and only 33% of owners having a compliance rate greater than 80%, owners need to be made aware of the importance of consistent therapy. In addition to providing important insights into medication compliance in patients with canine epilepsy, this study is the first in the veterinary literature to document medication compliance in a long-term, medically managed disease. Further studies into compliance in veterinary medicine should focus on methods and interventions to help improve compliance.

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REFERENCES

1. Charalambous M, Brodbelt D, Volk HA. Treatment in canine epilepsy – a systematic review. BMC Vet Res. 2014;10:257.
2. Bhatti SFM, de Risio L, Muñana K, Penderis J, Stein VM, Tipold A, et al. International Veterinary Epilepsy Task Force consensus proposal: medical treatment of canine epilepsy in Europe. BMC Vet Res. 2015;11:176.

3. Charalambous M, Shivapour SK, Brodbelt DC, Volk HA. Antiepileptic drugs' tolerability and safety – a systematic review and meta-analysis of adverse effects in dogs. BMC Vet Res. 2016;12:79.
4. Podell M, Volk HA, Berendt M, Volk HA. 2015 ACVIM small animal consensus statement on seizure management in dogs. J Vet Intern Med. 2016;30:477-90.
5. Boothe DM, Dewey C, Carpenter DM. Comparison of phenobarbital with bromide as a first-choice antiepileptic drug for treatment of epilepsy in dogs. J Am Vet Med Assoc. 2012;240:1073-83.
6. De Amici D, Klersy C, Ramajoli F, Brustia L, Politi P. Impact of the hawthorne effect in a longitudinal clinical study. Control Clin Trials. 2000;21:103-14.
7. Berendt M, Gredal H, Ersbøll AK, Alving J. Premature death, risk factors, and life patterns in dogs with epilepsy. J Vet Intern Med. 2007;21:754-9.
8. Arrol L, Penderis J, Garosi L, Cripps P, Gutierrez-Quintana R, Gonçalves R. Aetiology and long-term outcome of juvenile epilepsy in 136 dogs. Vet Rec. 2012;170:335.
9. Horne R, Weinman J, Barber N, Elliott R. Concordance, adherence and compliance in medicine taking. London, UK: National Co-ordinating Centre for NHS Service Delivery and Organisation; 2005.
10. Lutfey KE, Wishner WJ. Beyond "compliance" is "adherence". Improving the prospect of diabetes care. Diabetes Care. 1999;22:635-9.
11. Aronson JK. Compliance, concordance, adherence. Br J Clin Pharmacol. 2007;63:383-4.
12. De las Cuevas C. Towards a clarification of terminology in medicine taking behavior: compliance, adherence and concordance are related although different terms with different uses. Curr Clin Pharmacol. 2011;6:74-7.
13. French J. The long-term therapeutic management of epilepsy. Ann Intern Med. 1994;120:411–22.
14. Lannon SL. Using a health promotion model to enhance medication compliance. J Neurosci Nurs. 1997;29:170-8.
15. Jones RM, Butler JA, Thomas VA, Peveler RC, Prevett M. Adherence to treatment in patients with epilepsy: associations with seizure control and illness beliefs. Seizure. 2006;15:504-8.
16. Boothe DM. Anticonvulsant therapy in small animals. Vet Clin North Am Small Anim Pract. 1998;28:411-48.
17. Isoherranen N, Yagen B, Soback S, Roeder M, Schurig V, Bialer M. Pharmacokinetics of levetiracetam and its enantiomer (R)-α-ethyl-2-oxo-pyrrolidine acetamide in dogs. Epilepsia. 2001;42:825-30.
18. Beasley MJ, Boothe DM. Disposition of extended release levetiracetam in normal healthy dogs after single oral dosing. J Vet Intern Med. 2015;29:1348-53.
19. Barter LS, Maddison JE, Watson ADJ. Comparison of methods to assess dog owners' therapeutic compliance. Aust Vet J. 1996;74:443-6.
20. Amberg-Alraun A, Thiele S, Kietzmann M. Study of the pet-owners compliance in a small animal clinic. Kleintierpraxis. 2004;49:359–66.
21. Wareham KJ, Brennan ML, Dean R. Systematic review of the factors affecting cat and dog owner compliance with pharmaceutical treatment recommendations. Vet Rec. 2019;184:154.
22. Malek N, Heath CA, Greene J. A review of medication adherence in people with epilepsy. Acta Neurol Scand. 2017;135:507-15.
23. Farrukh MJ, Makmor-Bakry M, Hatah E, Jan TH. Use of complementary and alternative medicine and adherence to antiepileptic drug therapy among epilepsy patients: a systematic review. Patient Prefer Adherence. 2018;12:2111-21.
24. Hovinga CA, Asato MR, Manjunath R, Wheless JW, Phelps SJ, Sheth RD, et al. Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: Survey of patients with epilepsy and physicians. Epilepsy Behav. 2008;13:316-22.
25. Cramer JA, Glassman M, Rienzi V. The relationship between poor medication compliance and seizures. Epilepsy Behav. 2002;3:338-42.
26. Kutlu G, Erdal A, Gomceli YB, Inan LE. Pseudo-refractory epilepsy. Neurosciences (Riyadh). 2013;18:284–6.
27. Hülsmeyer V, Zimmermann R, Brauer C, Sauter-Louis C, Fischer A. Epilepsy in border collies: clinical manifestation, outcome, and mode of inheritance. J Vet Intern Med. 2010;24:171-8.
28. Thomas WB. Idiopathic epilepsy in dogs and cats. Vet Clin North Am Small Anim Pract. 2010;40:161-79.
29. Maddison JE. Medication compliance in small animal practice. Ir Vet J. 2011;64:39–43.
30. Packer RMA, McGreevy PD, Pergande A, Volk HA. Negative effects of epilepsy and antiepileptic drugs on the trainability of dogs with naturally occurring idiopathic epilepsy. Appl Anim Behav Sci. 2018;200:106-13.
31. Trimble MR. Anticonvulsant drugs and cognitive function: a review of the literature. Epilepsia. 1987;28(s3):S37–S45.
32. Stanaway L, Lambie DG, Johnson RH. Non-compliance with anticonvulsant therapy as a cause of seizures. N Z Med J. 1985;98:150–2.
33. Modi AC, Rausch JR, Glauser MD. Patterns of nonadherence to antiepileptic drug therapy in children with newly diagnosed epilepsy. J Am Med Assoc. 2011;305:1669–76.
34. Getnet A, Woldeyohannes SM, Bekana L, Mekonen T, Fekadu W, Menberu M, et al. Antiepileptic drug nonadherence and its predictors among people with epilepsy. Behav Neurol. 2016;2016:1.
35. Greenberg RN. Overview of patient compliance with medication dosing: a literature review. Clin Ther. 1984;6:592–9.
36. Cramer JA, Mattson RH, Prevey ML, Scheyer RD, Ouellette VL. How often is medication taken as prescribed? J Am Med Assoc. 1989;261:3273–7.
37. Eisen SA, Miller DK, Woodward RS, Spitznagel E, Przybeck TR. The effect of prescribed daily dose frequency on patient medication compliance. Arch Intern Med. 1990;150:1881–4.
38. Buck D, Jacoby A, Baker GA, Chadwick DW. Factors influencing compliance with antiepileptic drug regimes. Seizure. 1997;6:87–93.
39. Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. Clin Ther. 2001;23:1296-310.
40. Wang S, Alfieri T, Ramakrishnan K, Braunhofer P, Newsome BA. Serum phosphorus levels and pill burden are inversely associated with adherence in patients on hemodialysis. Nephrol Dial Transplant. 2014;29:2092-9.
41. Adams VJ, Campbell JR, Waldner CL, Dowling PM, Shmon CL. Evaluation of client compliance with short-term administration of antimicrobials to dogs. J Am Vet Med Assoc. 2005;226:567-74.
42. Berendt M, Farquhar RG, Mandigers PJJ, Pakozdy A, Bhatti SFM, De Risio L, et al. International veterinary epilepsy task force consensus report on epilepsy definition, classification and terminology in companion animals. BMC Vet Res. 2015;11:182.
43. Baker GA, Jacoby A, Buck D, Stalgis C, Monnet D. Quality of life of people with epilepsy: a European Study. Epilepsia. 1997;38:353-62.
44. Yang C, Hao Z, Yu D, Xu Q, Zhang L. The prevalence rates of medication adherence and factors influencing adherence to antiepileptic drugs in children with epilepsy: a systematic review and meta analysis. Epilepsy Res. 2018;142:88–99.
45. Bautista RED, Rundle-Gonzalez V. Effects of antiepileptic drug characteristics on medication adherence. Epilepsy Behav. 2012;23:437-41.
46. Ferrari CMM, de Sousa RMC, Castro LHM. Factors associated with treatment non-adherence in patients with epilepsy in Brazil. Seizure. 2013;22:384-9.
47. Carpay JA, Aldenkamp AP, van Donselaar CA. Complaints associated with the use of antiepileptic drugs: results from a community-based study. Seizure. 2005;14:198–206.
48. Sweileh WM, Ihbesheh MS, Jarar IS, Taha ASA, Sawalha AF, Zyoud Sa'H, et al. Self-reported medication adherence and treatment satisfaction in patients with epilepsy. Epilepsy Behav. 2011;21:301-5.
49. Wessmann A, Volk HA, Packer RMA, Ortega M, Anderson TJ. Quality-of-life aspects in idiopathic epilepsy in dogs. Vet Rec. 2016;179:229.

50. Bialer M. Extended-release formulations for the treatment of epilepsy. CNS Drugs. 2007;21:765-74.
51. Callegaro M. Social desirability. In: Lavrakas PJ, editor. Encyclopedia of survey research methods. Thousand Oaks, CA: SAGE Publications, 2008.
52. Adams AS, Soumerai SB, Lomas J, Ross-Degnan D. Evidence of self-report bias in assessing adherence to guidelines. Int J Qual Health Care. 1999;11:187-92.
53. Anghel LA, Farcas AM, Oprean RN. An overview of the common methods used to measure treatment adherence. Med Pharm Rep. 2019;92:117–22.
54. Berk BA, Packer RMA, Law TH, Volk HA. Investigating owner use of dietary supplements in dogs with idiopathic epilepsy. Res Vet Sci. 2018;119:276-84.
55. Packer RMA, Lucas R, Volk HA. Owner perception of focal seizures in canine epilepsy. Vet Rec. 2017;180:150.

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