Evaluation of relationships between pretreatment patient variables and duration of isolation for radioiodine-treated hyperthyroid cats

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Objective—To determine relationships between commonly measured pretreatment variables and duration of isolation for unrestricted dismissal after oral administration of iodine 131 (^{131}I) for treatment of hyperthyroidism in cats.

Animals—149 hyperthyroid cats treated with ^{131}I.

Procedure—A dose of ^{131}I (2.9 to 6.04 mCi [1.07 to 2.23×10^8 Bq]) was administered orally to all cats after hyperthyroidism was confirmed by evaluation of serum total thyroxine (T_4) concentrations. Forward stepwise regression analysis was used to determine whether pretreatment total T_4 concentration, serum creatinine concentration, body weight, age, ^{131}I dose, or concurrent administration of cardiac medication (specifically excluding thyroid suppression drugs) could be used as pretreatment predictors of duration of isolation in a clinical setting. Gamma radiation emission rate at dismissal was < 2.0 mR/h at skin surface over the thyroid region.

Results—Mean ± SD duration of isolation was 16.67 ± 4.42 days (95% confidence interval, 9.2 to 24.1 days). The regression equation for duration of isolation calculated on the basis of dose of ^{131}I (duration of isolation [days] = 3.2 + [2.66 $\times$ mCi – ^{131}I dose]) yielded a regression line with a 95% confidence interval of ± 3.3 days; only 15% of the variation was explained.

Conclusions and Clinical Relevance—A pretreatment estimate for duration of isolation could be determined only from an equation based on the orally administered dose of ^{131}I. These findings suggest that administration of the lowest efficacious dose possible is the dominant factor in reduction of duration of isolation for cats treated with ^{131}I. (*Am J Vet Res* 2003;64:425–427)

Radioiodine treatment as an alternative to medical and surgical treatment for feline hyperthyroidism has been discussed in detail.[1-17] Despite numerous reports of radioiodine treatment, there is no information available on whether the pretreatment total **thyroxine (T_4)** concentration, serum creatinine concentration, body weight, age, and concurrent administration of cardiac medication (specifically excluding thyroid suppression drugs) have any clinically exploitable relationship to the duration of patient isolation (acknowledging that dismissal criteria may vary by facility). Mean duration of isolation is specified by individual treatment facilities on the basis of administration route, dose of radioiodine, past experience of the treatment facility, and interpretation of applicable regulations governing radioactive emission levels (or calculated absorbed dose to household members) at dismissal. Other factors that may influence treatment success and potentially the duration of isolation include renal function and prior treatment with thyroid suppression drugs.[18-20] Because in some facilities the duration of isolation is a factor in not only the cost of the radioiodine treatment but also the duration of separation from the owner, a more precise estimate of projected duration of isolation may influence the owner's treatment decision or at least minimize the uncertainty of the duration of separation. The lower that the maximum γ emissions for dismissal (restricted vs unrestricted) are for a given facility, the more relevant this prediction may become.

The purpose of the study reported here was to determine whether estimates of duration of isolation based on thyroid surface emissions at dismissal can be refined by use of pretreatment parameters in an empirical-dose, constant-route (oral) administration protocol. Specifically, the study was designed to determine whether a significant relationship exists between pretreatment total T_4 concentration, serum creatinine concentration, body weight, age, **iodine 131 (^{131}I)** dose, or concurrent administration of medication (excluding thyroid suppression drugs) and duration of isolation for unrestricted dismissal from the hospital after radioiodine treatment in hyperthyroid cats.

Materials and Methods

Cats and data collection—Cats (n = 149) included in this study were evaluated for hyperthyroidism and, following permission from the owner, were treated with radioiodine at a privately owned inpatient facility. Pretreatment parameters analyzed were serum creatinine concentration, serum total T_4 concentration (not free T_4), body weight, age, and presence or absence of concurrent drug administration by the referring veterinarian for cardiac problems presumed to be secondary to hyperthyroidism. Only total T_4 values from 2 national-regional commercial veterinary clinical laboratories, in which strict quality control measures have been documented, were used in this study. Samples from 97 cats were analyzed by 1 laboratory, and the other laboratory analyzed samples from 52 cats. Statistical analyses were performed on data with and without indexing from each laboratory independently and after pooling the data from both laboratories.

The numeric values for all laboratory parameters, including those for total T_4 concentration, were indexed as a function of the specified reference range for that parameter in that laboratory. The indexing process consisted of setting all individual values for each parameter to 1.0, if the value was

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within the specified reference range for that laboratory. If a value exceeded the upper limit of that laboratory's specified reference range, it was divided by the maximum reference limit value and expressed as a value > 1.0. Similarly, if a value was less than the lower reference limit of that laboratory's reference range, the value was divided by the minimum reference limit value and expressed as a value < 1.0. Thus, the resulting indexed values for all parameters were intended to minimize any influence caused by the use of 2 laboratories.

Treatment—None of the cats were receiving concurrent thyroid suppression medications, and all had a minimum withdrawal period of 2 weeks from these medications, if applicable. Each cat was treated with 1.07 to 2.23 $\times 10^8$ Bq (2.9 to 6.04 mCi) of ^{131}I orally in a gelatin capsule and isolated until γ radiation emissions were < 0.00000026 coulomb/kg/h (2.0 mR/h) at the skin surface immediately adjacent to the thyroid glands. The activity in the gelatin capsule was calibrated from a commercial source to be given to the cat at a specific time. The typical dose was 5.0 mCi/cat given on an empirical basis. Adjustment of the ^{131}I dose included the option for clinical and qualitative judgment by the senior author (RCWF) after owner consultation and examination of the cat. Some dosage variation occurred because of the timing of the isotope delivery to the facility and the physical administration. No specific calculations were performed involving body weight, T_4, or any other variables. However, with increasing experience during the course of the study, smaller doses (eg, 3.0 to 4.0 mCi) were given to smaller cats (eg, 2.0 to 3.0 kg).

Radiation measurement—Radiation was detected with a calibrated Geiger-Mueller instrument.[a,b] Radiation emission levels from the cats were checked at least every other day during the initial part of the isolation and then daily as needed to define the time (within ± 1 day) when each cat's γ emission rate at skin surface was less than Nuclear Regulatory Commission guidelines[21] for an unrestricted area (potential γ radiation dose < 0.02 **millisievert [(mSv)]**/h from external sources). We conservatively interpreted this for the cats (considered the external source to their owners) as < 2.0 mR/h at skin surface over the thyroid region at dismissal from the hospital (acknowledging that millisievert is a unit of absorbed dose whereas coulomb per kilogram and milliroentgen are units of exposure).

Statistical analyses—Pretreatment numeric values (serum creatinine concentration, serum total T_4 concentration, concurrent nonthyroid medication [eg, β adrenergic blocker, afterload reduction drug] administration, age, ^{131}I dose, and body weight) reported from the laboratories and those pretreatment values after indexing were used to predict the duration of isolation (days) by use of a forward stepwise linear regression analysis.[c] This analysis included all of the described parameters as independent variables; duration of isolation was the dependent variable. For a variable to be included in the stepwise linear regression analysis, the probability of the F-value being 0 had to be < 5.0%. For a variable to then be excluded from the stepwise linear regression analysis, the probability of the F-value being 0 had to be > 10.0%. To be considered significant, the outcome of the derived relationship between an individual variable and duration of isolation time (as well as any derived prediction equation for duration of isolation) had to have a probability that the null hypothesis was true (ie, there was no association among the studied parameters) of < 5.0% ($P < 0.05$).

Results

One hundred forty-nine cats ranging from 7 to 18 years of age were studied. Mean ± SD age of the cats was 12.9 ± 2.28 years. Mean ± SD weight of the cats before treatment was 4.12 ± 1.2 kg (9.1 ± 2.6 lb; range, 2.2 to 8.2 kg [4.8 to 18.0 lb]). There were 86 (57.7%) females or spayed females and 63 (42.3%) males or neutered males. Whether the cat was spayed, neutered, or sexually intact was not recorded in the database, but the cats typically were not sexually intact. Most of the cats were domestic shorthair (n = 89; 59.7%), but there were domestic mediumhair (24; 16.1%), domestic longhair (16; 10.7%), and Siamese/Siamese-cross (10; 6.7%) in the group. Other breeds comprised only 6.8% of the cats. Of the 149 cats, 38 were known to be receiving cardiac-related medication. One hundred ten cats were known not to be receiving cardiac-related medication; for 1 cat, this information was incomplete.

Mean dose administered to the cats was 4.99 ± 0.48 mCi (range, 2.9 to 6.07 mCi). Duration of isolation ranged from 10 to 38 days; mean ± SD duration of isolation was 16.67 ± 4.42 days (95% confidence interval, 9.2 to 24.1 days). Mean indexed pretreatment total T_4 concentration was 2.45 ± 1.4 mg/dL (range, 1.1 to 14.9 mg/dL). Mean indexed pretreatment serum creatinine concentration was 0.99 ± 0.14 mg/dL (range, 0.42 to 1.84 mg/dL). Only 1 independent variable (^{131}I dose) was sufficiently significant to be included in any of the linear regression analyses. The resulting equation from the pooled, indexed laboratory data was

$$T \text{ (duration of isolation [days])} = C + [b \times {}^{131}\text{I dose (mCi)}];$$
$$\text{analysis of data yielded } T = 3.2 + [2.66 \times \text{mCi–I}^{131}]$$

where C is 3.2 with a SE of 2.67, and b is 2.66 with a SE of 0.52.

This equation, although significant, had an adjusted R^2 of 0.143. The minimum 95% confidence limit from this predicted duration of isolation equation was ± 3.35 days from the predicted line. If the ^{131}I dose was removed from the list of independent variables and the stepwise linear regression performed again, of all other independent variables, only the serum total T_4 concentration was sufficiently significant (F-value probability, < 4.6%) to be entered in an equation; however, the adjusted R^2 for that equation was 0.02. Prediction equations based on separated (by laboratory) and pooled (across the 2 laboratories) laboratory data that were not indexed and the separated, indexed laboratory data yielded the same conclusion, although with less explanation of the variation and somewhat different equation coefficients.

Discussion

Based on results of this study, refinement of predictions of duration of isolation before treatment with ^{131}I in hyperthyroid cats is possible to a limited extent. Although a significant duration of isolation prediction equation was developed, < 15.0% of the variation in duration of isolation was explained. However, the ± 3.4-day span in the 95% confidence interval for the equation-derived duration of isolation was considerably better than using the mean ± SD duration of isolation of 16.7 ± 4.4 with the 95% confidence interval of ± 7.47 days. It was disappointing that the derived duration of isolation equation was based only on ^{131}I dose, and that it could not be further refined by use of the other parameters. Observations or parameters that were not quantified in this study may have some predictive value and should be further investigated. These include semiquantitative assessment of pretreatment hydration, appetite, water intake, general body condition, thyroid γ emission rate 12 to 24 hours after radioiodine administration, and cardiac function (from echocardiograms), because individually or collectively, they may have relevant relationships to duration of isolation. A subjective observation on the part of the senior author (RCW) was that those cats that ate and drank more readily seemed to have shorter duration of isolation, and that fluid supplementation also helped to shorten duration of isolation. These could be not quantified or statistically investigated in our study.

Our conservative interpretation of Nuclear Regulatory Commission Regulations regarding unrestricted dismissal of radioiodine-treated cats has not been uniformly accepted among our peers. Alternative interpretations (based on exposure) involving the calculated absorbed human radiation dose may also be used as a basis for determining duration of isolation. In addition, differences exist in the interpretation of the Nuclear Regulatory Commission Regulations for radiation emission limits (eg, 2.0 mR/h as used in our study)[21] and the permissible unlabeled microcurie limits calculated to be contained in the radioiodine-treated cats for either uncontrolled release or confined (indoor) release.[22] It was not our intent to establish criteria for determining duration of isolation for radioiodine-treated cats; we wished to report our attempt to predict duration of isolation by use of the γ emission parameters we used. The data used in our study do not define any relationship between surface γ emission rate and the concentration of radioiodine in the urine or feces; those data are yet to be investigated beyond 24 hours in cats.[23] However, some landfill dumpsites are installing highly sensitive radiation detection devices to screen for low-level radioactive waste.[24] Therefore, defining any relationship between surface γ emission rate and a maximum possible level of radioiodine contamination in urine is germane to dismissal restrictions.

Our intent is to continue the search for a clinically relevant mathematical model to refine the duration of isolation equation with a straightforward γ emission endpoint. However, in tandem with this, we hope to determine whether there is a useful correlation or threshold between skin surface γ emission and urine radioiodine contamination so that home and environmental contamination risks can be addressed in the dismissal criteria.

[a]Model 3 survey instrument, Ludlum Measurements Inc, Sweetwater, Tex.

[b]Model 44-9CE "pancake" probe, Ludlum Measurements Inc, Sweetwater, Tex.

[c]V8.0, SPSS Inc, Chicago, Ill.

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