

CRITICALLY APPRAISED TOPIC:

Comparison of the clinical efficacy of radioiodine, oral methimazole and transdermal methimazole in the treatment of feline hyperthyroidism

Radioiodine, oral methimazole and transdermal methimazole are all effective in the treatment of feline hyperthyroidism.

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CLINICAL QUESTION

In cats newly diagnosed with hyperthyroidism, do radioiodine, oral methimazole and transdermal methimazole have similar clinical efficacy?

CLINICAL BOTTOM LINE

Radioiodine, oral methimazole and transdermal methimazole are all effective treatment options for feline hyperthyroidism. Determination of the most effective therapy, however, is not possible due to a lack of published controlled trials comparing efficacy between agents. Studies evaluating individual treatments are not directly comparable due to different research methods. Client and patient factors (*e.g.*, cooperation, compliance and follow-up), combination protocols (*e.g.*, pre-treatment with methimazole before radioiodine administration), differences in side effects and cost make clinical judgment and communication the key factors in choosing and monitoring treatment for this disease.

EVIDENCE SUMMARY

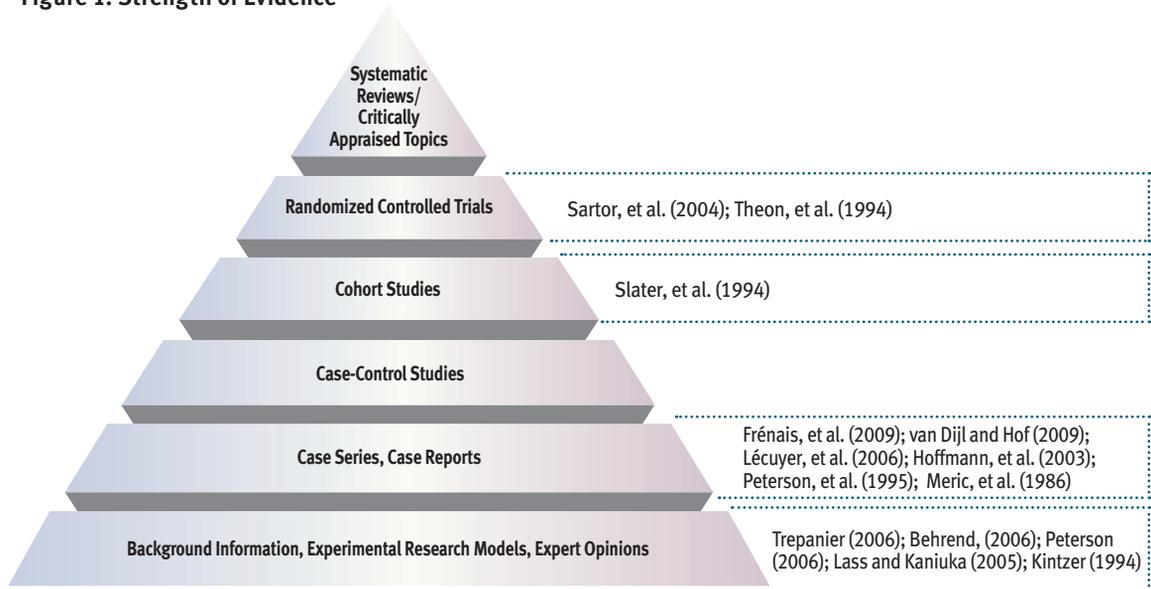
PubMed database search details (inception through current):

- Feline hyperthyroidism (veterinary subset): (“felidae”[MeSH Terms] OR “felidae”[All Fields] OR “feline”[All Fields]) AND (“hyperthyroidism”[MeSH Terms] OR “hyperthyroidism”[All Fields])

MAIN RESULTS

- One randomized controlled trial has compared oral and transdermal methimazole. Oral methimazole was more effective after two weeks of therapy, but by four weeks the difference was not statistically significant.¹
- There is a limited amount of moderate-quality research on each individual agent. These studies show that oral methimazole, transdermal methimazole and radioiodine can all be effective treatments for feline hyperthyroidism.²⁻⁹
- Radioiodine was found to be an effective treatment; however, some studies included cats that had been pre-treated with methimazole. Thus, a comparison of efficacy between radioiodine and either oral or transdermal methimazole is not possible.^{2,3,5,8,9}
- The nature and severity of side effects, longevity of results and ease of administration vary greatly between treatments.¹⁰⁻¹⁴

Figure 1: Strength of Evidence*



*See corresponding Evidence Summary, Table 1, pages 6-8.

COMMENTS

- For each individual patient, selection of an appropriate therapy depends on balancing ease of administration, owner and patient compliance, potential for side effects, nature of side effects and cost.
- For example, a single treatment with radioiodine is likely to be effective. However, there is a small risk of hypothyroidism and treatment requires access to

specialized facilities and, hence, may be expensive. Conversely, treatment with methimazole is lifelong, requires excellent patient cooperation and owner compliance and is associated with more side effects than radioiodine.

CAT Appraiser: Patrick Shearer, BVMS, PhD

Date CAT was “born”/expiration date: 12/08/2010

References

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Table 1: Evidence Summary

Author, Year	Participants (n)	Study Design & Measures	Intervention	Findings/Conclusions	Limitations
Frénais R, Rosenberg D, Burgaud S, et al. (2009)	Forty-four client-owned cats with history and clinical signs consistent with hyperthyroidism	Multicenter, self-controlled case series. Cats had a history and clinical signs consistent with hyperthyroidism and total T4 > 50 nmol/L. Primary measures were total T4 concentration and clinical assessment (hypo-, eu- or hyperthyroid). Clinicians were blinded to total T4 measurements when making clinical assessments.	Treatment was started at 15 mg carbimazole once daily; clinical response was assessed after 10 days, and 3, 5, 8, 26 and 53 weeks and dose adjusted as required.	Twenty cats completed the study period. The median maintenance dose of carbimazole was 10 mg (range 10 to 15 mg) and 15 mg (5 to 25 mg) once daily after 3 and 53 weeks, respectively. Median total thyroxine concentration dropped significantly from 118 nmol/L (50 to 320 nmol/L) at presentation to 33 nmol/L (n=40) after 10 days, 31 nmol/L (n=34) at 3 weeks and 21 nmol/L (n=18) at 53 weeks. Clinical signs improved or resolved in almost all cats within 3 weeks after starting treatment.	Limited follow-up on some cases, leading to a small sample size
van Dijk IC, Hof AJ (2009)	Eighty-three cats, diagnosed as hyperthyroid by referring veterinarians (based on clinical signs and total T4)	Self-controlled case series. Blood samples for measurement of plasma concentrations of total thyroxine (total T4), urea, and creatinine were collected prior to, 10 days after and several months after treatment. In addition, arterial blood pressure was measured before and 10 days after treatment.	Cats treated with 131I at between 4-6 mCi	Ten days and several months after 131I treatment, plasma total T4 concentrations had decreased below the upper limit of the reference range in 64 (77%) and 72 cats (87%), respectively. In four cats, the plasma total T4 concentration had decreased below the lower limit of the reference range, but only two cats had symptoms of hypothyroidism.	Study identified or described incorrectly. Sixty-five cats (78%) had been pre-treated with antithyroid drugs, with a washout period of only 3 days before 131I. Analysis did not account for the effect of pre-treatment antithyroid drugs. Blood samples analyzed by different labs with different reference ranges.
Trepanier (2006)	n/a	Review		Oral methimazole, oral carbimazole, transdermal methimazole, effective in treatment of hyperthyroidism. Radioiodine is preferred, because it has fewer side effects and is curative, although methimazole is better tolerated in cats with renal disease and treatment may be easier to arrange.	
Behrend (2006)	n/a	Review		Oral and transdermal methimazole effective in treatment of hyperthyroidism.	
Lécuyer M, Prini S, Dunn ME, et al. (2006)	Thirteen client-owned cats newly diagnosed with hyperthyroidism	Self-controlled case series. Baseline hematologic and biochemical values, along with serum thyroxine (total T4) levels, were obtained on presentation (day 0). Cats were evaluated at 14 d (D14) and 28 d (D28) following transdermal therapy. At each visit, a physical examination, a complete blood cell count, a serum biochemical analysis, and a serum total T4 evaluation were performed.	5 mg (0.1 mL) (concentration of 50 mg/mL) applied to the internal ear pinna every 12 h for 28 d.	Ten cats completed the study. Clinical improvement, as well as a significant decrease in total T4, was noted in all cats. Serum total T4 measured at D14 and D28 were significantly lower at 27.44 nmol/L, s = 37.51 and 14.63 nmol/L, s = 10.65, respectively (P < 0.0001), as compared with values at D0 (97.31 nmol/L, s = 37.55).	Small sample size

Table 1: Evidence Summary (cont'd)

Author, Year	Participants (n)	Study Design & Measures	Intervention	Findings/Conclusions	Limitations
Peterson ME (2006)	n/a	Review		Radioiodine effective	
Lass P, Kaniuka S (2005)	n/a	Review		Radioiodine is effective treatment	Obscure journal
Sartor LL, Trepanier LA, Kroll MM, et al. (2004)	Forty-seven client-owned cats newly diagnosed with hyperthyroidism	Randomized controlled trial. Cats were evaluated at weeks 0, 2, and 4 with a physical exam, body weight determination, CBC, biochemical panel, urinalysis, measurement of total levothyroxine (total T4) concentration, indirect Doppler blood pressure determination, and completion of an owner questionnaire. Data between the two groups and over time were compared by nonparametric methods.	Cats received either transdermal methimazole in pluronic lecithin organogel (PLO; applied to the inner pinna), or oral methimazole (2.5 mg q 12 h for either route).	Forty-four cats followed the protocol (17 oral and 27 transdermal). Significantly more cats treated with oral methimazole had serum total T4 concentrations within the reference range after 2 weeks (14 of 16 cats) compared to those treated by the transdermal route (14 of 25; P 5.027). This difference was no longer significant by 4 weeks of treatment (9 of 11 for oral versus 14 of 21 for transdermal), possibly because of inadequate numbers evaluated by four weeks. Cats treated with oral methimazole had a higher incidence of gastrointestinal (GI) adverse effects (four of 17 cats) compared to the cats treated with transdermal methimazole (1 of 27; P 5.04), but no differences were found between groups in the incidence of neutropenia, hepatotoxicity or facial excoriations.	Low numbers of participants in the 4-week follow-up group
Hoffmann G, Marks SL, Taboada J, et al. (2003)	Thirteen client-owned cats, identified from records of an endocrine diagnostic laboratory	Self-controlled case series. During the treatment period, cats were re-evaluated at a mean of 4.3 weeks (recheck-1), and again at a mean of 5.4 months (recheck-2).	Methimazole was formulated in a PLO-based vehicle and was applied to the inner pinna of the ear at a dosage ranging from 2.5 mg/cat q 24 h to 10 mg/cat q 12 h.	Clinical improvement was observed, and significant decreases in thyroxine concentrations were measured at recheck-1 (mean 39.57 nmol/L, SEM: 14.4, SD: 41.2) and recheck-2 (mean: 36.71 nmol/L, SEM: 13.9, SD: 45.56) compared to pretreatment concentrations (mean: 97.5 nmol/L, SEM: 11.42, SD:39.5). No adverse effects were reported.	Inconsistent follow-up times, low numbers of patients at follow up visits. Two patients were pre-treated with oral methimazole
Peterson ME, Becker DV. (1995)	524 client-owned cats diagnosed with hyperthyroidism at the Animal Medical Center and treated with radioiodine at Cornell University Medical College.	Self-controlled case series. Cats administered methimazole had the treatment stopped 1-2 weeks before radioiodine. Fourteen cats had partial surgical thyroid ablation. Cats were divided into three groups based on a score given according to clinical signs, size of thyroid gland and magnitude of total T4 concentration. Total T4 was measured on the day of discharge, 2 to 3 months post discharge and 6 to 12 months post-discharge, then once per year thereafter.	Cats with low, moderate or high scores were treated with either 2-3.4 mCi, 3.5-4.4 mCi or 4.5-6 mCi, respectively.	When discharged from the hospital, 80 cats (15.3%) still had high total T4 concentrations but by 6 months post-treatment only eight cats (1.5%) were persistently hyperthyroid. Eleven cats (2.1%) developed clinical and clinicopathologic signs consistent with hypothyroidism and required thyroxine supplementation.	Materials and methods didn't mention a blocking design, statistical analysis doesn't account for the design.

Table 1: Evidence Summary (cont'd)

Author, Year	Participants (n)	Study Design & Measures	Intervention	Findings/Conclusions	Limitations
Théon AP, Van Vechten MK, Feldman E (1994)	120 client-owned cats with confirmed hyperthyroidism	Randomized controlled trial. Total T4 measured at 1, 3 and 6 months post-treatment.	Cats received a dose of radioiodine by either IV or SC administration that delivered 150 Gy to the thyroid.	85% of cats treated IV and 84% treated SC were euthyroid 4 years after treatment. SC administration is as effective as IV, safer to personnel and less stressful to cats.	
Kintzer P (1994)	n/a	Review		Oral methimazole and radioiodine effective	
Slater M, Komkov A, Robinson LE, et al. (1994)	255 client-owned cats referred to the Texas A&M Veterinary Teaching Hospital between January 1985 and December 1990	Retrospective study using data from a referral institute plus follow-up telephone consultations with veterinarians and owners. Outcome was defined as either: 1) asymptomatic, 2) continued hyperthyroid or 3) hypothyroid. Standard questions were asked about outcome, diseases ongoing or diagnosed at the time of hyperthyroidism diagnosis and survival.	The dose of radioactive iodine administered was estimated by taking into consideration the size and number of the thyroid nodules and the total body weight of the cat. For example, a 4.5 kg cat with three large nodules would get a higher dose (e.g., 222 MBq or 6 mCi) but a 3 kg cat with a single nodule would receive 111 to 148 MBq (3 to 4 mCi). The median dose of I-131 was 18.13 MBq (4.9 mCi) [range 103.6 to 329.3 MBq (2.8 to 8.9 mCi)]	Cats with hyperthyroidism were significantly older than the control population ($P \leq 0.001$). Among cats 7 years and older, there was no significant breed predisposition to hyperthyroidism. When neuter status was used in the gender analysis, there was a significant association between gender and hyperthyroidism. However, when all females combined and all males combined were compared, no association with hyperthyroidism was found ($P = 0.45$). Eighty-five percent (200/236) of treated cats became euthyroid after treatment. Four percent (10/236) were hyperthyroid and 9% (22/236) were hypothyroid at the conclusion of the study. Age at diagnosis, total dose of I-131, duration of treatment, peak radiation level and median time that methimazole treatment was discontinued prior to radioactive iodine therapy.	A single multivariate analysis may have been more suitable than multiple bivariate analyses
Meric SM, Hawkins EC, Washabau RJ, et al. (1986)	Thirteen client-owned cats referred to the UC Davis Veterinary Medical Teaching Hospital	Self-controlled case series. Total T4 measured before treatment, at 12 h intervals after treatment in 10 cats and 48 h intervals in 21 cats. Also measured one month after therapy in 29 cats.	1.5 to 6.13 mCi, resulting in a dose of 20,000 rads to the thyroid.	Total T4 concentrations before administration were 5.3 to 51 µg/dL with a median of 11 µg/dL. 16 cats (55%) were euthyroid by day 4 after administration and 23 (74%) by day 8. Of the 29 cats evaluated 1 month after treatment, all were clinically improved and 24 (83%) were euthyroid. Three cats (10%) remained hyperthyroid and 2 (7%) were hypothyroid.	

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