Feline Hyperthyroidism- Choosing the Best Therapy

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Pathogenesis

Hyperthyroidism or thyrotoxicosis is the disorder that results from excessive production and secretion of active thyroid hormones (T4 and T3). Feline hyperthyroidism is most commonly the result of benign adenomatous hyperplasia, which accounts for 96-98% of cases. In the majority (~70%) of cats both lobes of the thyroid gland are affected, and the enlargement is typically asymmetrical. Thyroid carcinoma is a rare cause of hyperthyroidism in cats and only accounts for about 2% of cases.

The cause of the changes in the thyroid gland that lead to the development of hyperthyroidism remains unclear, but it is likely multifactorial. Studies have identified numerous nutritional and environmental factors that may contribute to the development of hyperthyroidism in cats.

Clinical Features

- Middle-aged to older cats
  - Median age 12-13 years
  - Approximately 5% of hyperthyroid cats are less than 10 years of age
- Domestic short-haired and long-haired cats are most commonly affected
- Males and females are equally affected
- Occurs less commonly in pure-bred cats, specifically Siamese cats

Hyperthyroidism is the most common endocrinopathy of middle-aged to older cats and has the potential to cause a variety of non-specific clinical signs. For this reason, hyperthyroidism should be considered in any middle-aged to older cat with medical problems.

The most common clinical signs associated with hyperthyroidism include weight loss (85-95%), polyphagia (60-75%), polyuria/polydipsia (45-60%), and increased activity or restlessness (30-55%). Clinical signs reported with less frequency include vomiting (may be associated with overeating), diarrhea (intestinal hypermotility and/or malabsorption), and coat changes (dull, matted, alopecia). Rarely cats develop apathetic hyperthyroidism and are lethargic, weak, and have a decreased appetite.

Diagnosis

Physical Examination

The nervous and aggressive behavior associated with hyperthyroidism may become more obvious during restraint and physical examination. Physical examination abnormalities commonly associated with hyperthyroidism include palpable enlargement of the thyroid gland (80-95%), a decreased body condition score (60-70%), tachycardia (50-60%), heart murmur (35-55%), gallop rhythm (15-25%), and hypertension (10-15%).
Two techniques that can be used to palpate the thyroid gland include the classic palpation technique (thumb and index finger on each side of the trachea in a sitting cat with an extended neck) and the Norsworthy technique, which involves extending the neck and turning the head to the left and right while palpating the ventral neck. An inability to palpate thyroid gland enlargement does not rule out hyperthyroidism. Confirmation of bilateral involvement by palpation alone is challenging and insensitive because of asymmetrical enlargement.

The physical examination may be unremarkable in cats with early clinical or sub-clinical hyperthyroidism. In these cats, evaluation of the medical record may allow documentation of subtle weight loss and owners should be questioned about the presence of mild supportive clinical signs.

**Laboratory Testing**

A baseline evaluation (complete blood count, serum biochemistry profile, urinalysis, blood pressure measurement, and thoracic radiographs) is recommended for all cats with suspected or confirmed hyperthyroidism. In many instances, the results of these tests are normal although they may support a diagnosis of hyperthyroidism. Occasionally, a concurrent disease is discovered that alters the treatment recommendations and prognosis.

In most cases, diagnosis is based on appropriate clinical signs, +/- palpation of a thyroid nodule, and documentation of an increased serum T4 concentration.

**Serum total T4 (TT4) concentration**

- Preferred initial screening test
- >90% of hyperthyroid cats will have an increased TT4 concentration
- ~10% of hyperthyroid cats will have TT4 concentrations within the reference interval (usually in the upper half of the reference interval)
- In early or mild cases, TT4 may fluctuate in and out of reference interval
- Cats with mild hyperthyroidism and concurrent nonthyroidal illness may have TT4 concentrations within the upper half of the reference interval

**Serum free T4 (FT4) concentration**

- More sensitive than TT4
- 98% of hyperthyroid cats have increased FT4
- FT4 should not be used alone as a routine screening test
  - Nonthyroidal illness can increase the FT4 concentration in euthyroid cats.
  - FT4 should always be evaluated in conjunction with a TT4 measured on the same blood sample
Serum TSH concentration

- Commonly used in people to diagnosis hyperthyroidism
- Expected to be low in the early stages before the T4 is increased and suppressed (undetectable) when the T4 concentration is increased
- Current canine assay only detects about 35% of feline recombinant TSH so difficult to distinguish low (suppressed) from low-normal TSH
- A normal (detectable with the current assays) concentration may aid in excluding hyperthyroidism as a diagnosis

Serum total T3 concentration is not recommended and dynamic thyroid function testing is rarely performed. If the total T4 and free T4 concentrations do not support a diagnosis of hyperthyroidism, other potential causes for the observed clinical signs should be considered. If hyperthyroidism is still suspected, reassess the total and free T4 concentrations in 4 to 8 weeks or consider performing thyroid scintigraphy.

Differential Diagnoses

Hyperthyroidism is a multisystemic disease that can cause a variety of nonspecific clinical signs. For this reason, it is often necessary to consider a number of other diseases that are common in older cats as the primary or concurrent illness.

- Diabetes mellitus
- Chronic kidney disease
- Liver disease
- Gastrointestinal disease
- Primary cardiac disease
- Neoplasia

Treatment

Long-term medical management is a reasonable option for many cats and owners. It is not invasive, effective, and well tolerated in many cats. It also does not require special facilities or isolation like treatment with radioactive iodine and unlike thyroidectomy, has low risk for complications. There are a number of disadvantages associated with medical management including the need for cat and owner compliance, treatment intolerance, and the cost associated with lifelong treatment and monitoring. Another disadvantage is a lack of direct cytotoxic effect on the hyperplastic or neoplastic tissue. Temporary medical management can also be used to alleviate or eliminate medical complications and to allow assessment of renal function while euthyroid prior to definitive therapy.

Methimazole

- Licensed for treatment of feline hyperthyroidism (Felimazole™ Dechra Veterinary Products)
• Inhibits synthesis of thyroid hormones
• Does not block the release of stored hormone or have antitumor/cytotoxic effects
• Recommended starting dose is 2.5 mg every 12-24 hours
• Dosage adjustments are usually made in 1.25-2.5 mg/day increments
• Goal of therapy is to maintain the thyroid hormone concentration within the reference interval
• Transdermal formulations are an effective alternative

Adverse reactions typically occur within the first 2-3 months of treatment and may require discontinuation of the medication.

• Vomiting, decreased appetite (may be transient)
• Neutropenia, thrombocytopenia, anemia (discontinue)
• Facial excoriations (discontinue)
• Hepatotoxicity (discontinue)
• Myasthenia gravis/neuromuscular weakness (discontinue)

Cats should be examined every 2-3 weeks during the first 2-3 months of treatment. The evaluation should include a serum T4 concentration, complete blood count, and serum biochemistry profile. Following thyroid hormone regulation and establishment of an appropriate methimazole dose, monitoring (T4, CBC, serum biochemistry) should be performed every 3-6 months for the duration of therapy.

**Thyroidectomy**

• Curative treatment
• Can be associated with significant morbidity and mortality
• Should only be considered for cats that are not an anesthetic risk and not known/suspected to have underlying renal disease
• Bilateral thyroidectomy is often indicated since the majority of cats have bilateral disease

Complications include:

• Hypothyroidism
• Hypoparathyroidism
• Laryngeal nerve damage
• Horner’s syndrome
• Persistent or recurrent hyperthyroidism
Radioactive Iodine

- Considered the treatment of choice by most veterinarians
- $^{131}$Iodine is the radionuclide of choice
  - 2-4 mCi administered subcutaneously
- Concentrates primarily in the hyperplastic or neoplastic cells and destroys the hyperfunctioning tissue
- Safe and effective treatment for cats with hyperthyroidism
- Normal tissue is normally not affected because it is suppressed/atrophied and only receives a small dose of radiation
- Hyperthyroidism may recur in a small number (rare) of cats ≥ 2 years after treatment

Advantages:

- Curative/restores euthyroidism in most (95-98%) cats with a single treatment
- No perioperative or anesthetic concerns or complications
- Does not require routine monitoring once euthyroidism is restored
- Eliminates the need for daily administration of medication

Disadvantages:

- Treatment availability and the need for special licensing
- Inpatient isolation following treatment (duration is facility dependent) and isolation in the home for 2 weeks following discharge
- Permanent hypothyroidism occurs in a small number (< 5%) of cats
  - Levothyroxine supplementation (0.1 mg per day) should be administered in cats with subnormal serum $T_4$ and high TSH concentrations following $^{131}$I
- ~5% of cats fail to respond and remain hyperthyroid following treatment
  - The second treatment is often effective in these cats

Nutritional Management

- Feeding an iodine restricted diet (Hill’s Prescription Diet y/d®) can be used to establish euthyroidism in most hyperthyroid cats
- The diet is deficient in iodine (level is below minimum daily requirement)
- Majority of cats will be euthyroid after eating the diet for ≤ 12 weeks
- Diet must be fed exclusively, and most treatment failures are related to compliance (consuming other foods or treats)
• Approximately 10% of cats fed exclusively Hill’s Prescription Diet y/d® will fail to become euthyroid
• Should be considered a treatment option for cats that are not candidates for definitive therapy, cannot tolerate methimazole, and/or have moderate to severe concurrent chronic kidney disease

Treatment Considerations
Treatment considerations should include the presence of concurrent illness, availability of treatment, morbidity associated with the treatment, treatment success rate, and the ability of the owner to tolerate and comply with the treatment recommendations. If medical management is not effective or is not well tolerated, definitive therapy such as $^{131}$I or thyroidectomy should be considered/recommended.

Prognosis
• Good to excellent for most cats with appropriate treatment
• Prognosis for individual cats depends on age, overall condition at the time of diagnosis, and concurrent medical problems/diseases as well as the treatment type and response to therapy
• Earlier diagnosis and treatment may be contributing to a better overall prognosis

References