Hypothyroid-mediated insulin resistance in the dog

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1. INTRODUCTION
Hypothyroidism and diabetes mellitus are two common endocrine disorders in the dog but they do not usually appear concurrently. Hypothyroidism has been suggested to be a cause of insulin resistance through different mechanisms and can lead to the development of diabetes mellitus. Besides, if hypothyroidism emerges in a diabetic dog, glycemic control and insulin dosage become hard to manage. Therefore, knowledge of the role of hypothyroidism on glucose homeostasis may be crucial to success in glycemic control in diabetic dogs and to avoid later development of diabetes mellitus in a hypothyroid dog.

2. OBJECTIVES
✓ Understand the mechanisms of how hypothyroidism can affect insulin sensitivity.
✓ Be aware of glucose tolerance alterations in hypothyroid dogs.
✓ How to diagnose hypothyroidism in a diabetic dog showing insulin resistance, and to early detect diabetes mellitus emerging in a hypothyroid dog.
✓ How to treat insulin resistance mediated by hypothyroidism.

3. MECHANISMS
Marked impaired insulin sensitivity in hypothyroid dogs is mediated by different factors, such as decreased glucose transporter protein 4 (GLUT4), excess of insulin and reduced endothelium-dependent vasodilatation.

- Decreased expression of triiodothyronine-responsive region in glucose transporter protein 4 (GLUT4)
- Decreased somatostatin secretion (GH inhibitory hormone)
- Absence of a positive thyroid hormone responsive element (TRE) or presence of a negative TRE in the GH gene
- Transdifferentiation of somatotrophs to “thyrosomatotrophs” and secrete GH and TSH

4. DIAGNOSTIC

Hypothyroidism in diabetic dogs
- Insulin > 1.5 U/kg
- Blood glucose concentration > 300 mg/dl
- Erratic glycemia control and changing insulin requirements
- Historical, physical and clinicopathologic findings (may also be found in euthyroid dogs with poorly controlled diabetes)
- TSH or TRH stimulation test (more accurate than baseline serum thyroid hormone concentration)

Insulin resistance in hypothyroid dogs
- Initial euglycemia → Increased insulin secretion + unchanged glucose effectiveness
- Later decompensation → Diabetes mellitus

Early detection of diabetes mellitus:
- Monitoring hypothyroidism therapy
- Glycosuria and periodic blood fructosamine levels
- GH measurement

5. TREATMENT
Insulin resistance is reversible targeting the concurrent disease, so in the diabetic dog:
- Treatment with sodium levothyroxine has to be initiated
- Insulin dose must be adjusted

In the hypothyroid dog developing diabetes mellitus, sodium levothyroxine treatment needs to be rechecked.

6. CONCLUSIONS
- Pathogenesis of hypothyroid-mediated insulin resistance seems to be multifactorial.
- Hypothyroidism causes marked insulin resistance but glycemia is initially unaffected. However, diabetes mellitus may develop if the compensatory mechanisms collapse and its early detection is not straightforward or well established.
- Diagnosis of hypothyroidism in a diabetic dog must be initiated when insulin resistance is suspected but its recognition is difficult because many findings compatible with hypothyroidism are not specific of thyroid hormone deficiency.
- Treatment of insulin resistance consists in treating hypothyroidism with sodium levothyroxine, and later adjusting insulin dose in the diabetic dog.