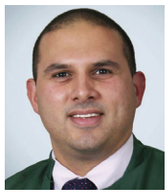
The management of hypertriglyceridaemia in dogs



***Isuru Gajanayake*, from Willows Veterinary Centre and Referral Service, discusses canine hypertriglyceridaemia and how to manage the condition.**

Hyperlipidaemia refers to the concurrent increases in both triglycerides (hypertriglyceridaemia) and cholesterol (hypercholesterolaemia). Lipaemia refers to the presence of grossly visible turbid serum. This begins to occur at around 3 to 3.5 mmol/l of serum triglycerides, and latescent (grossly white) serum is seen at around 11 to 11.5 mmol/l of serum triglycerides. Hypercholesterolaemia does not cause visibly lipaemic serum because HDL particles (which carry cholesterol) do not refract light.

Lipid metabolism

Triglycerides are compounds composed of three fatty acids linked to a glycerol molecule. The fatty acids can vary in structure and function based on their length (i.e., short chain, medium chain and long chain), presence of double bonds (i.e., saturated versus unsaturated), and the location of the first double bond (i.e., omega 3, omega 6, omega 9). The digestion and absorption of dietary lipids involves gastric lipases, bile salts and pancreatic lipases.

Lipoproteins are formed between proteins and lipids to enable transport around the body. These include chylomicrons which are made in the intestine and essentially contain lipid, as well as very low-density lipoprotein (VLDL), low density lipoprotein (LDL) and high-density lipoprotein (HDL) containing increasing proportions of protein and decreasing proportions of lipid.

Cholesterol is found only in animal fats, rather than plant oils. In dogs, most of the cholesterol is carried as HDL, whereas in people cholesterol is carried on HDL to the liver ('good' cholesterol) and on LDL to the arteries ('bad' cholesterol). Hypercholesterolaemia, although important in human medicine as a cause of atherosclerotic disease, is not usually a cause for concern in canine medicine.

Causes of hypertriglyceridaemia

The causes of hypertriglyceridaemia can be broadly categorized into artefactual, secondary and primary. Postprandial blood sampling (artefactual) can lead to increased serum triglycerides, but this is usually mild and transient. The most common secondary causes of hypertriglyceridaemia include endocrine disease (especially diabetes mellitus, hypothyroidism and hyperadrenocorticism), kidney disease (protein-losing nephropathy), pancreatitis and obesity. Primary idiopathic hypertriglyceridaemia usually occurs in specific breeds due to a genetic disorder or by an unknown mechanism. This is best characterized in the Miniature Schnauzer, but also reported in other breeds (e.g. Beagles, Shetland Sheepdogs).

Consequences of hypertriglyceridaemia

The reported detrimental consequences of hypertriglyceridaemia include:

- Pancreatitis
- Proteinuria
- Seizures
- Liver disease (vacuolar hepatopathy, gall bladder mucocele)
- Peripheral neuropathies
- Insulin resistance
- Retinal pathology (lipaemia retinalis)
- Skin lesions (cutaneous xanthomas).

Of these manifestations, pancreatitis has been the most commonly reported, and a link between hypertriglyceridaemia and pancreatitis has been demonstrated in Miniature Schnauzers (Figure 1).[1]

Targets for treatment

The normal serum triglyceride concentration in dogs is usually less than 2 mmol/l. Generally, treatment is recommended when the values are greater than 5 to 5.5 mmol/l. Normalization of triglyceride values is considered the therapeutic target.

Dietary fat restriction

Dietary fat is an essential part of a balanced diet and is needed to provide energy and essential nutrients. Dietary fat provides more than twice the energy (per gram) compared to the other two macronutrients (protein and carbohydrate). It is also vital in food to provide essential fatty acids (linoleic acid in dogs) and fat-soluble vitamins (A, D, E and K).

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FIGURE 1: A 6-year-old Miniature Schnauzer hospitalized for management of pancreatitis secondary to primary idiopathic hypertriglyceridaemia.

Comparing fat contents of diets

Dietary fat restriction is the mainstay of managing hypertriglyceridaemia; however, this is complicated by the difficulties in assessing and comparing the fat contents of diets. This is because the fat content of diets is usually expressed on an 'as fed' basis. This is the least accurate way to compare diets because the 'as fed' amount is affected by the moisture content of the food (e.g. dry versus canned/pouch food) as well as the relative amounts of protein and carbohydrate in the food.

Comparison of fat contents on a 'dry matter' basis, accounts for the moisture content but is still influenced by relative amounts of the other two macronutrients. For example, a diet with a relatively low carbohydrate content can give a falsely low impression about the fat content of a diet. For this reason, the most accurate way to analyse and compare dietary fat contents is on an 'energy or calorie' basis. The conversion of the dietary fat content from an as fed basis to calorie basis requires knowledge about its protein, fat, moisture, fibre and mineral (ash) content. Online calculators are available to simplify this process.[2]

Commercial fat restricted diets

A dietary fat content of less than 20% of the total calories is generally considered to be a fat restricted diet. Feeding commercial fat restricted diets are the cheapest and most effective way to provide dietary fat restriction. There are currently at least two commercial diets which meet these criteria, including Royal Canin Gastrointestinal low fat canned (16.9% fat per calorie basis) and dry food (19.9% fat), as well as Hill's i/d low fat canned (18.9% fat) and dried food (20.9% fat).

Balanced home-cooked fat restricted diets

The feeding of a balanced home-cooked diet allows more severe fat restriction compared to commercial diets. With this method of feeding, dietary fat contents as low as 10–12% on energy basis can be achieved (hence sometimes called ultra-low-fat diets). It is vital that ultra-low-fat home-cooked diets are formulated by a veterinary nutritionist because nutritional deficiencies (e.g. of the essential fatty acids) are possible with severe fat restriction. Apart from utilizing low-fat protein (meat) sources, balanced home-cooked diets also require the addition of a vitamin and mineral supplement to ensure the diets are complete and balanced. Home-cooked diets also enable concurrent nutritional modulations alongside fat restriction to manage simultaneous disorders (e.g. protein and phosphorus restriction concurrent for kidney disease).

Nutritional supplements

Fish oil supplements

The two omega-3 fatty acids found in fish oils, eicosapentanoic acid (EPA) and docosahexanoic acid (DHA) can be used to manage hypertriglyceridaemia. This is based on evidence from human medicine and healthy dogs showing that fish oil supplementation reduces serum triglycerides. A small study into the use of EPA and DHA in 18 Miniature Schnauzer dogs with primary hyperlipidaemia showed triglyceride and cholesterol-reducing effects with a fat-restricted diet as well as a maintenance diet.[3] The mechanism of action of fish oil supplementation in reducing serum triglycerides is postulated to be a combination of effects via altered gene transcription.

The therapeutic effect of serum triglyceride reduction appears to be dose dependent but in most clinical situations an EPA dose of 40 mg/kg/day and a DHA dose of 30 mg/kg/day is recommended. Fish oil supplementation is usually well-tolerated but possible adverse effects including gastrointestinal upsets and blood clotting disorders have been raised. Potent high-dose fish oil supplementation has also been used in people.

Niacin

Niacin or nicotinic acid is a water-soluble B vitamin. This nutrient has been used in human medicine as both a cholesterol and triglyceride-reducing medication. There are a handful of reports using niacin as a triglyceride-reducing medication in dogs. The mechanism of action of this therapy is thought to be via inhibition of triglyceride synthesis. The main adverse effects noted include skin erythema and pruritus. These adverse effects are dose dependent so gradual dose escalation of this supplement from 50 to 200 mg per day is recommended while monitoring tolerance closely.

Chitosan

This phosphate binding supplement used to manage hyperphosphataemia in chronic kidney disease has been shown to have lipid reducing effects in research animals. There are, however, no clinical studies using chitosan to manage hypertriglyceridaemia in dogs.

Medical therapy

Fibrates

Fibrates are medications used in people to lower serum triglycerides. These medications have been reported to lower the serum triglycerides by up to 50% in people. The mechanism of action includes inhibition of the enzymes which synthetize and metabolize (oxidize) fatty acids, as well as those involved in the synthesis and metabolism of triglycerides.

Bezafibrate

Bezafibrate is readily available as tablets (200 mg and 400 mg strengths) and is administered once daily. A canine study from 2017 reported the effect of bezafibrate in 46 dogs, including 16 with primary hypertriglyceridaemia and 30 with secondary disease.[4] All dogs were treated with a median dose of 6 mg/kg and 91% of dogs had normal serum triglycerides after 30 days. Serum cholesterol concentrations also normalized in 67% dogs with this abnormality. Adverse effects were not reported.

Fenofibrate

Fenofibrate is a fibric acid derivative with enhanced potency. A study by Miceli and others (2021) compared the effect of this medication and a fat restricted diet for the management of severe hypertriglyceridaemia in 124 dogs.[5] Although both treatment approaches resulted in a reduction of serum triglycerides, a greater proportion of fenofibrate treated dogs (86%) had resolution of hyperlipidaemia compared to the diet treated group (27%). Diarrhoea was noted in two fenofibrate treated dogs.

Gemfibrozil

Gemfibrozil is a commonly used medication in people, but it has not been extensively investigated in dogs. Anecdotally, it appears to be well tolerated in dogs with few adverse effects.

Statins

Statins are commonly used in people as cholesterol reducing medications. These medications are reversible inhibitors of a key enzyme (HMG-CoA reductase) in the formation of cholesterol. The action of statins is primarily in reducing blood cholesterol, not triglyceride, concentrations. For this reason, statins are rarely useful in the management of canine hypertriglyceridaemia.

Cholestyramine

Cholestyramine is a bile acid sequestrant used to manage bile acid induced diarrhoea (e.g. in short bowel syndrome following extensive intestinal resection). Cholestyramine has also been demonstrated to have a cholesterol-reducing effect.

Introducing, monitoring and escalating therapy for hypertriglyceridaemia

Nutritional modulation of hypertriglyceridaemia is generally preferred as the first intervention. Due to their availability and palatability, a commercial fat restricted diet is a sensible first step. This may be augmented by fish oil supplementation. The monitoring of effectiveness of treatment will require fasting blood tests after 4–6 weeks of the diet change.

If the initial step(s) fail to improve the magnitude of hypertriglyceridaemia, an ultra-low-fat home-cooked diet can be considered provided a board-certified veterinary nutritionist is available to formulate the recipe. Otherwise, medical therapy with bezafibrate or fenofibrate would be the logical next step. If those approaches fail, combination therapy with an ultra-low-fat home-cooked diet and a fibrate medication would need to be considered.

References and further reading are available at: **www.bsavalibrary.com**.

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