Is There a Role for Dietary Polyunsaturated Fatty Acid Supplementation in Canine Renal Disease?¹,²

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ABSTRACT Dogs with spontaneous renal diseases frequently develop progressive uremia. After partial nephrectomy, a similar pattern of progressively declining renal function develops. This pattern may be attributed in part to the development of glomerular hypertension in remnant canine nephrons. Changes in the composition of dietary polyunsaturated fatty acids (PUFA) modify glomerular hemodynamics in normal rats and affect the chronic course of renal disease in partially nephrectomized rats. Thus, dietary PUFA supplementation might alter progressive canine nephropathies. However, the response of dogs with renal insufficiency to dietary manipulations frequently differs substantially from that of laboratory rodents, and the effects of dietary PUFA composition have been poorly characterized in dogs with chronic renal disease. Here we address the hypothesis that dietary PUFA supplementation may delay the progression of chronic renal insufficiency in dogs. In particular, dogs ingesting diets supplemented with (n-6) PUFA exhibited severe glomerular hypertension associated with rapidly progressive renal failure. In contrast, dietary supplementation with (n-3) PUFA prevented deterioration of the glomerular filtration rate and preserved renal structure. The results of these model studies demonstrate that dietary PUFA supplementation may alter renal hemodynamics and the long-term course of renal injury in dogs. Clinical trials to address the potential benefits of dietary (n-3) PUFA supplementation in a variety of spontaneous renal diseases seem warranted. J. Nutr. 128: 2765S–2767S, 1998.

KEY WORDS: • polyunsaturated fatty acids • renal disease • hypertension • glomerulosclerosis • dogs

Spontaneous renal diseases are a frequent cause of illness and death in dogs, affecting ~1% of all dogs (MacDougall et al. 1986). The prevalence is higher in geriatric dogs, with chronic renal insufficiency reaching a peak prevalence of 10% in veterinary clinical patients >15 y of age (Polzin et al. 1992). Frequently, affected animals suffer progressive decrements in renal function, developing end-stage uremia. After marked, surgical reduction of renal mass in dogs, a similar progressive loss of glomerular filtration rate (GFR) associated with glomerulosclerosis and tubulointerstitial fibrosis ensues (Brown et al. 1991a). This process serves as a model of progressive renal injury in this species (Brown et al. 1991a, Finco et al. 1992a and 1992b) and of the effects of nutrients on progression of renal failure (Brown et al. 1991a, Finco et al. 1992a and 1992b, Polzin et al. 1983 and 1988, Robertson et al. 1986).

The composition of dietary polyunsaturated fatty acids (PUFA) modifies the course of induced renal disease in rats (Barcelli et al. 1986, Clark et al. 1991, Logan et al. 1992, Scharschmidt et al. 1987). In some laboratory studies (Barcelli et al. 1986, Clark et al. 1991), dietary supplementation with (n-3) PUFA is renoprotective; however, in others (Logan et al. 1992, Scharschmidt et al. 1987), PUFA supplementation was associated with worsening glomerulosclerosis and/or decrements in GFR. Results of studies in human beings are similarly conflictive, with benefits (Donadio et al. 1994) or no effect (Clark et al. 1993) reported. Because the response of dogs with renal insufficiency to dietary modification often differs from that observed in other species, several issues related to the effects of dietary PUFA supplementation in dogs remain unanswered.

ISSUE 1. ARE THERE EFFECTS OF DIETARY PUFA SUPPLEMENTATION IN DOGS WITH SPONTANEOUSLY OCCURRING CHRONIC RENAL DISEASES?

When dogs with a diverse array of spontaneous renal diseases were studied, they exhibited alterations in vasoactive urinary eicosanoid excretion, changes interpreted to support a role for glomerular hyperfiltration in progressive canine renal injury (Crocker et al. 1996). Because a variety of renal diseases were studied in this report, there is apparently a generalized effect of reduction in renal function on urinary eicosanoid metabolism. Eicosanoids produced from (n-3) PUFA are less vasoactive than those derived from (n-6) PUFA. Thus, dietary PUFA supplementation would be expected to alter renal production of eicosanoids and perhaps change the intrarenal hemodynamic response to disease. Accordingly, in short-term...
88% (n = 5) in dogs with naturally occurring renal diseases, supplementation with (n-6) PUFA led to increased GFR (Bauer et al. 1997).

ISSUE 2. WHAT IS THE MECHANISM OF THE INCREASE IN GFR OBSERVED AFTER SUPPLEMENTATION WITH (N-6) PUFA IN DOGS WITH RENAL INSUFFICIENCY?

Although studies in dogs with spontaneous renal diseases indicated that GFR might increase in response to (n-6) PUFA supplementation (Bauer et al. 1997), the mechanism of this increase in GFR was not determined. Such an increase in GFR is likely due to an increase in glomerular capillary pressure or glomerular ultrafiltration coefficient. Earlier micropuncture studies in our laboratory (Brown et al. 1990 and 1991a) demonstrated that glomerular capillary pressure is increased in dogs with induced renal insufficiency and that the magnitude of this intrarenal hypertension is proportional to the degree of renal insufficiency. Preliminary results of our studies demonstrated that dietary supplementation with (n-6) PUFA raised, and (n-3) PUFA lowered glomerular capillary pressure (Brown et al. 1996). Although there was no apparent increase in GFR in the group supplemented with (n-6) PUFA, an increase of glomerular capillary pressure would be expected to increase GFR in some settings.

ISSUE 3. DOES DIETARY SUPPLEMENTATION WITH PUFA MODULATE THE PROGRESSION OF CHRONIC RENAL DISEASE IN DOGS?

Our glomerular hemodynamic studies revealed that (n-6) PUFA increased, and (n-3) PUFA reduced the magnitude of glomerular capillary hypertension. Thus we reasoned that the long-term effects of these dietary manipulations might be more distinct. To address this hypothesis, we studied partially nephrectomized dogs randomly divided into three groups (n = 7 dogs in each group) and fed a diet supplemented with 15% fat from one of three alternate sources, i.e., safflower oil, beef tallow, or menhaden fish oil (Brown et al. 1998). Serial measurements of GFR were used to follow the chronic course of glomerular hypertension in dogs with induced renal insufficiency. Renal micropuncture studies demonstrate that glomerular capillary hypertension is likely due to an increase in glomerular capillary pressure or increase in GFR was not determined. Such an increase in GFR might alter intrarenal hemodynamics in dogs with renal insufficiency. To address this proposal, we studied the glomerular hemodynamic response to changes in dietary PUFA in dogs with induced renal insufficiency. Preliminary results of our studies demonstrated that dietary supplementation with (n-6) PUFA raised, and (n-3) PUFA lowered glomerular capillary pressure (Brown et al. 1996). Although there was no apparent increase in GFR in the group supplemented with (n-6) PUFA, an increase of glomerular capillary pressure would be expected to increase GFR in some settings.

Despite the findings of increased GFR in dogs with reduced renal mass, the long-term effects of these dietary manipulations might be more distinct. To address this hypothesis, we studied partially nephrectomized dogs randomly divided into three groups (n = 7 dogs in each group) and fed a diet supplemented with 15% fat from one of three alternate sources, i.e., safflower oil, beef tallow, or menhaden fish oil (Brown et al. 1998). Serial measurements of GFR were used to follow the chronic course of glomerular hypertension in dogs with induced renal insufficiency. Renal micropuncture studies demonstrate that glomerular capillary hypertension is likely due to an increase in glomerular capillary pressure or increase in GFR was not determined. Such an increase in GFR might alter intrarenal hemodynamics in dogs with renal insufficiency. To address this proposal, we studied the glomerular hemodynamic response to changes in dietary PUFA in dogs with induced renal insufficiency. Preliminary results of our studies demonstrated that dietary supplementation with (n-6) PUFA raised, and (n-3) PUFA lowered glomerular capillary pressure (Brown et al. 1996). Although there was no apparent increase in GFR in the group supplemented with (n-6) PUFA, an increase of glomerular capillary pressure would be expected to increase GFR in some settings.

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renal disease for 20 mo. Progressive deterioration of renal function occurred in dogs receiving the safflower oil, (n-6) PUFA supplementation (Fig. 2). These dogs also exhibited proteinuria; terminally, there was morphologic evidence of glomerular and tubulointerstitial injury. Dietary supplementation with beef tallow, a source of saturated fatty acids, was also associated with progressive decrements of renal function, although the rate of decline of renal function was slower in this group of dogs.

In contrast, dietary supplementation with menhaden fish oil, a source of (n-3) PUFA, prevented deterioration of GFR (Fig. 2). This renoprotective maneuver also lessened the magnitude of proteinuria and preserved renal structure. Our findings of stable or increasing GFR in dogs fed the (n-3)–supplemented diet contrasts with our previous reports in dogs fed a low protein, low phosphorus diet for 24 mo after 94% nephrectomy (Brown et al. 1991a). In that study, decrements of GFR leading to end-stage renal failure (25% prevalence) were evident. In contrast, dogs fed the (n-3) PUFA-enriched diet had a mean overall increase in renal function after 20 mo (Fig. 2) and no dogs of this group developed end-stage renal failure.

These results indicate that (n-3) PUFA were renoprotective, and (n-6) PUFA deleterious in dogs after partial nephrectomy; this is consistent with those studies of (n-3) PUFA demonstrating preservation of renal function and/or structure in rats after reduction of renal mass (Barcelli et al. 1986, Clark et al. 1991).

In conclusion, dogs with spontaneous renal diseases exhibit alterations in vasoactive urinary eicosanoid excretion, changes consistent with a role for glomerular hyperfiltration in progressive canine renal injury (Crockler et al. 1996). Interestingly, short-term studies in dogs with naturally occurring renal disease indicate that supplementation with (n-6) PUFA led to increased GFR (Bauer et al. 1997). On the basis of studies in dogs with induced renal disease (Brown et al. 1996), the mechanism of this increase in GFR appears to be an increase in glomerular capillary pressure. However, studies of the long-term course of renal injury in dogs indicate that dietary supplementation with (n-6) PUFA may hasten renal injury, perhaps through hypertensive glomerular injury (Brown et al. 1998). In contrast, dietary supplementation with (n-3) PUFA lowered glomerular capillary pressure and was renoprotective. On the basis of studies to date, there is reason for optimism about the potential use of (n-3) PUFA in the management of dogs with naturally occurring renal diseases. These potential benefits should be explored further in prospective clinical trials.

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LITERATURE CITED


