Nephrol Dial Transplant (2002) 17: 2033–2037

Nephrology
Dialysis
Transplantation

Letters

Fish oils and glomerulonephritis

Sir,
I agree that fish oils administered at high dosage will reduce access thrombosis [1] and that fish oils lower serum triglycerides [2] and so protect against atherosclerosis. However, the evidence that fish oils really benefit patients with glomerulonephritis deserves closer scrutiny. In spite of impressive lymphocyte suppression in mice or *in vitro*, results accumulated over two decades show only a modest benefit of fish oils on eicosanoid production and cytokine release and on the clinical status of persons with rheumatoid arthritis, and other Th-1 lymphocyte-mediated pathologies [3].

We were reliably informed that fish oils could reduce the decline of creatinine clearance, and yet not reduce proteinuria significantly [4]. At the ISN IgA Nephropathy Conference in Leiden in 1998 we noted that fish oils did not reduce urine thromboxanes, as anticipated. Now Grimble [5] reports that in UK subjects, fish oils will increase serum TNFα in half, and lower it in the other 50%!

Nephrologists should stop extrapolating results from dietary experiments in mice to what might happen in humans, and carry out more detailed investigations of their own patients who participate in trials.

21 Common Road
North Leigh
Oxford OX29 6RD, UK

E. Nigel Wardle

1. Schmitz PG, Antony KA. n-3 fatty acids in ERSD: should patients with ERSD eat more fish? *Nephrol Dial Transplant* 2001; 17: 11–14
2. Clarke SD. Polyunsaturated fatty acid regulation of gene transcription. *J Nutr* 2001; 131: 1129–1132
3. Tidow-Kebrithi S, Mobarhans S. Effects of diets containing fish oils and vitamin E on rheumatoid arthritis. *Nutr Rev* 2001; 59: 335–338
4. Donadio JV, Larson S, Bergstralh EJ, Grande JP. A randomised trial of high-dose compared with low-dose omega-3 fatty acids in severe IgA nephropathy. *J Am Soc Nephrol* 2001; 12: 791–799
5. Grimble RF. Nutritional modulation of immune function. *Proc Nutr Soc* 2001; 60: 389–397

Steroid therapy in chronic interstitial renal fibrosis: the case of Chinese-herb nephropathy

Sir,
Chinese-herb nephropathy (CHN) is a progressive interstitial renal fibrosis, initially reported to occur after exposure to herbal medicine containing aristolochic acids [1,2]. In some CHN patients, corticosteroid therapy (Cs) was successfully attempted to slow the rate of progression of the disease. The first pilot study involved 14 CHN patients treated with Cs, with 12 of them included in the 1-year follow-up study already published [3], whose clinical evolution was compared with 23 other control CHN patients not given corticosteroids (nCs). After 1 year of observation, only two of the 12 Cs CHN patients required renal replacement therapy (RRT) compared with 16 of the 23 nCs CHN control cases ($P=0.0045$). Interestingly, in a recent study dealing with the relationship between the rate of progression of the renal disease in our CHN patients and the cumulative dose intake of Chinese herbs, we found that Cs treatment had actually slowed the progression to end-stage renal disease (ESRD) in some CHN patients [4]. As this report raised some questions [5], we decided to investigate further the role of Cs therapy in the progression rate of CHN; first, by actualizing at 8 years the follow-up of the pilot study cohort (study 1); and secondly, by focusing on Cs therapy in the analysis of renal disease progression rate in the patient groups of the study of dose relationship (study 2).

According to the pilot study, Cs therapy (treatment is detailed in [3]) was actually proposed to all CHN patients referred to us with moderate but progressive renal failure. This means that Cs therapy was proposed neither to patients with preterminal renal failure [plasma creatinine (P_{creat}) >4 mg/dl] nor to patients with stable renal function. Fourteen CHN patients were included in the Cs group of the pilot study (study 1). They were also taken into account in study 2, as well as nine additional CHN patients having received Cs after completion of the pilot study. Two of these nine patients were given Cs despite the fact that P_{creat} was >4 mg/dl (4.1 and 5.8 mg/dl, respectively). For the nCs CHN control group of patients, there was a significant difference between study 1 and study 2. For study 1, according to the pilot study protocol, nCs CHN patients with preterminal renal failure or stable renal disease, similar to the Cs group, were excluded from the control group, while 11 patients cared for in other nephrology centres were included in the 23 nCs CHN control group. For study 2, on the other hand, all nCs CHN patients from our centre were included whatever the degree of renal failure, while patients from other centres were excluded. This means that studies 1 and 2 had only 12 patients of the control group in common.

For study 1, the results of the follow-up of the 37 CHN patients (14 Cs, 23 nCs) are shown in Table 1. After 1 year, 12 out of 14 Cs patients escaped RRT, in comparison with seven out of 23 nCs patients ($P=0.0019$). Three years later, the evolution of the same cohort was re-analysed: six of the 14 Cs CHN patients were still receiving conservative treatment, compared with two of the 23 nCs CHN patients ($P=0.0345$) [6]. At 8 years, the corresponding figures were three out of 14 and one out of 23, respectively (not significant, $P=0.1419$) (Table 1).

For study 2, a total of 22 CHN patients treated with Cs were finally identified in our database [4]. Fifteen of them belonged to the ESRD group ($n=44$), while the remaining seven were in the chronic renal failure (CRF) group ($n=27$). Within these two groups, no statistical difference was found between the mean ($\pm$SEM) cumulative dose of the so-called *Stephania tetrandra*—actually replaced by *Aristolochia fangchi* (symbolized by *ST-AF*)—ingested by Cs and nCs patients [ESRD group: 215 ± 24 *vs* 180 ± 15 g, respectively ($P=0.20$); CRF group: 125 ± 19 *vs* 143 ± 2.1 g, respectively ($P=0.64$)]. In contrast, among Cs-treated patients, significantly higher amounts of *ST-AF* had been ingested by patients who developed ESRD further (Table 2).

In this ESRD group, levels of P_{creat} at the initiation of Cs were significantly higher and a treatment with Cs was initiated more rapidly compared with CRF patients,

Table 1. Follow-up of the pilot study [3] on the effects of steroid therapy on progression of renal failure in CHN patients

Years of follow-up	Number of patients escaping RRT		*P* value[a]
	Cs	nCs	
0	14	23	
1	12	7	0.0019
3	6	2	0.0345
8	3	1	0.1419

[a]Fisher's exact test.

Table 2. Characteristics of CHN patients (with CRF or ESRD) treated with corticosteroids

	CRF ($n=7$)	ESRD ($n=15$)	*P* value
Dose of *ST-AF* (g)	125 ± 19.0	215 ± 23.7	0.025
ΔT (months)	33.7 ± 7.2	15.1 ± 4.2	0.027
Duration of Cs treatment (months)	17.0 ± 6.9	10.3 ± 1.7	0.22
P_{creat} [start Cs] (mg/dl)	1.96 ± 0.24	3.33 ± 0.42	0.043
P_{creat} [end Cs] (mg/dl)	1.87 ± 0.19	4.35 ± 0.42	<0.001
ΔPcr	-0.09 ± 0.11	$+1.02 \pm 0.25$	0.007
Slope (1/mg/dl/month)	-0.003 ± 0.003	-0.021 ± 0.006	0.046

ΔT, time interval between the end of *ST-AF* intake and the initiation of Cs.

indicating that the progression of the disease was worse. In CRF group, the slope of renal function deterioration ($1/P_{creat}$ *vs* time) was not significantly different in Cs patients compared with nCs patients (-0.0026 ± 0.003 *vs* -0.0031 ± 0.001, respectively; $P=0.84$) [4]. This observation does not contradict study 1; indeed, all the Cs patients showed evidence of progression of renal failure before Cs therapy (which was a condition for treatment), while in study 2, all the nCs patients were taken into account, including those with stable renal function. In contrast, in the ESRD group (the group with evolving disease, even in nCs patients), the slope was in favour of Cs patients compared with nCs patients (-0.021 ± -0.006 *vs* -0.037 ± -0.004, $P=0.034$) [4]. In patients given <200 g of *ST-AF*, the slope was greater than -0.02 in one out of eight Cs patients compared with 11 out of 20 nCs patients ($P=0.0882$). In patients given >200 g of *ST-AF*, the slope was greater than -0.02 in two out of seven Cs patients and eight out of nine nCs patients ($P=0.0350$). In other words, a beneficial effect of Cs in slowing renal failure progression could be demonstrated in the subgroup of CHN patients with more severe renal disease, as well as in those having ingested the greatest quantities of toxic compounds.

Taken together, studies 1 and 2 reinforced the conclusion that Cs therapy was able to slow the progression of renal failure in some CHN patients. This could appear surprising when considering the prominent feature of acellular fibrosis, which is particularly characteristic of CHN [7]. However, renal biopsies were often obtained in advanced stages of the disease. Interestingly, an earlier stage of the disease in an experimental rat model of CHN showed marked lymphocytic infiltrates [8]. We thus still recommend a trial of Cs treatment in rapidly progressive and severe chronic interstitial CHN nephritis. However, the benefit of Cs therapy (that is, at best, to delay ESRD from 1 to 3 years) remains to be weighed against the side effects of such a treatment.

Department of Nephrology Marie-Carmen Muniz Martinez
Hôpital Erasme Joëlle Nortier
Brussels Pierre Vereerstraeten
Belgium Jean-Louis Vanherweghem
Email: jnortier@ulb.ac.be

1. Vanherweghem JL, Depierreux M, Tielemans C *et al*. Rapidly progressive interstitial renal fibrosis in young women: association with slimming regimen including Chinese herbs. *Lancet* 1993; 341: 387–391
2. Vanhaelen M, Vanhaelen-Fastre R, But P *et al*. Identification of aristolochic acid in Chinese herbs. *Lancet* 1994; 343: 174
3. Vanherweghem JL, Abramowicz D, Tielemans C *et al*. Effects of steroids on the progression of renal failure in chronic interstitial renal fibrosis: a pilot study in Chinese herbs nephropathy. *Am J Kidney Dis* 1996; 27: 209–215
4. Muniz Martinez MC, Nortier J, Vereerstraeten P *et al*. Progression rate of Chinese-herb nephropathy: impact of *Aristolochia fangchi* ingested dose. *Nephrol Dial Transplant* 2002; 17: 408–412
5. Van Ypersele de Strihou C, Jadoul M. Progression rate of Chinese herb nephropathy: impact of *Aristolochia fangchi* ingested dose. *Nephrol Dial Transplant* 2002; 17: 1852
6. Vanherweghem JL. Prévention de la fibrose rénale interstitielle. In: Chatelain C, Jacobs C, eds. *Séminaires d'Uro-néphrologie*, 23ème série. Masson, Paris, 1997; 220–225
7. Depierreux M, Van Damme B, Vanden Houte K *et al*. Pathologic aspects of a newly described nephropathy related to the prolonged use of Chinese herbs. *Am J Kidney Dis* 1994; 24: 172–180
8. Debelle F, Nortier J, De Prez E *et al*. Aristolochic acids induce chronic renal failure with interstitial fibrosis in salt-depleted rats. *J Am Soc Nephrol* 2002; 13: 431–436

Comment on Dr Canaud's editorial

Sir,

Subsequent to the recent Editorial Comment by Prof. Canaud [1], Fresenius Medical Care wishes to respond to concerns and questions from patients and dialysis care personnel and hereby expressively confirm that perfluorocarbon-based fluids are not used in the manufacturing process of Fresenius Medical Care dialysers. Moreover, Fresenius Medical Care dialysers that fail the inline integrity test in the production process are rejected and are not reprocessed.

Furthermore, according to our market surveillance we do not share the opinion that 'perfluorohydrocarbons are well-known products that are widely used in the dialyser manufacturing industry ...'.

In the interest of all parties currently using Fresenius Medical Care dialysers we once again state that Fresenius Polysulfone® differs distinctly from the dialysers in question based on the raw materials used, the polymer, the manufacturing process, sterilization process and clinical performance characteristics.

Today, and in the future, every effort will be undertaken by Fresenius Medical Care to comply rigorously with the highest quality and safety guidelines and ensure the well being of our patients and all served by our company.

Fresenius Medical Care International Wolfgang Kummerle
Quality and Regulatory Affairs
Email: wolfgang.kuemmerle@fmc-ag.de