Fibrate treatment can increase serum creatinine levels

Sir,

We read with great interest the recently published article by Broeders *et al*. with regard to the fibrate-induced increase in blood urea and creatinine [1]. Taking into account these findings, we retrospectively reviewed the charts of patients treated with fibrates, in the lipid clinic of our university hospital. In the study we included patients without any evidence of renal dysfunction, not receiving nephrotoxic agents or drugs that could affect renal function (such as angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, non-steroidal anti-inflammatory drugs, aminoglycosides etc), with available serum urea and creatinine levels before and after treatment with fibrates.

Interestingly, in accordance to the results of Broeders *et al*. a significant increase in serum creatinine levels was observed after ciprofibrate and fenofibrate administration (Table 1). In addition, similar elevations were observed in serum urea levels after the administration of both drugs (by 17% and 8%, respectively). These increases in serum urea and creatinine levels were evident at the patients' first visit (after a mean period of 6 weeks of therapy) and remained unchanged or slightly elevated during a follow-up period of 8 months (3–18 months). However, as shown in Table 1, no significant change in serum creatinine levels was observed after gemfibrozil administration.

One possible explanation for these diverse effects of fibric acid derivatives could be the hypothesis that fibrates, such as fenofibrate, ciprofibrate and bezafibrate, impair the generation of vasodilatory prostaglandins, probably because of the activation of peroxisome proliferator-activated receptors (PPARs), which can down-regulate the expression of the inducible COX-2 enzyme [2–4]. Gemfibrozil, in contrast to the other fibrates, fails to bind and activate PPARs, which may account for the absence of nephrotoxicity observed [5].

We conclude that fibrates, possibly with the exception of gemfibrozil, can cause a small though significant increase in serum creatinine levels, which should be taken into account, especially in patients with underlying renal disease or in patients also receiving drugs that may affect renal function, such as kidney transplant recipients.

Table 1. Effect of fibrates on serum creatinine levels (expressed in mg/dl)

Fibrate	Serum creatinine levels		% change	Range of increase
	Before treatment	After treatment		
Fenofibrate ($n=60$)	0.92 ± 0.12	1.03 ± 0.14*	12	0–0.3
Ciprofibrate ($n=55$)	0.88 ± 0.14	1.03 ± 0.17*	17	0–0.4
Gemfibrozil ($n=15$)	0.96 ± 0.13	1.02 ± 0.16	6	0–0.1

Values represent mean ± SD. Statistical analysis was performed using paired *t*-test and a P value of less than 0.05 was considered to be significant.

*$P < 0.0001$ compared to the pretreatment values.

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