Thrombocytopenia induced by nicotinamide in hemodialysis patients

To the Editor: Recently, Takahashi [1] proposed in an article in *Kidney International* the prescription of nicotinamide in order to control phosphorus level in hemodialysis patients. Nicotinamide is a circulating form of nicotinic acid. It was suggested that nicotinamide is probably an effective inhibitor of phosphorus absorption in the intestine. Serum phosphorus level decreased in the study in 65 hemodialysis patients from $2.23 \pm 0.48$ mmol/L to $1.74 \pm 0.42$ mmol/L after 12 weeks of treatment. The authors concluded that nicotinamide may provide an alternative for controlling hyperphosphatemia in hemodialysis patients.

In our dialysis unit, where we treat 100 patients, the control of phosphoremia is essentially obtained by diet and prescription of sevelamer [2]. Mean phosphorus level during the last 6 months was $1.77 \pm 0.36$ mmol/L. Nevertheless, some patients did not reach this level. We prescribed nicotinamide in 6 of them at a dosage of 1000 mg/day. Because a transitory decline in platelet count was described in 1 out 65 patients in the Japanese study, we controlled the platelet count every 2 weeks. In 1 patient the platelet count remained stable, but in 5 of them we observed a dramatic decrease in the platelet count within 3 months of prescription.

Data are expressed as mean $\pm$ standart deviation in $\mu$L, and a $P$ value of less than 0.05 was considered statistically significant. The mean platelet count 3 months before the prescription of nicotinamide was $188,000 \pm 17,000$. The mean platelet count during the 3 months of prescription was $122,000 \pm 41,000$ ($P < 0.01$). Ten days after discontinuation of the drug the mean platelet count increased to $150,000 \pm 9100$ ($P < 0.01$). For each patient, the thrombocytopenia was significant ($P < 0.001$). We looked at the overall prescriptions of our 6 patients: the only one in common was the prescription of sevelamer, which is not described as inducing a thrombocytopenia. Nicotinamide has been given over the past 40 years at high doses for a variety of therapeutic applications [3]. Nicotinic acid and its derivatives were seldom reported to induce thrombocytopenia [4, 5]. The mechanism of this side effect has not been completely elucidated to date: thrombocytopenia may result from decreased levels of thyroxin-binding globulin induced by nicotinic acid or one of its derivatives. We suggest to control very carefully the prescription of nicotinamide in patients undergoing hemodialysis, and probably to insist more on diet prescription than on drugs to control hyperphosphatemia.
Muscle IGF-I levels in hemodialysis patients

To the Editor: We read with great interest Wang et al’s paper [1] describing reduced skeletal muscle mRNA levels for insulin-like growth factor (IGF)-IEa, IGF-II, and the IGF type 1 receptor in hemodialysis (HD) patients. While the low levels of IGF-IEa mRNA relative to healthy controls is anticipated, the elevated muscle IGF-I protein level (mIGF-I) reported is at odds with the diminished levels, relative to healthy controls previously reported in our HD patients [2] and animal models of chronic renal failure (CRF) (e.g. [3]). An obvious difference between these studies is that in contrast to our patients and CRF rats, the HD patients recruited by Wang et al were not muscle wasted. This supports our contention that mIGF-I may play an important role in muscle atrophy in CRF populations.

Notwithstanding species and methodologic differences, we were also surprised by the huge disparity in mean mIGF-I levels reported by this group for HD patients and CRF rats [1, 3]. Assuming a protein content of 15.5% in wet skeletal muscle for nonobese humans [4], the 131 and 100 ng IGF-I/mg wet muscle values reported by Wang et al convert to 845 and 645 ng IGF-I/mg muscle protein for HD patients and controls, respectively. These values are 1 to 2×10^3 greater than those reported by Ding et al (0.0042 and 0.0069 ng/mg muscle protein for CRF and control rats, respectively). Are the units correctly stated in these papers? Additionally, the serum IGF values in Wang et al’s paper need to be reported as ng/mL, not µg/mL, to be correct.

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Anti-proteinase 3 antibody binding to neutrophils as demonstrated by confocal microscopy

To the Editor: We read with great interest the article by Van Rossum et al [1] and wish to provide supplementary microscopic evidence of binding of anti-neutrophil cytoplasm antibodies (ANCA) to a subset of neutrophils. Following the report by Abdel-Salam et al [2] of a failure of ANCA to bind to neutrophils, we investigated binding of anti-PR3 antibody positive serum from patients with systemic vasculitis to human neutrophils using indirect immunofluorescence and confocal microscopy, as detailed in Figure 1. The priming and staining procedure was virtually identical to that used by Van Rossum et al, with the addition of an incubation step with the neutrophil marker CD16. Our results support their findings, with membrane staining of a fraction of neutrophils incubated with anti-PR3–positive serum. Thus, the hypothesis that ANCA binding in vivo results in dysregulated degranulation of neutrophils [3] remains viable.

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