The Normal Haematocrit Trial in dialysis patients with cardiac disease

Sir,

We wish to address some questions raised by two recent editorials [1,2] discussing our trial of normal haematocrit among haemodialysis patients with cardiac disease [3]. Ritz and Amann raised concerns that the normalization of haematocrit may have acutely reversed hypoxic vasodilation [1]. We do not believe that this phenomenon was prevalent during the trial, in light of the observations that it took more than 6 months to increase the mean haematocrit from 30.5% to 38.8% and that blood pressure did not increase.

Both editorials suggested that 24-h ambulatory blood pressure monitoring and post-dialysis haematocrit measurement would have been desirable during the trial [1,2]. We, too, considered these factors. There was no increase in 24-h ambulatory blood pressure at 2, 4, 8, or 12 months among 28 study subjects who underwent serial testing (haematocrit 42.0% ± 1.1% among the normal-haematocrit patients at 12 months) and no difference between the low-haematocrit group and the normal-haematocrit group at any of the test periods [4]. In a pilot study of normal haematocrit in 15 patients, haematocrit increased only 3.2 ± 3.3 volume-per cent following haemodialysis treatment (three sessions per patient) and none of the post-dialysis haematocrit values exceeded the upper limit of the normal range [5]. The mean weight loss during these sessions was 3.1 ± 1.0 kg (range, 1.4–4.6 kg). We therefore expected that post-dialysis polycythaemia would occur rarely, if at all, during the cardiac trial. Also it seems unlikely that higher haematocrit values following ultrafiltration contributed to mortality, in light of the finding that higher pre-dialysis values (which predispose to higher post-dialysis values) were associated with lower mortality rates.

Finally, Macdougall and Ritz expressed concern with ‘the choice of haematocrit rather than haemoglobin concentration to monitor the correction of anaemia’ [2]. We wish to reiterate that anaemia was in fact monitored by measuring haemoglobin concentration and all dosing decisions were based on haemoglobin concentrations [3]. Results were reported as [haemoglobin × 3], for an approximation of haematocrit, because clinicians in the United States are more familiar with haematocrit than haemoglobin values.

We agree with the editorialists that full publication of the recently completed prospective studies of normal haematocrit values in dialysis patients conducted in Scandinavia, Canada,
and Spain should provide new insights into a complex risk/benefit assessment. We also concur with the observation that data are needed regarding the effects of normal haematocrit on patients who do not have cardiac disease.

1Division of Nephrology and Hypertension Henry Ford Hospital Detroit Michigan
2Division of Nephrology University of Virginia Health Sciences Center Charlottesville Virginia
3Division of Nephrology University of California at Los Angeles Los Angeles California
4Nephrology Division Duke University Medical Center Durham North Carolina
5Clinical Research Amgen Thousand Oaks California USA

5. Data on file, Amgen

Reply

Sir,

We thank the authors for their comments on our ‘Comment’. It was certainly useful to have some clarification of the data on 24-h blood pressure monitoring and post-dialysis haematocrit measurements that were not included in their original publication.

We also accept that what was measured in this study was haemoglobin concentration, but that this was then multiplied by three to derive a ‘haematocrit’. We remain concerned, however, that it is scientifically inappropriate to report haematocrit measured by this means when in fact haematocrit was not directly measured. We are also aware of data which suggests that the haematocrit does not always accurately reflect three times the haemoglobin concentration (Brian Walters, personal communication), and this extrapolation is hugely dependent on factors such as the mean cell volume and intracellular haemoglobin content of the red cells. It is a pity that the only reason why haematocrit was reported rather than haemoglobin concentration was simply that this was an American study and that ‘clinicians in the United States are more familiar with haematocrit than haemoglobin values’. The New England Journal of Medicine is unarguably an international journal rather than an American one and its readership is worldwide including countries that are much more familiar with haemoglobin than with haematocrit.

Sadly, by choosing haematocrit for this paper, it appears that American bureaucracy was more important than scientific accuracy.

Our critique of the study was, however, not meant in any way to devalue the importance of this study. It was simply meant to stimulate thoughts and discussions about a result that was contraintuitive but that would influence treatment strategies for some time to come. It is likely that nephrologists worldwide will continue to debate this controversy, and any additional information (as was provided in the above letter) is indeed most welcome in helping to resolve the paradox.

1The Renal Unit King’s College Hospital Eberhard Ritz2 (Dulwich) London UK
2Sektion Nephrologie Med. Universitatsklinik Heidelberg Germany
3The Renal Unit Iain C Macdougall1

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