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>200 μM significantly enhanced CFU-E colony formation in mouse bone marrow cell cultures.

Although these observations are still preliminary, some conjecture may be offered regarding the potential effect of LC on differentiation during RBC maturation. Programmed cell death is known to occur during the differentiation of progenitor cells. Erythropoietin contributes to RBC maturation by retarding apoptosis, thus allowing erythroid progenitors to complete their differentiation programmes. Indeed, a major negative regulation of erythropoiesis is the caspase-mediated cleavage of GATA-1 or other erythropoietic factors [9]. Mutomba et al. [10] reported that LC at millimolar levels inhibits the activation of caspases at various point in the Fas ligation pathway in Jurkat cells. Collectively, these reports suggest that LC influences erythropoiesis, possibly by inhibiting the apoptosis of progenitor cells.

A better understanding of the mechanisms involved in LC-mediated effect on uremic anaemia, peripheral and/or central action, will help to clarify the role of LC in the treatment of renal anaemia.

Conflict of interest statement: A.A. is currently the Director of the Research and Development Department of Iperboreal Pharma Srl.

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Impact of calcium and vitamin D therapy on arterial and cardiac disease in young adults with childhood-onset end stage renal disease

Sir,

In the discussion of their well-documented study on cardiovascular disease in young adults with childhood-onset of end-stage renal disease (ESRD), the Berlin paediatricians Briese et al. [1] pointed out interesting differences with a quite similar study reported 4 years ago by their colleagues of Heidelberg [2]: the prevalence of coronary calcifications (10 vs 92%) and of calcified valve calcifications (0 vs 32%) was quite lower in the Berlin study than in the Heidelberg one, while the technique of evaluation was comparable (Table 1). This difference was all the more remarkable in that the population characteristics were quite similar regarding the proportion of transplant patients. However, the age was slightly younger (23 vs 27 years) while time on dialysis was shorter (2.9 vs 5 years) and that of transplantation longer (9.2 vs 7.8 years). In spite of these differences, at the time of cardiovascular evaluation, the classical cardiovascular risks [body mass index (BMI), smoking, low density lipoprotein (LDL) and high density lipoprotein (HDL) cholesterol] were comparable (with the exception of mean blood pressure which was 11 mmHg lower), as well as the non-classic risk factors such as albumin and homocysteine, with the exception of CRP that was 11 mg/l higher in the Berlin study. Regarding the serum mineral parameters, although their evaluation in the Berlin study was only punctual and not time-integrated as in the Heidelberg one, it is remarkable to note that the Ca × PO4 product was similar while the serum parathyroid hormone (PTH) levels were twice lower in Berlin, despite the fact that the cumulative doses of both calcium oral phosphate binder (Ca-OPB) and ‘active’ vitamin D (alfacalcidol or calcitriol) were much lower (respectively by 7- and 35- folds). Since the Berlin authors did not comment on such differences as calcium and vitamin D therapy and clinical results, we would like to propose the following comments.

We have noted that in contrast to the Heidelberg group, the Berlin group mentioned the use of cholecalciferol i.e. plain vitamin D at a dose of 2.1–108 IU per year i.e. 5.750 IU (or 143 μg) per day i.e. a dose that would certainly secure a serum 25 OH vitamin D level well above the recommended thresholds of 30–40 ng/ml [3]. Even though the 3 years difference in age and the 2 years less time on dialysis may have contributed to the 2-fold difference in PTH suppression, we think that a causal relationship between lower PTH levels and lower prevalence of cardiovascular calcifications with cholecalciferol use cannot be excluded. Indeed, there is a rational to relate this better PTH suppression to cholecalciferol use since the Slatopolsky group [4] recently evidenced in bovine parathyroid cell cultures that at a concentration of 40 ng/ml 25 OH vitamin OH-D was as efficient as calcitriol at a maximally PTH suppressive dose (40–80 ng/ml), for suppressing PTH. The reason for this efficiency is not only that the concentration of 25 OH vitamin D is about 103 higher, but that provided calcidiol concentration is sufficient, it can be taken up by the LR2-megalin receptor present in the parathyroid cells and presented to their mitochondrial 25 OH vitamin D-1 α hydroxylase, in order to synthesize 1.25(OH)2 vitamin D [5]. This in situ synthesized calcitriol can then suppress the