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A) COMMENTS ON PUBLISHED ARTICLES

A comment on the question 'Are the aims of the K/DOQI guidelines for mineral metabolism disorders in stages 3-5 chronic kidney disease unachievable or inadequate?'

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To the Editor:

I read with much attention and a great deal of interest the editorial by Dr. Elvira Fernández[1] on whether the aims of the K/DOQI guidelines on mineral metabolism disorders in stages 3-5 chronic kidney disease are unachievable or inadequate. Dr. Fernández concludes that the recommended values are adequate but unachievable at the time the OSERCE I study was conducted, since no drugs such as oral paricalcitol, sevelamer carbonate or lanthanum carbonate were available for use in pre-dialysis.

However, I believe that the evidence on the adequacy of the mineral metabolism parameter values is not clearly defined by any prospective study as the KDIGO guidelines demonstrate: neither are stage 3 and 4 parathyroid hormone values clear, nor is it clear whether or not we should maintain 25(OH)D values > 30ng/ml or whether or not we should use non-calcium chelating agents in pre-dialysis. The study by Block GA et al.[2] on the effects of phosphorus chelating agents in moderate renal failure using calcium and non-calcium chelating agents is very disturbing, given the association between high levels of phosphorus and mortality. The conclusion of that study was that phosphorus chelating agents significantly lowered serum and urinary phosphorus and slowed the progression of secondary hyperparathyroidism in patients with moderate chronic renal failure (CRF) with normal or near normal levels of phosphorus, but that it nevertheless promoted progression of vascular calcification, which called into question the effectiveness and safety of phosphorus chelating agents in stage 3-4 CRF. We require well-designed comprehensive prospective studies that use hard endpoints such as total and cardiovascular mortality to assess what mineral metabolism values are adequate and what interventions can be carried out to achieve them safely.

Conflicts of interest

The author declares potential conflicts of interest.

Lecture fees: Abbot; Sanofi.

Council Membership: Consejo de Metabolismo Mineral de la Asociación Nefrológica de Buenos Aires.

1. Fernández E. ¿Son inalcazables o inadecuados los objetivos de las guías K/DOQI en las alteraciones del metabolismo mineral en pacientes con enfermedad renal crónica 3-5? Nefrologia 2013;33(1):1-6.
2. Block GA, Wheeler DC, Persky MS, Kestenbaum B, Ketteler M, Spiegel DM, et al. Effects of phosphate binders in moderate CKD. J Am Soc Nephrol 2012;23(8):1407-15.

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Response to the Comment 'Are the aims of the K/DOQI guidelines for mineral metabolism disorders in patients with stage 3-5 chronic kidney disease unachievable or inadequate?'

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To the Editor:

I thank Dr Armando Negri for his interest in and Comment on the editorial 'Are the aims of the K/DOQI guidelines for mineral metabolism disorders in patients with stage 3-5 chronic kidney disease unachievable or inadequate?',[1] written with the aim of putting into context the original published in the same issue on the adequacy of the K/DOQI guidelines to stage 3 to 5 chronic kidney disease patients (OSERCE II).[2]

Dr Negri disagrees with the term "adequate" applied by me to the values recommended in the K/DOQI guidelines, owing to a lack of evidence in prospective studies. I justify using the term for two reasons: 1) the credibility that we owe guidelines for which the literature has been thoroughly revised in order that experts of recognised prestige may determine the best evidence available and 2) the adjective "adequate" is not equivalent to "ideal". I understand that when it is applied to medicine, there is a slight distinction, with it being understood as something that is not perfect, although it may be "reasonable" or "advisable".

Nevertheless, the concern of Dr Negri has obliged me to reflect on the word and agree with his evaluation. The term "adequate" cannot be applied to aims that are unachievable. The acronym S.M.A.R.T. is employed as a mnemonic resource to remind us what properties

must meet the aims (specific, measurable, achievable, result-oriented).

Dr Negri summarises by attributing the fact that they are unachievable due to the unavailability of drugs such as oral paricalcitol, sevelamer carbonate and lanthanum carbonate for their use in predialysis. This is a simplification of the reasons that I presented, of which there are various, although I still continue to consider this reason as highly important (it is an opinion).

I agree with Dr Negri that the study by Block et al.[3] is disturbing. The methodological criticisms for this are obvious and numerous.[4] This is not the place to analyse it in detail. However, I believe that it is having excessive impact due to the fact that it has been published in one of the most prestigious journals in our specialty and because it has been signed by authors with great scientific backgrounds. We should wait for more solid evidence, without neglecting the best evidence available.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

1. Fernández E. ¿Son inalcanzables o inadecuados los objetivos de las guías K/DOQI en las alteraciones del metabolismo mineral en pacientes con enfermedad renal crónica 3-5? Nefrologia 2013;33(1):1-6
2. Górriz JL, Molina P, Bover J, Barril G, Martín-de Francisco AL, Caravaca F, et al., en nombre de los investigadores del estudio OSERCE. Características del metabolismo óseo y mineral en pacientes con enfermedad renal crónica en estadios 3-5 no en diálisis: resultados del estudio OSERCE. Nefrologia 2013;33(1):46-60.
3. Block GA, Wheeler DC, Persky MS, Kestenbaum B, Ketteler M, Spiegel DM, et al. Effects of phosphate binders in moderate CKD. J Am Soc Nephrol 2012;23(8):1407-15.
4. Drueke TB, Massy ZA. Phosphate binders in CKD: bad news or good news? J Am Soc Nephrol 2012;23:1273-82.

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B) BRIEF PAPERS ON RESEARCH AND CLINICAL EXPERIMENTS

Treatment with megestrol acetate increases muscle mass in uraemic patients

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To the Editor:

Megestrol acetate is an appetite stimulant used in the treatment of uraemic patients' anorexia. When administered in appropriate doses, it achieves an increase in weight and the improvement of other nutritional parameters without significant side effects.[1]

The body compartment responsible for weight gain induced by megestrol acetate is a subject of controversy. Very few studies have examined this issue and the results are conflicting. While the work by Golebiewska et al. observed a tendency to retain hydrosaline,[2] other authors observed increased fat mass[3,4] and increased fat free mass.[5]

We had the opportunity to analyse body composition with electrical bioimpedance techniques in 9 patients who experienced significant weight gain after treatment with megestrol acetate.

Our patients are 4 males and 5 females, between 40 and 80 years of age. None had residual renal function and they were treated with three weekly sessions of haemodialysis. All received a daily dose of 160mg megestrol acetate.

The baseline electrical bioimpedance analysis was performed immediately before the start of treatment with megestrol acetate and it was repeated before withdrawal of the treatment when the patients were considered to have overcome a state of malnutrition and experienced a significant increase in weight. We used a single frequency bioimpedance model with the standard tetrapolar technique (EFG ElectroFluidGraph analyzer, Akern SRL, Florence, Italy). Bioimpedance studies were performed after the haemodialysis session, following a five minute rest period in the supine position, using a current of 300 microA a 50kHz.

The duration of treatment with megestrol acetate ranged between 2 and 12 months (6.5±3.8, mean ± standard deviation). The dose of dialysis did not change during this time period (Daurgidas unicompartmental Kt/V: baseline 1.48 end 1.50). After the treatment, patients experienced an increase in weight which varied between 2 and 9kg associated with an increase in the protein catabolic rate (1.25 compared with 0.97g/kg/day, $P<.05$) , albumin concentration (3.9 compared with 3.50g/dl, $P<.05$), serum creatinine (10.1 compared with 8.34mg/dl, $P<.05$) and urea (198 compared with 175mg/dl, $P<.05$), without there being variations in the concentration of phosphorus (4.9 compared with 4.8mg/dl) and the dialysis dose (Daurgidas spKt/V 1.47 compared with 1.49). Table 1 shows the body composition data provided by the bioimped-