How do the KDIGO Clinical Practice Guidelines on CKD - MBD apply to the UK?

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Introduction

This report briefly summarises the likely relevance and utility of the recently published global KDIGO Clinical Practice Guidelines for the diagnosis, evaluation, prevention and treatment of Chronic Kidney Disease – Mineral and Bone Disorder (CKD-MBD) (Kidney Int. 2009; vol 76 suppl 113, s1-132) with respect to UK clinical practice. CKD-MBD is a ubiquitous disorder in patients with impaired renal function. However, according to the Registry Report of December 2008, only 25% of haemodialysis patients in the UK currently achieve Renal Association targets for PTH.

The KDIGO report is a comprehensive and systematic review of available evidence in this important area, but emphasises the current lack of robust level 1 evidence that informs this component of clinical practice. In fact, the two recommendations within the report that are graded 1A are in areas that fall within paediatric nephrology.

Chapter 3.1: Diagnosis of CKD-MBD: biochemical abnormalities

The guidelines appear reasonable and reflect what would probably be considered standard current practice in most UK renal units apart from the recommendation to measure serum PTH concentrations in all patients with CKD stage 3 as this contradicts the guidance in recommendation 64 in NICE 73 Chronic Kidney Disease 2008 www.nice.org.uk/Guidance/CG73. NICE 73 states that there is no requirement to routinely measure serum PTH concentrations in CKD stages 1-3A and serum PTH measurement is not usually necessary in CKD stage 3B unless there is a specific indication such as hypercalcaemia or symptoms suggestive of hyperparathyroidism. The KDIGO recommendation is mostly based on the evidence that moderate elevations of PTH are observed in CKD stage 3 and it is unclear whether measurement of serum PTH concentrations in CKD stage 3 would result in a change in treatment. Routine measurement of serum PTH concentrations in CKD stage 3 would add significantly to NHS laboratory workload and costs with little evidence of benefit.

The guideline recommends the removal of CaxP as a routine parameter, with which we concur. It suggests that serum 25-hydroxyvitamin D is measured routinely in CKD stages 3-5D, but this assertion is not well supported by evidence and there remains no consensus on what represents an adequate, or inadequate, level. In this regard the guideline does not advance the ongoing debate around screening for, and correction of, nutritional vitamin D deficiency in CKD. Current practice is hindered by uncertainties regarding the appropriate threshold for intervention and by a lack of

evidence that supplementation will impact on end points beyond the serum 25-hydroxyvitamin D level.

Chapter 3.2: Diagnosis of CKD-MBD: bone

This chapter mainly concerns the performance and utility of bone biopsy and histological/histomorphometric diagnosis and classification of CKD-MBD. This chapter also includes recommendations on Bone Mineral Density measurement (BMD), saying that BMD does not predict fracture in CKD and so should not be used routinely. As such, it is unlikely to alter clinical practice in the UK.

Chapter 3.3: Diagnosis of CKD-MBD: vascular calcification

It is recommended that lateral abdominal radiographs are used to assess the burden of vascular calcification. This is unlikely to alter current UK clinical practice, but may be a relatively simple tool for clinical research. The role of screening (and management strategies) for vascular calcification remain uncertain.

Chapter 4.1: Treatment of CKD-MBD targeted at lowering high serum phosphate and maintaining serum calcium

This highlights the importance of phosphate control, with target ranges that are familiar from current practice. It is recommended that serum calcium is kept within the normal physiological range, which, although a departure from previous international guidelines, perhaps represents a more pragmatic approach given available evidence.

Chapter 4.2: Treatment of abnormal PTH levels in CKD-MBD

This represents a noteworthy departure from previous national and international guidelines and is perhaps the real 'headline' from this KDIGO report. The target for serum PTH in CKD pre-dialysis is effectively removed, beyond treating a progressively rising value. For dialysis patients a level of 2-9x the normal physiological range is recommended. This acknowledges that there is no current data to underpin an ideal range for PTH in the CKD 3-5D patient group and is based on the avoidance of risk at extremes of PTH. The value of this guideline will obviously come under scrutiny, both by the authors of this module and the wider renal community, prior to the revised RA guidelines in 2010.

Chapter 4.3: Treatment of CKD-MBD: treatment with bisphosphonates, other osteoporosis medications and growth hormone

There is a clinical disconnect between the assertion that bone mineral density (BMD) measurement in CKD 3 does not help predict fracture risk and advocating the use of bisphosphonates where BMD is demonstrably low. The recommendation to consider a bone biopsy in such situations, prior to embarking on bisphosphonate therapy, is unlikely to impact on current UK practice - and unlikely to persuade UK nephrologists to use bisphosphonates more widely. This has also become a significant area of confusion in primary care and this new guideline does not provide enough new insight to remove current uncertainty.

The strongest recommendation in this section concerns current standard paediatric practice with respect to growth hormone.

Chapter 5: Evaluation and treatment of kidney transplant bone disease

The monitoring of biochemical bone parameters and the appropriate selection for (and timing of) BMD measurement is appropriate for UK practice. It is suggested that serum 25-hydroxyvitamin D is measured (and insufficiency corrected) as for the general population. This may represent a departure from many transplant units current local policy.

Chapter 6: Summary and research recommendations

Recommendations for research cover all aspects of the guideline and highlight the need for randomised controlled trials to inform clinical practice - as well as future guidelines. A comprehensive summary of peer reviewed publications is given. It is immediately apparent that many of these studies are short term and that those extending into the longer term contain relatively small numbers of patients. It must be hoped that these guidelines can act as a catalyst and stimulate further clinical research in this area in the UK and elsewhere.

Summary

Guidelines in chapters 3.1, 4.1 (perhaps 4.2) and 5 are the most likely to be endorsed and supported by renal units in the UK**.**

Acknowledgement

This report on the utility and predicted implementation of the KDIGO CKD-MBD guideline within the UK has been reported to KDIGO and the authors of the KDIGO CKD-MBD guideline. KDIGO has requested that this feedback is made available on the Renal Association's website.

References

KDIGO Clinical Practice Guideline for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (Kidney International 2009, volume 76, supplement 113, s1-132)