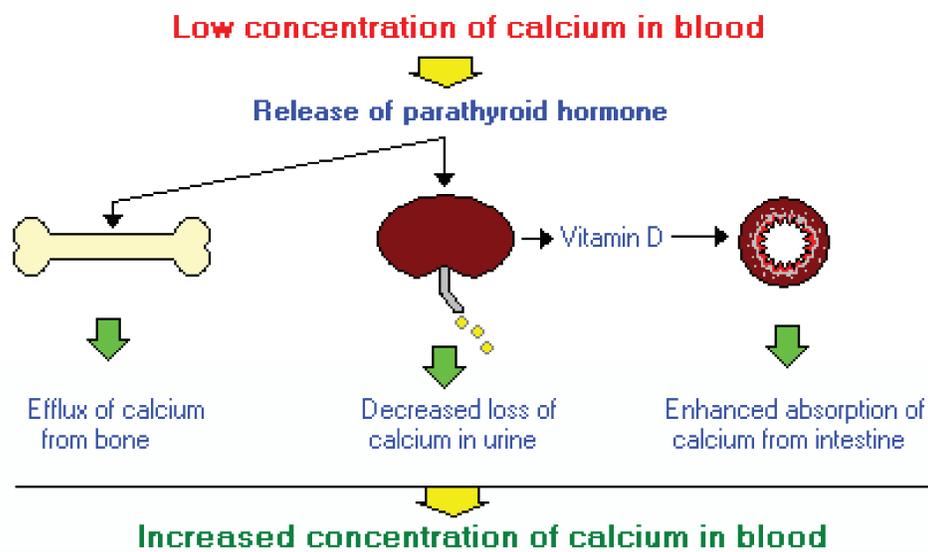


Bisphosphonates in kidney transplant patients: Time for a holiday?

Betty Pham, Jess Lloyd, Alex Bongaarts, Michael Arao
Pharmacy Dept, Princess Alexandra Hospital, Brisbane, Queensland

Background

Patients with chronic kidney disease are predisposed to renal osteodystrophy or renal bone disease, due to long term hyperparathyroidism. Following a kidney transplant, patients are subject to additional osteoporotic changes through their exposure to anti-rejection medications known to impact bone health including glucocorticoids and calcineurin inhibitors.



Bisphosphonates are a group of antiresorptive agents commonly used to treat osteoporotic changes following kidney-transplantation. In the general population, bisphosphonate therapy is continued for 5 years before a drug free period or 'holiday' is considered. This approach is based on evidence from the FLEX study. The justification for this is that bisphosphonates have a long half-life in bone and ongoing therapy beyond this time point may not provide further benefit, especially in the elderly population given their generally shorter life expectancy. There is also additional concerns about the risk of atypical femur fractures with prolonged therapy with bisphosphonates.

In the transplant population, the optimum duration of bisphosphonate therapy is not yet well-defined. There is uncertainty about whether in fact therapy *should* cease after 5 years as the patient population are often younger and likely to require ongoing therapy with glucocorticoids.

This uncertainty means there is a risk that patients may remain on therapy without timely review. Treatment guidelines are needed to ensure clinicians can confidently assess and document the appropriateness of ongoing therapy.

Aim

To identify the number of post kidney transplant patients currently receiving a bisphosphonate in which the treatment duration is greater than five years. To establish if the extended duration was a conscious decision.

Methods

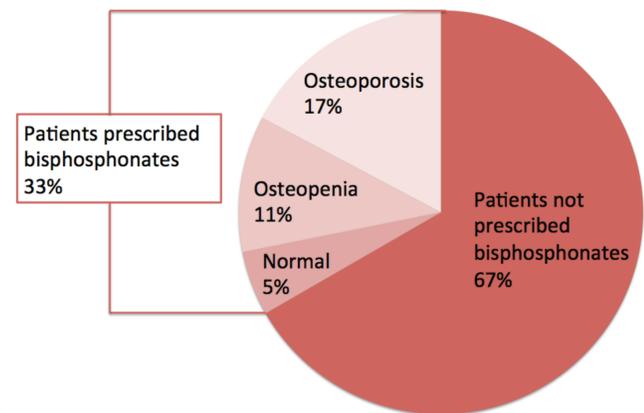
A retrospective point prevalence study was performed at the Princess Alexandra Hospital (PAH). The study identified patients who had undergone kidney transplantation between 2008 and 2013 and that were commenced on an oral bisphosphonate, specifically alendronate or risedronate.

Data collected included

- Bisphosphonate initiation date
- Duration of therapy
- Markers of bone turnover (P1NP, CTX, PTH)
- Bone Mineral Density Score

Results

Of the 189 patients screened, 62 (33%) were prescribed a bisphosphonate post-transplant. Using the WHO classification, 32 patients (17%) had osteoporosis and 21 patients (11%) had osteopenia.



11 of the 62 patients were identified as having received bisphosphonate therapy for greater than five years. For all 11 patients, there was no bisphosphonate initiation date documented by the pharmacist, demonstrating an area for improvement. Eight of the eleven patients had no documentation in their medical records discussing duration of therapy. In three patients, documentation indicated an intention to cease the bisphosphonate however it appeared this was not executed. The following cases demonstrate that current practice is individualised based on patients T-scores.

	Case 1					Case 2						
	<ul style="list-style-type: none"> • 56 year old male • Kidney transplant in 2011 • Alendronate for 6 years presently 					<ul style="list-style-type: none"> • 53 year old male • Kidney transplant in 2008 • Risedronate for 10 years presently 						
		T Lumbar Spine	T L femur total	T R femur total	Additional risk factor score	WHO classification		T Lumbar Spine	T L femur total	T R femur total	Additional risk factor score	WHO classification
Baseline		-0.6	-0.2	-1.2	1	Osteopenia	Baseline	-3.7	-3.0	-3.4	0	Severe Osteoporosis
Current		1.4	0.2	-1.4	1	Osteopenia	Current	-2.1	-2.2	-2.5	1	Severe Osteoporosis
	Improvement in T score observed from baseline						Worsening T score observed from baseline					
	Outcome: cease bisphosphonate						Outcome: continue bisphosphonate					

Conclusion

The optimal duration of bisphosphonate therapy post kidney transplant is not well defined. Pharmacist should flag patients who are approaching the five-year mark for timely review and discussion regarding the ongoing appropriateness of therapy.

At the PAH, the pharmacist work instructions have been updated to ensure bisphosphonate initiation date is well documented in both the digital system and discharge summary to facilitate this review.

References

1. Black DM, Schwartz AV, Ensrud KE, et al; FLEX Research Group. Effects of continuing or stopping alendronate after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (FLEX): a randomized trial. *JAMA*. 2006;296(24):2927-2938.
2. National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *American Journal of Kidney Diseases* [Internet]. 2003 Oct [cited 2018 Jun 1]; 42(4):S1-201. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/14520607>
3. Hawley C, Porter S. 2.4 Management of Bone Complications after Renal Transplantation. Australia: Queensland Renal Transplant Service. 2012 [cited 2018 Jun 2].
4. Therapeutic Guidelines. eTG: T-scores and Z-scores: diagnosing osteoporosis. Melbourne: Therapeutic Guidelines Limited [Internet]. 2017 [cited 2018 Jun 2]. Available from: https://tgldcdp-tg-org-au.ezpo1.library.qut.edu.au/viewTopic?topicfile=osteoporosis&guidelineName=Endocrinology#toc_d1e73
5. Watts N. Long-term risks of bisphosphonate therapy. *J Endocrinol* [Internet]. 2014 Jul [cited 2018 Jun 1]; 58(5):1677-1689. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-27302014000500523&lng=en&nrm=iso&tng=en