Use of vitamin D during pregnancy

Dear Editor,

In "Vitamin D supplementation: navigating the debate" (BPJ 36, June 2011) you mention the Australian and New Zealand College of Obstetricians guidelines recommending vitamin D supplementation for pregnant women considered to be at risk of deficiency. This advice is alluded to again in "Routine laboratory testing during pregnancy" (Best Tests, July 2011).

I have recently seen a patient who was prescribed vitamin D in pregnancy but the patient leaflet she was given with the prescription advised against the taking of cholecalciferol in pregnancy and the datasheet (dated 26/8/10) includes the following advice:

> *"**Use in Pregnancy**: Problems in humans have not been documented with intake of normal daily requirements. Maternal hypercalcaemia during pregnancy in humans may be associated with increased sensitivity to effects of vitamin D, suppression of parathyroid function, or a syndrome of peculiar (elfin) facies, mental retardation and congenital aortic stenosis in infants.*
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> *Overdosage of vitamin D has been associated with foetal abnormalities in animals. Animal studies have shown calcitriol to be teratogenic when given in doses 4 and 15 times the dose recommended for human use. Excessive doses of dihydrotachysterol are also teratogenic in animals. Animal studies have also shown calcifediol to be teratogenic when given in doses of 6 to 12 times the human dose.*
>
> *FDA Pregnancy Category C"*

I would be grateful to know how we should be advising patients regarding the safety of vitamin D supplements in pregnancy given the contradictory nature of the advice given in the Guidelines and the medicine information sheets. Also is the FDA category C equivalent to the Australian category C?

***Dr Phil White, General Practitioner,** Dunedin*

The Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) recommends that women with known vitamin D deficiency or who are at risk of deficiency (e.g. dark skinned, women who are veiled), should receive vitamin D supplementation during pregnancy.[1, 2] The recommended treatment is with cholecalciferol. Calcitriol is not routinely used during pregnancy and would only be considered in the case of hypocalcaemia or chronic renal failure.[2] Calcium supplementation is recommended in women whose dietary intake is inadequate.

Cholecalciferol is considered safe to use during pregnancy when used at therapeutic levels.[3] The United States Food and Drug Administration (FDA) pregnancy Category C is different from the Australian Drug Evaluation Committee pregnancy Category C. The FDA Category C is: "Animal reproduction studies have shown an adverse effect on the foetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks."

There appears to be a lack of consensus as to the exact dose and regimen of cholecalciferol recommended for pregnant women. A normal regimen for an adult with vitamin D deficiency would be a loading dose of 2 x 1.25 mg cholecalciferol followed by 1 x 1.25 mg cholecalciferol

per month. Ideally women, at risk of vitamin D deficiency, should be treated pre-conceptually with this dose.

National Health and Medical Research Council guidelines for nutrient reference values for Australia and New Zealand recommend that a daily amount of 80 µg (3200 I.U) cholecalciferol should not be exceeded during pregnancy. The guidelines recommend a supplement of 10 µg (400 I.U) cholecalciferol per day for pregnant women at risk of vitamin D deficiency.[4] Guidance from the Royal College of Obstetricians and Gynaecologists (United Kingdom) and the National Institute for Health and Clinical Excellence (United Kingdom), is in accord with this recommendation.[5, 6]

However, a recent study found that higher doses of cholecalciferol (100 µg / 4000 I.U) given daily are safe during pregnancy (i.e. no evidence of hypercalcaemia and hypercalcuria), and resulted in higher vitamin D status in women and neonates than the currently recommended 10 µg per day.[7]

Some practitioners are recommending that the usual adult dose of cholecalciferol (a loading dose of 2 x 1.25 mg cholecalciferol followed by 1 x 1.25 mg cholecalciferol per month) is used for pregnant women with vitamin D deficiency. However, there is no evidence of the safety of this dose in pregnancy.

Although guidelines may change in the future, at this time it would be reasonable to recommend that pregnant women at risk of vitamin D deficiency obtain their vitamin D requirements through a daily pre-natal multivitamin supplement that contains approximately 10 µg (400 I.U) cholecalciferol. Pregnant women are often already taking a multivitamin in order to meet requirements for folic acid and iodine, therefore this recommendation avoids the addition of an extra medicine.

There are currently no subsidised pre-natal multivitamins available, therefore this may be a barrier for some women. Pregnant women, especially those at risk of deficiency, are recommended to eat foods rich in vitamin D and to receive adequate sunlight.

Elevit with Iodine contains 12.5 µg (500 IU) cholecalciferol per tablet. Several other pre-natal vitamins contain cholecalciferol, but at lower than recommended doses.

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Vitamin D in patients with impaired renal function

Dear Editor,
I enjoyed reading "Vitamin D supplementation: navigating the debate" (BPJ 36, June 2011), however, I am hoping that you might further clarify when I might prescribe calcitriol for my patients.

In the article it refers to calcitriol being used for patients with chronic kidney disease, however, most of my elderly patients with some degree of chronic kidney disease are currently being prescribed cholecalciferol. Do I need to switch them over to calcitriol? At what level of renal impairment should I do so?

***General Practitioner**, Dunedin*

In "Vitamin D supplementation: navigating the debate" (BPJ 36, June 2011), it was stated that:

> "Patients with severe renal impairment, who require vitamin D supplementation, should be prescribed hydroxylated derivatives of vitamin D such as alfacalcidol and calcitriol. Doses of these medicines vary from patient to patient and require careful monitoring of serum calcium levels to prevent hypercalcaemia. These patients are most likely to be treated in secondary care".

Cholecalciferol is the form of vitamin D, most frequently recommended for people who require supplementation. However, cholecalciferol is not recommended in people with severe renal impairment as they are unable to convert it to its active metabolite – calcitriol. For this reason, some people with severe renal impairment who require vitamin D supplementation, are recommended to use calcitriol as it does not require metabolism by the kidneys.[1, 2]

Calcitriol should not be used routinely in patients with chronic kidney disease. Calcitriol is most appropriate for patients with confirmed metabolic disturbances resulting from chronic renal failure including patients under-going dialysis (or pre-dialysis), in renal osteodystrophy and secondary hyperparathyroidism.[2, 3, 4]

If considering use of calcitriol, it is recommended to first consult with a renal physician and the patient should have appropriate assessment of their parathyroid hormone, calcium, vitamin D and phosphate status.

Cholecalciferol may be used in people with mild to moderate renal impairment, but it is recommended to monitor their plasma calcium levels more frequently.[2, 5]

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