WHO recommendation regarding Vitamin D supplementation during pregnancy

12 December 2016

Recommendation

Vitamin D supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.

Publication history

First published: October 2011

Updated: December 2016

Assessed as up-to-date: December 2016

Remarks

- This recommendation supersedes the previous WHO recommendation found in the 2012 Guideline: vitamin D supplementation in pregnant women(1)
- Pregnant women should be advised that sunlight is the most important source of vitamin D. The amount of time needed in the sun is not known and depends on many variables, such as the amount of skin exposed, the time of day, latitude and season, skin pigmentation (darker skin pigments synthesize less vitamin D than lighter pigments) and sunscreen use
- Pregnant women should be encouraged to receive adequate nutrition, which is best achieved through consumption of a healthy, balanced diet, and to refer to guidelines on healthy eating.(2)
- For pregnant women with documented vitamin D deficiency, vitamin D supplements may be given at the current recommended nutrient intake (RNI) of 200 IU (5 µg) per day.
- According to the Cochrane review, there are 23 ongoing or unpublished studies on vitamin D supplementation in pregnancy.(3) Evidence from these trials should help to clarify the current uncertainties regarding vitamin D effects, particularly the effect on preterm birth, and any other associated benefits or harms of vitamin D when combined with other vitamins and minerals, particularly calcium.

Background

Hypertensive disorders of pregnancy are an important cause of severe morbidity, long-term disability and
death among both mothers and their babies. Worldwide, they account for approximately 14% of all maternal deaths, whereas in Latin America and the Caribbean, they contribute to approximately 22% of all maternal deaths.(4)

Among the hypertensive disorders that complicate pregnancy, pre-eclampsia and eclampsia stand out as major causes of maternal and perinatal mortality and morbidity. The majority of deaths due to pre-eclampsia and eclampsia are avoidable through the provision of timely and effective care to the women presenting with these complications.

Methods

The recommendation was developed using standardized operating procedures in accordance with the process described in the “WHO handbook for guideline development”, guided by the GRADE approach.(5, 6) Outcomes used for this recommendation were aligned with the prioritized outcomes from the WHO recommendations on prevention and treatment of pre-eclampsia and eclampsia (2011), and WHO recommendations on antenatal care for a positive pregnancy experience.(7, 8)

A Cochrane systematic review was conducted, on the effects on pregnancy outcomes of vitamin D supplementation during pregnancy.(3) In the review, randomized controlled trials relevant to the key question were screened by review authors, and data on relevant outcomes and comparisons were extracted. Evidence profiles (in the form of GRADE tables) were prepared for comparisons of interest, including the assessment and judgments for each outcome, and the estimated risks.

WHO convened a Guideline Development Group (GDG) meeting on recommendations for prevention and treatment of pre-eclampsia or eclampsia in April 2011, where this recommendation was first developed. The recommendation was reviewed and updated at a GDG meeting on antenatal care recommendations in March 2016.

Both GDGs comprised of a group of independent experts, who used the evidence profiles to assess evidence on effects on the pre-specified outcomes. GDG members discussed the balance between desirable and undesirable effects, overall quality of supporting evidence, values and preferences of stakeholders, resource requirements, cost-effectiveness, acceptability, feasibility and equity, to formulate the recommendation. Remarks were added to clarify the recommendation, and aid implementation.

Recommendation question

For this recommendation, we aimed to answer the following question/s:

- in pregnant women (P), does a supplementation with vitamin D alone or with other supplements (I) compared to placebo or no change to diet (C), affect the maternal and neonatal outcomes (O)?

Evidence Summary

The evidence was derived from a Cochrane systematic review that included 15 trials assessing 2833 women.(3) Nine trials were conducted in LMICs (Bangladesh, Brazil, China, India and the Islamic Republic of Iran) and six were conducted in HICs (France, New Zealand, Russia and the United Kingdom). Sample sizes ranged from 40 to 400 women. Nine trials compared the effects of vitamin D alone versus placebo or no supplementation, and six trials compared the effects of vitamin D plus calcium versus
placebo or no supplementation. The dose and regimen of vitamin D varied widely among the trials.

**Effects of vitamin D supplements alone versus placebo or no supplement (EB Table A.9)**

Nine trials contributed data to this comparison. Six trials evaluated daily vitamin D with daily doses ranging from 400 IU to 2000 IU. Two trials evaluated a single dose of 200 000 IU given at about 28 weeks of gestation, one trial evaluated a weekly dose of 35 000 IU during the third trimester, and one trial administered 1–4 vitamin D doses (60 000–480 000 IU in total) depending on the participants’ baseline serum 25-hydroxy-vitamin D levels.

**Maternal outcomes**

The evidence on pre-eclampsia, GDM, maternal mortality, caesarean section and side-effects is very uncertain (i.e. all findings were assessed as very low certainty evidence).

**Fetal and neonatal outcomes**

Low-certainty evidence suggests that vitamin D supplementation may reduce low-birth-weight neonates (3 trials, 493 women; RR: 0.40, 95% CI: 0.24–0.67) and preterm birth (< 37 weeks of gestation) (3 trials, 477 women; RR: 0.36, 95% CI: 0.14–0.93), but may have little or no effect on neonatal deaths (2 trials, 282 women, RR: 0.27; 95% CI: 0.04–1.67) and stillbirths (3 trials, 540 women; RR: 0.35, 95% CI: 0.06–1.99).

**Effects of vitamin D plus calcium supplements versus placebo or no supplement (EB Table A.9)**

Six trials contributed data to this comparison. Vitamin D doses ranged from 200 IU to 1250 IU daily and calcium doses ranged from 375 mg to 1250 mg daily.

**Maternal outcomes**

Moderate-certainty evidence shows that vitamin D plus calcium probably reduces pre-eclampsia (3 trials, 798 women; RR: 0.51; 95% CI: 0.32–0.80), but low-certainty evidence suggest that it may have little or no effect on GDM (1 trial, 54 women, 1 event; RR: 0.43, 95% CI: 0.05–3.45).

**Fetal and neonatal outcomes**

Moderate-certainty evidence indicates that vitamin D plus calcium probably increases preterm birth (< 37 weeks of gestation) (3 trials, 798 women; RR: 1.57, 95% CI: 1.02–2.43). Low-certainty evidence suggests that vitamin D plus calcium has little or no effect on neonatal mortality (1 trial, 660 women; RR: 0.20, 95% CI: 0.01–4.14).

**Additional considerations**

- Due to the limited evidence currently available to directly assess the benefits and harms of the use of vitamin D supplementation alone in pregnancy for improving maternal and infant health outcomes, the use of this intervention during pregnancy as part of routine ANC is not recommended

The moderate-certainty evidence showing that adding vitamin D to calcium supplementation probably increases preterm birth is of concern and this potential harm needs further investigation.

**Implementation considerations**

- The successful introduction of this recommendation into national programmes and health-care services depends on well-planned and participatory consensus-driven processes of adaptation and
implementation. The adaptation and implementation processes may include the development or revision of existing national guidelines or protocols based on this recommendation.

- The recommendation should be adapted into a locally appropriate document that can meet the specific needs of each country and health service. Any changes should be made in an explicit and transparent manner.
- A set of interventions should be established to ensure that an enabling environment is created for the use of the recommendations and that the behaviour of the healthcare practitioner changes towards the use of this evidence-based practice.
- In this process, the role of local professional societies is important and an all-inclusive and participatory process should be encouraged.
- The WHO antenatal care guidelines outline the 2016 WHO ANC model, which includes timing, content and frequency of antenatal care contacts.

Research implications

The 2011 GDG identified the following high-priority research question on this intervention:

- Vitamin D supplementation alone should be evaluated for the prevention of hypertensive disorders of pregnancy.

A further research priority was identified by the 2016 antenatal care GDG:

- Does vitamin D increase the risk of preterm birth when it’s combined with calcium?

Related Links

WHO recommendations on prevention and treatment of pre-eclampsia and eclampsia (2011) - full document and evidence tables (EB Table 51)

Pregnancy, Childbirth, Postpartum and Newborn Care: A guide for essential practice

Managing Complications in Pregnancy and Childbirth: A guide for midwives and doctors

Supporting systematic review:


References


Citation


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