WHO recommendation against the use of diuretics for the prevention of pre-eclampsia during pregnancy

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Recommendation

Diuretics, particularly thiazides, are not recommended for the prevention of pre-eclampsia and its complications.

(low-quality evidence, strong recommendation)

Publication history

First published: October 2011

Updated: prioritized for updating

Assessed as up-to-date: October 2011

Remarks

- In not recommending diuretics, particularly thiazides, for the prevention of preeclampsia and its complications, the group noted that this recommendation applies only to women at risk of developing preeclampsia who are not currently under treatment with diuretics. It does not apply to the use of diuretics for non-pre-eclampsia-related indications.

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.(1)

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.

A range of drug options are used for treatment of hypertension, such as thiazide diuretics, ACE inhibitors,
angiotensin receptor blockers, calcium channel blockers and beta blockers. Many antihypertensive medications have been tested in pregnant women with varying levels of hypertension (mild, moderate and severe).

**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.(2, 3) Outcomes used for this recommendation were aligned with the prioritized outcomes from the WHO recommendations on prevention and treatment of pre-eclampsia eclampsia (2011).(4)

A Cochrane systematic review was conducted, on the use of diuretics for preventing pre-eclampsia.(5) In the reviews, 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 developed. The GDG 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 with or without normal blood pressure (P), does treatment with diuretics (I) compared to placebo or no treatment (C), reduce the risk of developing pre-eclampsia and improve maternal and perinatal outcomes (O)?
- If so, which drug/s and route of administration optimizes outcomes?

**Evidence Summary**

*Diuretics for preventing pre-eclampsia*

Evidence related to the effects of diuretics on the prevention of pre-eclampsia came from a Cochrane systematic review of five RCTs involving 1836 women in the USA.(5) Both primiparous and multiparous women with gestations from first to the third trimester were recruited into the trials. Two trials (347 women) recruited only women with normal blood pressure, one trial (20 women) recruited only those with chronic hypertension while the other two trials (1658 women) did not report on blood pressure status at trial entry. In all trials thiazide diuretics were compared with placebo or no treatment. When diuretics were compared with placebo or no treatment, there were no statistically significant differences in the critical (or proxy) outcomes: new or worsening hypertension (two trials, 1475 women; RR 0.85, 95% CI 0.68–1.08), pre-eclampsia (four trials, 1391 women; RR 0.68, 95% CI 0.45–1.03), severe pre-eclampsia (two trials, 1297 women; RR 1.56, 95% CI 0.26–9.17), use of antihypertensive drugs (one trial, 20 women; RR 2.00, 95% CI 0.21–18.69), adverse events (two trials, 1217 women; RR 1.85, 95% CI 0.81–4.22), perinatal death (five trials, 1836
women; RR 0.72, 95% CI 0.40–1.27) and 5-minute Apgar score less than seven (one trial, 20 women; RR 3.00, 95% CI 0.14–65.90). There was no case of eclampsia in both the intervention and control arms of one trial that reported it as an outcome measure. All the trials providing this evidence had moderate risk of bias, relatively small sample sizes and sparse events resulting in generally low overall quality of evidence for the critical outcomes.

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 (including, for example, the availability of low-dose aspirin in antenatal care settings), 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.

Research implications

The 2011 GDG identified that further research on the following high-priority questions is needed:

- For mild to moderate high blood pressure, there is a need to determine whether treatment is better than no treatment.
- Further research is needed on the relative effectiveness of available drugs for severe acute hypertension.

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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