WHO recommendations on antiplatelet agents for the prevention of pre-eclampsia.

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World Health Organization (WHO)

World Health Organization (WHO). WHO recommendations on antiplatelet agents for the prevention of pre-eclampsia. Geneva (Switzerland): World Health Organization (WHO); 2021. 70 p. [16 references]

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Overview

Guideline Objective

To update recommendations on the use of antiplatelet agents for the prevention of pre-eclampsia

Patient Population

All pregnant women

Recommendations

Recommendation Statements

Low-dose acetylsalicylic acid (aspirin, 75 mg per day) is recommended for the prevention of pre-eclampsia in women at moderate or high risk of developing the condition. (**Recommended**)

Remarks:

- Evidence from the systematic review supports the use of aspirin in all at-risk groups (low, moderate and high). However, the Guideline Development Group (GDG) noted that a much larger number of women at low risk of developing pre-eclampsia would need to be treated to prevent one case of pre-eclampsia compared with women at moderate or high risk. Based on the risk-benefit assessment of the use of aspirin among women at low risk of pre-eclampsia, additional resource constraints on a health system, and the impact on equity, the GDG recommends restricting treatment to only women at moderate or high risk of pre-eclampsia.

- For the purpose of this recommendation, women are regarded as being at moderate risk of developing pre-eclampsia if they have any two of the following risk factors: primiparity, family history of pre-eclampsia, age greater than 40 years, or multiple pregnancy; and at high risk of developing pre-eclampsia if they have one or more of the following risk factors: diabetes, chronic or gestational hypertension, renal disease, autoimmune disease, positive uterine artery Doppler, previous history of pre-eclampsia, or previous fetal or neonatal death associated with pre-eclampsia. This is not an exhaustive list of factors for moderate- or high-risk stratification for pre-eclampsia and can be adapted or complemented based on the local epidemiology of pre-eclampsia.

- The GDG acknowledged that in settings where 75 mg aspirin tablets are not available, the dose nearest to 75 mg that is available should be used.

- Although there is evidence to suggest that a daily dose of aspirin of 75 mg and above (up to 150 mg) may be more beneficial compared to an aspirin dose less than 75 mg in terms of reduction of pre-eclampsia, the GDG was concerned about the potential for increased risk of postpartum haemorrhage and the plausibility that the risk could be increased with higher doses of aspirin. Therefore, the GDG selected 75 mg as the optimal dose in terms of risk-benefit considerations (details described in the Evidence to Decision framework). In making this decision, the GDG acknowledged the lack of evidence on the comparative risk of postpartum haemorrhage among women who received 75 mg compared with those who received 150 mg of aspirin for pre-eclampsia prevention and noted it as a research priority. In view of the potential for a small increase in risk for postpartum haemorrhage among women treated with aspirin it is important to counsel women

who are eligible for aspirin for the prevention of pre-eclampsia on the potential risks to encourage informed decision-making by the women and their families.

- Aspirin should not be used by women for whom it is contraindicated.
- The GDG emphasized that this recommendation applies to the use of aspirin in women with gestational hypertension as a secondary preventive measure against developing pre-eclampsia.
- This recommendation supersedes recommendation 7 in the 2011 *WHO Recommendations for the Prevention and Treatment of Pre-eclampsia and Eclampsia* guideline.

Low-dose acetylsalicylic acid (aspirin, 75 mg per day) for the prevention of pre-eclampsia and its related complications should be initiated by 20 weeks' gestation or as soon as antenatal care is started. (**Context-specific recommendation**)

Remarks:

- Evidence from the systematic review shows that women appeared to have a decreased risk of developing pre-eclampsia and its complications with the use of antiplatelet agents whether they began the intervention before or after 20 weeks' gestation. However, in view of the pathophysiology of pre-eclampsia, the GDG supports the initiation of treatment early in a pregnancy. The GDG noted that in most of the trials providing evidence on the benefit of aspirin in early pregnancy, treatment was initiated at 12 weeks' gestation and therefore consider this an appropriate time to initiate aspirin treatment.
- While antenatal care is ideally initiated by 12 weeks' gestation, in situations where antenatal care is started later than 20 weeks in pregnancy, GDG suggests initiating treatment at the time it begins.
- Irrespective of when treatment is initiated, appropriate counselling on the risks and benefits of preventative treatment is paramount - both to improve adherence and to inform the woman of warning signs which should be reported (such as bleeding or abdominal pain).
- There is scant evidence on the optimal time to discontinue aspirin treatment for the prevention of pre-eclampsia. In addition, the GDG is aware that, in some settings, the use of aspirin around the time of birth may preclude the use of epidural or spinal anaesthesia at the time of delivery. The GDG suggests that aspirin should be discontinued in line with local practice on the use of anticoagulants in pregnancy. The GDG notes the need for research in this area to clarify the benefits of prevention

of pre-eclampsia with the potential risks of postpartum and neuroaxial haemorrhage with the use of lowdose aspirin late in pregnancy.

- This recommendation supersedes recommendation 8 in the 2011 *WHO Recommendations for the Prevention and Treatment of Pre-eclampsia and Eclampsia* guideline.

Evidence Rating Scheme

Certainty of evidence assessments are defined according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach:

- **High certainty**: We are very confident that the true effect lies close to that of the estimate of the effect.
- **Moderate certainty**: We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- **Low certainty**: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
- **Very low certainty**: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Recommendation Rating Scheme

The GDG classified the recommendations into one of the following categories:

- **Recommended**: This category indicates that the intervention should be implemented.
- **Not recommended**: This category indicates that the intervention should not be implemented.
- **Recommended only in specific contexts ("context-specific recommendation")**: This category indicates that the intervention is applicable only to the condition, setting or population specified in the recommendation, and should only be implemented in these contexts.
- **Recommended only in the context of rigorous research ("research-context recommendation")**: This category indicates that there are important uncertainties

about the intervention. In such instances, implementation can still be undertaken on a large scale, provided that it takes the form of research that is able to address unanswered questions and uncertainties related both to effectiveness of the intervention or option, and its acceptability and feasibility.

Related Content

Supporting Documents

- Antiplatelet Agents for Preventing Pre-eclampsia and its Complications; 2019 Oct 30.
- WHO Handbook for Guideline Development, 2nd Edition; 2014.

Implementation Tools

No implementation tools available.

Patient Education

No patient education materials available.

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these Guideline Profiles is responsible for evaluating the appropriateness of applying them in a clinical setting.

TRUST Scorecard

Composition of Guideline Development Group (GDG)

Multidisciplinary GDG Members	**Yes**
Methodologist Involvement	**Yes**
Incorporation of Patient and Public Perspective	★★★★★

Systematic Review of Evidence

Literature Search	★★★★★
Study Selection	★★★★★
Evidence Synthesis	★★★★★

Foundations for Recommendations

Strength of Evidence Grade	★★★★☆
Description of Benefits and Harms of Recommendations	★★★★☆
Summary of Evidence Supporting Recommendations	★★★★★
Strength of Recommendations Rating	★★★☆☆
Clear Articulation of Recommendations	★★★★★

Funding Source — **Yes**

Disclosure and Management of Financial Conflicts of Interests — ★★★★★

External Review — ★★★★★

Updating — ★★★☆☆

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