UK NATIONAL SCREENING COMMITTEE

Policy Review

Screening for Pre-eclampsia

17 November 2011

Aim

1. This note provides background to the agenda item addressing the review of the evidence for screening for pre-eclampsia. It proposes a policy statement for consideration by the UK National Screening Committee (UK NSC).

2. The current review is attached for information.

Context of the review

UK NSC

3. This is the first time the UK NSC has formally considered the evidence for screening for pre-eclampsia.

4. The current policy is that 'Screening for risk factors for pre-eclampsia is part of routine antenatal care.'

5. This was adopted in 2003 following discussion with the National Institute for Health and Clinical Excellence (NICE).

6. A Health Technology Assessment (HTA) study, Methods of prediction and prevention of pre-eclampsia: systematic reviews of accuracy and effectiveness literature with economic modelling, was published in 2008. The current review is a summary of the findings of that study and subsequent systematic reviews.

NICE Guidance

7. The NICE Routine Antenatal Care Guideline (2008) recommends that:

8. Blood pressure measurement and urinalysis for protein should be carried out at each antenatal visit to screen for pre-eclampsia.

9. At the booking appointment, the following risk factors for pre-eclampsia should be determined:

- age 40 years or older
- nulliparity
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- previous history of pre-eclampsia

- body mass index 30 kg/m^2 or above
- pre-existing vascular disease such as hypertension
- pre-existing renal disease
- multiple pregnancy.

More frequent blood pressure measurements should be considered for pregnant women who have any of the above risk factors.

10. The presence of significant hypertension and/or proteinuria should alert the healthcare professional to the need for increased surveillance.

11. Blood pressure should be measured as outlined below:

- remove tight clothing, ensure arm is relaxed and supported at heart level
- use cuff of appropriate size
- inflate cuff to 20–30 mmHg above palpated systolic blood pressure
- lower column slowly, by 2 mmHg per second or per beat
- read blood pressure to the nearest 2 mmHg
- measure diastolic blood pressure as disappearance of sounds (phase V).

12. Hypertension in which there is a single diastolic blood pressure of 110 mmHg or two consecutive readings of 90 mmHg at least 4 hours apart and/or significant proteinuria (1+) should prompt increased surveillance.

13. If the systolic blood pressure is above 160 mmHg on two consecutive readings at least 4 hours apart, treatment should be considered.

14. All pregnant women should be made aware of the need to seek immediate advice from a healthcare professional if they experience symptoms of pre-eclampsia. Symptoms include:

- severe headache
- problems with vision, such as blurring or flashing before the eyes
- severe pain just below the ribs
- vomiting
- sudden swelling of the face, hands or feet.

15. Although there is a great deal of material published on alternative screening methods for pre-eclampsia, none of these has satisfactory sensitivity and specificity, and therefore they are not recommended.

Review process

16. The review has been received by the UK NSC at a previous meeting and was posted on the UK NSC website for three months. It was also sent directly to the Royal College of Obstetricians and Gynaecologists and Action on Pre-eclampsia.

17. One response was received from PerkinElmer. This company is developing a test for pre-eclampsia based on biochemical markers. The response is given in full below

	Comment
PerkinElmer Ms Tarja Ahola, Global Business Director, Maternal Fetal Health, PerkinElmer	The expert review refers to Meads et al. HTA published in March 2008: Methods of prediction and prevention of pre-eclampsia:systematic reviews of accuracy and effectiveness literature with economic modeling. It is based on literature that was published mainly before 2005 (there are 11 publications which were published in 2005 and 1 which was published in 2006). Since 2005 new results have been published both in the area of screening methods and prevention of pre-eclampsia. In 2009 Bujold et al. described a meta-analysis to assess the influence of gestational age at the time of starting the aspirin treatment on the incidence of PE. They found that there was 52% reduction in the risk of PE if the treatment was started before 16 weeks of pregnancy among women at increased risk for PE. In fact, guidelines in several countries recommend low dose aspirin for high risk pregnancies (NICE 2010, CNGOF-SFAR-SFMP-SFNN/France 2009, DGGG/Germany 2010, SOGC/Canada 2008). Regarding the safety question for aspirin, this is an important question and ideally, pregnant women should not be exposed unnecessarily to low dose aspirin. Therefore, it is important to select the high risk group using an approach which maximises detection rate for a relatively low FPR. This cannot be achieved by history alone, but may be achieved by the addition of other bioph ysical (uterine artery doppler ., mean arterial blood pressue) and biochemical markers (PAPP-A, PlGF). Recent studies on placental pathology suggests that early-onset disease is more likely to be associated with abnormal villous and vascular morphology while late-onset pre-eclampsia may be related to impaired glucose metabolism. This theory is supported by new placental markers that predict early-onset PE better than late-onset PE. Combining several markers have shown good predictive value especially for early-onset PE (Foidart et al 2010, Poon et al. 2010, Akolekar et al 2009). Based on these case-control studies for the prediction of early-onset pre-eclampsia it was proposed that a performance similar to that for 1st Trimester Trisomy21 screening (90%DR /5% FPR) could be achieved.. A prospective study presented by Professor Nicolaides at FMF World Congress in June 2011 confirms the results of the case-control studies. Regarding the economic evaluation presented by Meads et al. I would like to bring to your attention Professor Lieven Annemans comments, presented at the Children's Health 2010 . Prof Annemans is a health economist, director of the independent research organisation HEDM (Health Economics and Disease Management), Professor of Health Economics at the Medical Faculty and Pharmacoepidemiology at the Pharmaceutical Faculty at Ghent University. He is also Chairman of the Flemish Health Council, and advisory board to the Minister of Public Health. He reviewed Mead et al, and made the following observations: 1) An extremely simplistic decision tree was developed 2) No consideration was given to the timing of the screening i.e 1st T v 2nd T 3)No consideration of the gestation of onset of pre-eclampsia i.e ,34wks (early on-set) v > 34wks (late on-set) and the relative performance of markers, 4) No consideration of the use of combinations of markers 5) This

	area of research is prolific and the HTA was outdated.

18. The response and the publications have been considered by the reviewer.

19. Regarding low dose aspirin, this was covered in the review. Since then NICE have issued recommendations on the use of low dose aspirin in high risk groups as a means of preventing pre-eclampsia. However the guideline is cautious because evidence on the indications for treatment (eg how to define and handle moderate risk), timing of initiation and discontinuation of treatment and the optimum dosage.

20. There is also some evidence of fine and gross motor problems in treated women and in their children.

21. Regarding the test, the studies cited focus on testing in early pregnancy using a combination of ultrasound and biochemical markers. The results suggest a good detection rate but are small and other references identify the need for large scale trials before considering the introduction of screening.

22. While the studies highlight an evolving area they do not provide sufficient evidence to change the recommendations of the review at this point.

Proposed policy position statement

23. A nationally managed screening programme for pre-eclampsia is not recommended. There are currently no appropriate predictive tests or preventive treatments with suitably safe profiles. There is also insufficient information on the natural history of pre-eclampsia.

24. Current management is based on pragmatic assessment and management of risk factors throughout pregnancy.

25. The policy should be reviewed in three years time unless there is significant new peer reviewed evidence in the meantime.

Recommendations

26. The review suggested that audits of current practice, based on the NICE guideline, and assessment of its outcomes are required to establish whether current clinical practice has been optimised.

27. It is recommended that studies of tests using ultrasound and biochemical markers should be kept under review along with the evidence regarding treatment with anitiplatelet agents.

Action

28. The UK NSC is asked to agree to the proposed policy position statement and recommendations.