Placental Growth Factor based testing in suspected Preeclampsia

Population: Women presenting with suspected preeclampsia at 20+0-36+6 week's gestation

Introduction

Pre eclampsia (PE) is a multisystem hypertensive disorder of pregnancy that affects approximately 3% of pregnancies. The disease is a major cause of maternal and fetal morbidity and to date the best indicators of PE have been hypertension and elevated protein in the urine (proteinuria). This places significant economic and capacity burdens on maternity systems as around 10% of women in pregnancy will experience hypertension in pregnancy.

In view of the seriousness of the disease and the impact on women and their families, clinical teams have a high degree of suspicion for PE and a low threshold to admit pregnant women with suspected PE, although only a relatively small proportion go on to develop the disease. Placental Growth factor (PlGF) based testing reduces the time taken to diagnose PE, reduces adverse outcomes and is cost effective. NICE guidelines NG133 (2019) and DG23 (2016) recommend PlGF testing for suspected PE in pregnant women.

PlGF based testing does not replace existing local or national guidance in the assessment and management of hypertension in preeclampsia and suspected PE. Testing is integrated alongside standard management of suspected PE and in particular hypertension should be managed as per local guidance.

The main role for PlGF testing is at present a 'rule out' test for preterm preeclampsia

Guideline

Read in conjunction with the hypertension in pregnancy guideline

Initial Management of suspected preeclampsia

Diagnose preeclampsia on the basis of the criteria according to NICE 2019 (detailed in the Hypertension in pregnancy guideline).

See women with suspected PE in Triage (MAC) or DAU for full clinical assessment including:

- Blood pressure
- assessment of proteinuria automated reader dipstick
- abdominal palpation and auscultation and confirmation of normal fetal movements
- assessment of symptoms
- Additional tests may include CTG, fetal USS, quantification of proteinuria and maternal PET bloods (FBC, UE, LFT)

PIGF based testing

Offer PlGF testing to women with a singleton pregnancy at 20-36+6 weeks gestation with suspected preeclampsia / clinical uncertainty about the diagnosis.

- Take an additional EDTA tube along with maternal PET bloods (standard venepuncture technique)
- Label the EDTA sample with patient name and hospital number and time
- Order the blood test via ICE 'PET screen' and 'Placental Growth Factor'
- Send the sample to the lab within 1 hour of venupuncture (The sample MUST be processed or frozen within 4 hrs)
- The result will be reported on ICE in line with the PET screen

Further management

- Manage hypertension as per the hypertension in pregnancy guideline.
- Follow the flow chart (Appendix 1)

PIGF>100pg/ml - Normal level

- Do not admit to hospital
- Consider alternative diagnoses for symptoms
- Community midwife BP and urine check in 1 week
- NB if new diagnosis gestational hypertension follow up and fetal USS as per local guideline

PIGF <100pg/ml but >12pg/ml – low level

- Do not admit to hospital
- Arrange fetal USS for growth and Dopplers unless done within the past two weeks
- Continue to check BP twice weekly in DAU
- If no proteinuria or PCR <30, for dipstick check at each visit

PIGF < 12pg/ml – Very Low

- Placental dysfunction (PET / small baby or both)
- Arrange fetal USS for growth and Dopplers unless done within the past two weeks
- Senior obstetric Review (Reg or Consultant)
- Consider admission

- Do not deliver on the basis of PlGF result alone

Additional guidance for women at gestation 35-36+6 weeks

The PARROT study (Duhig et al Lancet 2019) included women with suspected preeclampsia up to 36+6 weeks gestation. In women with a PlGF level >100pg/ml there was a 97.1% negative predictive value for preeclampsia requiring delivery before 37 weeks in this group (35-36+6 weeks). If the level is >100 97.1% of women do NOT develop preeclampsia needing delivery before 37 weeks. In comparison the negative predictive value for the test up to 34+6 is 98% (PELICAN study).

The test performance appears to be satisfactory to allow its use at these gestations and there is some evidence that its use may improve the timely detection of PE.

Repeat testing

- There is no available data on the role of serial PlGF measurements.
- PlGf testing can be offered again if there is a new 'episode of care' and new clinical uncertainty about the diagnosis of pre-eclampsia.
- If the woman presents again >14 days after a previous test then follow the flow chart and guideline
- If less than 14 days have elapsed manage the woman according to the Hypertension guideline. If it is felt PlGF testing may be of value then seek Consultant advice given the limited evidence available.

Recommended cut-off values for the Triage PlGF test

Adapted from Duhig et al Lancet 2019 and NICE 2016

Result	Classification	Interpretation
PlGF ≥100 pg/ml	Normal	Normal -unlikely to progress to delivery within 14 days of the test
PlGF ≥12 pg/ml and <100 pg/ml	Low	Abnormal - increased risk for preterm delivery Increased surveillance
PlGF <12 pg/ml	Very Low	Highly abnormal - suggestive of patients with severe placental dysfunction and at increased risk for preterm delivery Assume / manage as preeclampsia
Abbreviations: PlGF, placental growth factor; pg/ml, picograms per millilitre.		

References:

ISSHP (2014) The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the ISSHP. Pregnancy Hypertension; 4:97-104

National Institute for Health and Care Excellence (2019) Hypertension in pregnancy: diagnosis and management NG133.

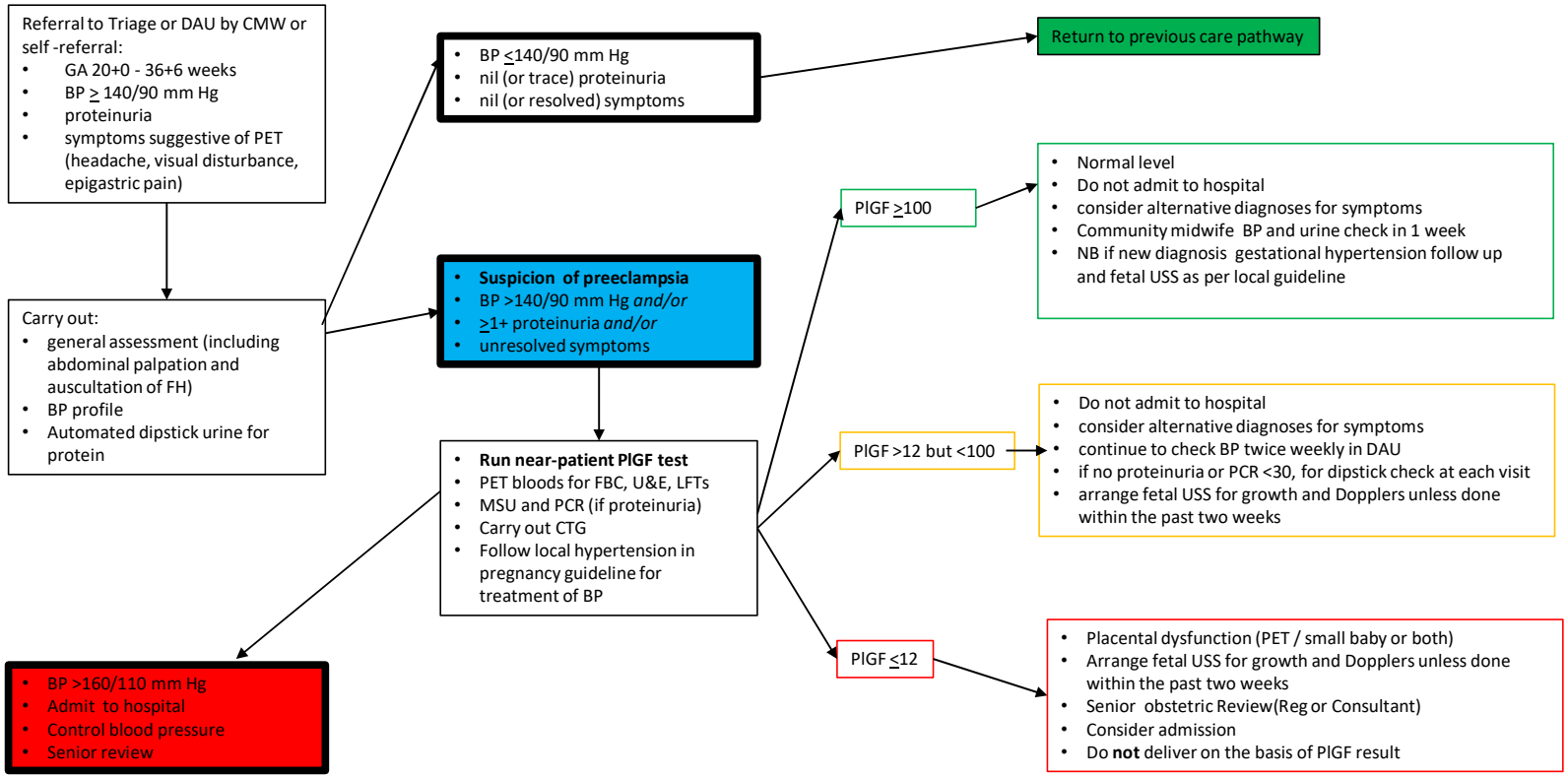
Placental growth factor testing to assess women with suspected preeclampsia. PARROT trial group. Duhig et al, Lancet 2019

Diagnostic accuracy of Placental growth factor PELICAN trial group Chappell et al, Circulation 2013

Appendix 1

Flowchart for PlGF testing

PlGF flowchart ASPH 2019



Based on Duhig et al Lancet 2019, integrated with NICE 2019 (NG133)

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