

# Multidisciplinary Management of Severe PreEclampsia (PE)

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## **Methodology:**

These updated guidelines are based on the experts meeting held in year 2000, and was initiated by the steering committee of SFAR (French Society of Anaesthesiology and Intensive Care) and supported by the administrative council.

They are an accomplishment of a multidisciplinary task group composed of experts in the fields of Anaesthesia & Intensive Care, Obstetricians, Internists, Nephrologists, Hepatologists, Paediatricians and Pathologists.

Chosen for their experience in the clinical management of eclampsia by their respective colleges, these experts produced a set of two documents, using the GRADE [1-2] method:

- An essay (detailed argumentation) comprising 22 chapters & considering all aspects of the management of PE
- Every chapter is backed by an adequate set of bibliographical references.  
The essay will be available in the electronic version of the Annales Francaise d'Anesthesie Reanimation.
- A summary of the essay or guidelines designed to address practical issues affecting the clinicians confronted by this complication.  
This work will be published in the journals of the participating disciplines.

These recommendations reflect most of the chapters making up the essay.

At first, they have been constructed as a set of statements formulated by the experts in the respective disciplines.

As much as was feasible, these statements were backed by concurring evidence published in the literature. Where this was not possible, their backing was achieved through professional consensus.

Each expert has defended both the substance and form of every statement he formulated during a preliminary session.

During this session, modifications were carried out by the panel.

Every statement then underwent a rating, according to the RAND/UCLA rating method proposed by the SFAR. This was done in order to document the endorsement of each formulated statement by the group in its entirety.

During the months of July and August 2008, each expert was invited to personally rate every single statement using a scaling method ranging from 0 to 9, according to a rating form, allowing for a personalized vote.

After a first round of ratings, statements which did not obtain full endorsement (agreement) among the experts were submitted back to the steering group and were reformulated, and subjected to a second round of ratings.

Ratings were interpreted as follows:

A median rating score of 7 or above was considered to indicate strong agreement among all experts.

One from 4 to 6 was considered indecisive and a median rating with a lower value was considered to show disagreement.

The agreement was considered high and strong if the dispersion of the ratings was narrow (i.e. no rating less than 7). Otherwise it is qualified as weak.

Endly, 154 of the initial statements were agreed on (i.e. a median rating > 7).

Out of these, 139 were rated as strong (i.e. no rating < 7) and 15 as weak, printed in italics, but none was left equivocal following the second round.

For the purpose of clarity, the statements were regrouped by topic in order to obtain 76 guidelines.

Strength of each recommendation was labelled as one of 4 different levels.

**(G1+)** : "It should / Must be done..." - 48 guidelines

**(G2+)** : "It is possible to do / May be done" - 18 guidelines

**(G1-)** : "It is possible not to do" - 10 guidelines

**(G2-)** : "It must not be done" 0 guideline

These guidelines have been regrouped under 7 headings:

1. Definitions
2. Information and training
3. Prevention and prediction
4. Managing PE
5. Managing the complications of PE
6. Anaesthesia for the woman with PE
7. After PE

## 1. DEFINITIONS (PROFESSIONAL CONSENSUS)

(G1+) The use of the following definitions is recommended.

**Gestational Hypertension (GHT):** Systolic BP  $\geq$  140 and/or diastolic BP  $\geq$  90 mmHg, arising after the 20<sup>th</sup> week of GA (gestational amenorrhoea) up till 6 weeks post partum.

**Pre-eclampsia (PE):** the association of GHT with proteinuria ( $> 300\text{mg}/24\text{h}$ )

**Severe PE:** PE together with at least one of the following:

- Severe systemic hypertension (HT) : systolic BP  $\geq$  160 and/or a diastolic BP  $\geq$  110
- Renal impairment : oliguria ( $< 500\text{ ml}/24\text{ hours}$ ) or elevated blood creatinine levels ( $>135\ \mu\text{mol.L}^{-1}$ ) or proteinuria  $> 5\text{g}/\text{day}$ .
- Acute Pulmonary Oedema or epigastric pain or HELLP syndrome
- Eclampsia or other neurological impairment (visual disturbances, hyper-reflexia, permanent headache)
- Thrombocytopenia (Platelet count  $< 100.10^9 . \text{L}^{-1}$ )
- Abruptio placenta or foetal heart decelerations.

**Early PE:** Within the 32 first weeks GA

**HELLP syndrome:** The association of Haemolysis, Elevated Liver enzymes and Low Platelet count.

**Eclampsia:** The outbreak of a tonic-clonic seizure in the setting of gestational hypertension.

**High risk patient:** A patient with a previous history of at least severe and early PE.

## 2. Information and training (Professional consensus)

(G1+) It is recommended to sensitise community (GPs, Midwives) to the signs and symptoms suggestive of PE and to encourage the identification of the high risk patient.

(G1+) It is recommended that all pregnant women be systematically informed on the necessity to seek immediate medical attention at the first tell tale signs, even in the absence of any particular antecedents.

Information to women about the ante natal facilities available as well as possibility of in-utero transfer between facilities must be provided.

(G1+) It is suggested that healthcare providers involved in the management of PE patients be perfectly accustomed with:

- a) The systematic checking of hypertension, *especially systolic hypertension*, at each consultation.
- b) The adequate use of magnesium sulphate.
- c) Organizing a prompt delivery in the setting of rapidly deteriorating PE or following established PE

*(G2+) It is advisable to systematically perform a pathological examination of every placenta specimen following a PE.*

(G1+) It is recommended to have a pathology examination of the placenta specimen as well as a maternal and/or foetal autopsy, following a maternal and/or foetal death as a result of PE.

### **3. Prevention and prediction:**

*(G1+) No clinical or biological criteria will predict the occurrence of PE in the pregnant women and therefore no investigation may be recommended which bears a predictive value.*

*(G2+) Uterine artery doppler velocimetry may only be envisaged for the high risk patient.*

(G1+) The prevention of PE through low dose aspirin (i.e. 75-160 mmHg/day) is recommended in the high risk patient and is to be initiated before the 20<sup>th</sup> week of GA.

The use of low molecular weight heparin is not recommended as a preventive method (G1-) but it may be used in the patient at risk of thrombotic events.(G2+)

*(G1-) Antioxidant supplementation as well as the use of an NO dispenser are not recommended.*

*(G2+) The administration of Ca<sup>++</sup> (1.5g / day) is only indicated if there is demonstrated calcium deficiency.*

## **4. Managing PE**

### **4.1. Organising the management of PE in the community (Professional consensus)**

(G2+) In the case of a patient with a previous history of PE, for whom the current pregnancy is uneventful, it is possible that she may be followed up at community level on the condition that a primary consultation was made, ideally pre-conceptually, with an

obstetrician/gynaecologist (OG), producing a series of written recommendations for this patient's follow up.

(G1+) In case of non-severe PE, it is advised that investigations be carried out by the OG as an in-patient basis and that a tight follow-up be organized (convention or written protocol)

(G1+) In case of severe PE, immediate admission is mandatory.

(G1+) It is recommended to choose the place of birth according to gestational age, criteria for maternal and foetal distress and the eventual necessity for post-partum intensive care admission.

(G1+) It is recommended that the protocols be set up in common in the perinatal networks, with the ability to self-assess the quality of the multidisciplinary patient management and adherence to the protocols.

## **4.2 Pre-hospital management and inter-hospital transfer.**

(G1+) Prior to an in-utero transfer, information should be provided jointly by the OG and paediatrician to the parents, regarding its maternal and foetal implications.

(G1+) It is recommended that all senior medical staff involved in the transfer (obstetrician, paediatrician, anaesthesiologist & intensivist, emergency physician) come to an agreement and that appropriate means are implemented without delay, in accordance with the protocols in effect within the perinatal network.

(G1+) It is recommended to continue the treatment of severe HT during transport in order to maintain its level during this period, in accordance with fig.1

(G1+) It is possible to maintain the magnesium sulphate infusion as a primary preventive measure against PE during transport.

(G2+) It is possible to use i.v. benzodiazepines for the treatment of eclampsia in the pre-hospital setting.

(G1+) During the transport, it is recommended to set up surveillance of the patient's level of consciousness, monitor heart and respiratory rates, pulse oxymetry, blood pressure via non-invasive continuous intermittent measure and, if the patient is intubated, capnometry.

(G2+) In case of foetal heart rhythm anomaly, the delivery at the initial admitting facility, whichever type, needs to be considered.

## **4.3 In-patient management of PE (professional consensus)**

(G1+) Monitoring of the foetal heart rhythm, performing ultrasonic foetal biometry and foetal Doppler velocimetry are recommended for the evaluation of foetal well-being.

(G1+) It is recommended to initiate a corticosteroid therapy at an appropriate gestational age (2 doses of 12 mg Betamethasone at 24 hours interval) for foetal maturation, as soon as possible after the diagnosis of PE has been made, especially prior to a transfer.

(G1+) During a severe PE episode, it is recommended to manage the arterial hypertension according to the flowchart in fig. 1

(G1+) When the diastolic blood pressure exceeds 110 mmHg or the systolic blood pressure exceeds 160 mmHg, it is recommended to begin an anti-hypertension treatment.

(G1-) It is not recommended to systematically perform fluid expansion since this has failed to demonstrate any improvement of maternal or foetal outcome and could induce an acute pulmonary oedema.

(G2+) Careful circulatory expansion is warranted in case of a sudden and significant drop in arterial blood pressure secondary to the introduction of an antihypertensive treatment.

(G1+) Whenever the haemodynamic status of the PE patient needs to be assessed, the use of ultrasound should be preferred.

Invasive measurements of pulmonary arterial blood pressure are only justified in exceptional cases.

(G1+) In case of severe PE, the prevention of an eclamptic crisis through use of magnesium sulphate is recommended when neurological signs appear (i.e. persistent resistant headache, hyper-reflexia and visual disturbances) and in the absence of contra-indications (i.e. renal failure, neuromuscular disorders).

(G2+) The initial treatment plan comprises a loading dose of 4g magnesium sulphate, followed by a continuous iv infusion at a rate of 1g/h.

(G1+) The surveillance during the magnesium sulphate therapy must consist of frequent level of consciousness charting (GCS=15), *respiratory rate charting (>12bpm)*, urine output charting (>30 ml/h), and checking for the presence of deep tendon reflexes.

(G1+) In the event of a clinical manifestation of an over-dosage, the infusion must be stopped, the injection of calcium gluconate considered and magnesium blood levels checked.

(G1+) A regular platelet count must be performed in severe PE cases.

#### **4.4 Criteria for the interruption of pregnancy (professional consensus)**

(G2+) In case of non-severe PE beyond 36 GA , interruption of the pregnancy must be considered.

(G1+) In case of severe PE beyond the 34<sup>th</sup> GA , the interruption of pregnancy is indicated.

(G1+) In case of severe PE within the first 24 GA , the performing of a medical interruption of pregnancy must be clearly discussed with the parents.

(G1+) Indications to interrupt the pregnancy in severe cases of PE between 24 and 34 GA can be either maternal or foetal:

❖ **For maternal reasons:**

• **Immediate:**

- Hypertension that cannot be controlled
- Eclampsia
- Acute pulmonary oedema
- Abruption placenta
- *Thrombocytopenia < 50.10<sup>9</sup> . L<sup>-1</sup>*
- Intra-capsular liver haematoma

• **Following corticosteroid therapy for foetal maturation (if the foetal and maternal conditions permit the prolongation of pregnancy by 48 hours):**

- Rapidly deteriorating of the renal failure and/or oliguria (i.e. <100 ml in 4 hours) resistant to appropriate fluid expansion
- Persistent signs of imminent eclampsia (i.e. headache or visual disturbances)
- Persistent epigastric pain
- HELLP syndrome which deteriorates

❖ **Foetal reasons:**

- Repeated foetal heart rate (FHR) decelerations
- Short term variability in FHR < 3 bpm, controlled,
- *Severe intra-uterine growth retardation beyond 32 GA*
- *Inverted diastolic flow in the umbilical artery beyond 32 GA.*

(G2+) If the interruption of the pregnancy has been decided, but there is no absolute need for an immediate interruption, it is possible to induce the delivery through cervical maturation.

## **5. Managing the complications of PE:**

### **5.1. Eclampsia:**

(G1+) In case of persistent visual disturbances, it is recommended to perform a fundoscopy and an MRI when available, otherwise perform a CT scan.

(G1+) Magnesium sulphate is recommended since it is superior to diazepam, phenytoin and the association of *phenergan, dolosal & largactyl*, for the management of ongoing seizures or to prevent their relapse.

(G2+) *In case of a critical relapse, the administration of a further 1.5 to 2 g of i.v. magnesium sulphate is possible.*

(G1+) Following the last crisis, it is recommended to set up a continuous magnesium sulphate infusion for 24 hours.

## **5.2 Pre-eclampsia & renal impairment:**

(G1+) It is recommended as early as the first ante-natal visit to look for signs of kidney disease and to perform a urine dipstick test.

If the latter are abnormal, investigations must include a 24 hour urinary protein count (cut-off at 300 mg / 24 hours) and an MSU for microscopy and cytology with a cut-off value at 10 RBC.mm<sup>-3</sup>

(G1+) It is recommended to assess the renal function if there is any predisposing factor for nephropathy (previous history, early hypertension, nephrotic syndrome) bearing in mind that in the second half of the gestational period, creatinine levels over 90 µmol.L<sup>-1</sup> are pathological and that the Cockcroft formula is not applicable.

(G1+) A renal consultation must be organized if there are signs of nephropathy, whatever the gestational age. This must lead to a multidisciplinary management (OG, nephrologists, anaesthesiologist & intensivist) of the pregnancy and include counselling of the mother with regard to the risk to herself and her foetus.

Indications for the use of diuretics, and ultimately, *the termination of the pregnancy in case of an acute renal failure or Thrombotic & Thrombocytopenic Purpura or Haemolytic-Uremic Syndrome (HUS)* must be discussed with the patient.

## **5.3 Pre-eclampsia & liver impairment:**

(G1-) *The administration of steroids is not recommended for the treatment of HELLP syndrome because it does not improve the maternal or the neonatal outcome.*

(G1-) Plasmapheresis does not improve maternal morbidity or mortality outcome and is therefore not recommended in cases of established HELLP syndrome.

## **5.4 Abruptio placenta:**

(G1-) *Ultrasound is not recommended for the screening of retroplacental haematomas in the at-risk patient.*

(G1-) Having a history of an isolated retroplacental haematoma is not an indication for any specific preventive therapeutic measure for subsequent pregnancies.



## 6. Anaesthesia for the woman with PE:

(G1+) An assessment of the patient must take place as early as possible in view of anaesthesia.

(G1+) It is recommended to perform a clotting screen as close as possible to the performing of an epidural anaesthesia.

(G2+) The use of aspirin, if indicated for the prevention of PE, does not as such, constitute a contraindication to performing an epidural anaesthesia if:

- ❖ No other medication altering the homeostasis is being used concomitantly.
- ❖ If her clotting screen (INR, ATTP, Fibrinogen levels, platelet count) is compatible with such a technique.

(G2+) With regards to the minimum platelet count, the recommended cut-off values for the performing of an epidural or a spinal anaesthesia are 75 & 50.10<sup>9</sup>.L<sup>-1</sup> respectively, only if all the following conditions are fulfilled:

- The thrombocytopenia is stable on several consecutive counts.
- The procedure will be carried out by an experienced operator.
- Post partum neurological monitoring will be performed.
- The patient did not, over the previous 3 days, take aspirin.

(G1+) It is recommended to quickly set up an epidural anaesthesia because this will improve the blood pressure levels, the uteroplacenteric haemodynamics as well as facilitate the management in case of a caesarean section.

(G2+) It is possible to use oxytocin (Syntocinon ®) during & after labour.

(G1-) Methylergometrine (Methergin ®) is contraindicated in the PE patient.

(G1+) Before performing a spinal anaesthesia it is recommended to restrain the administration of crystalloids to a maximum of 1000ml.

The i.v. antihypertensive treatment should be reduced or interrupted until complete establishment of the anaesthetic.

(G1-) The adrenaline containing test dose is not recommended in the PE woman.

(G1+) In case a general anaesthesia is to be performed, an assessment of the criteria for difficult intubation should be performed immediately prior to the induction.

*The technique employed should be a rapid sequence induction with intubation*, while preventing a surge in blood pressure induced by the tracheal intubation. Difficulties to extubate should be systematically anticipated.

(G2+) It is possible to perform a loco-regional anaesthesia following an eclamptic crisis if the following conditions are met:

- The woman has regained consciousness
- She doesn't have any neurological deficit
- She is clinically stable

(G1+) In case of overlapping seizures and/or impaired consciousness, a general anaesthesia is recommended.

## **7. Outcome & Follow up care:**

### **7.1 Prognosis of children born to pre-eclamptic mothers (Professional consensus)**

(G1+) It is recommended to inform the paediatricians of the mother's past and present treatments.

(G1+) In case of preterm birth or intra uterine growth retardation, it is recommended that the paediatrician and the obstetrician jointly inform the parents of the risks to be encountered.

(G2+) In case of severe HELLP syndrome and especially if there is acute fatty liver of pregnancy, it is possible to consider an ante-natal long-chain-3-hydroxyacyl-coenzyme-A-dehydrogenase (LCHAD) deficiency.

In any case, an attentive surveillance of the newborn as well as a long chain fatty acid profile workup, are recommended.

### **7.2 Early follow-up (Professional consensus)**

(G1+) Following the delivery, a strict clinical & biological monitoring must be undertaken for at least 48 hours, including:

- Frequent blood pressure charting with appropriate treatment adjustments (ref to fig.1)
- Daily assessment of fluid intake, weight and diuresis

(G1+) Women with organ failure must be admitted in an intensive care unit.

(G1+) A twice weekly blood pressure charting and a medical consultation are recommended during the 2 to 3 first post partum weeks.

(G1+) During the compulsory post natal consultation, it is recommended to verify the normalization of the blood pressure values & and the complete resolution of the proteinuria.

(G2+) In the absence of risk factors or biological anomalies, it is possible to prescribe an oestro-progestative contraceptive medication at the post natal consultation.

### **7.3 Long term follow-up:**

(G1+) If the HT and/or the proteinuria persist for more than 3 months following the delivery, it is recommended to seek a specialist's advice.

(G1-) One must not perform a post partum renal biopsy except in the following cases:

- Persistent renal insufficiency
- Signs of systemic disease
- Persistent proteinuria lasting beyond 6 months post partum

(G1+) It is recommended to look for antiphospholipid antibodies following a severe & early onset of PE.

(G1-) It is not recommended to screen for hereditary thrombophilia, except in one of the following cases:

- Past history or family history of thrombo-embolic disease
- Early PE
- Association with severe intra-uterine growth retardation, abruptio placenta or intra-uterine death

(G1+) It is recommended to initiate a specialized follow-up early (before the 14<sup>th</sup> week GA) in subsequent pregnancies, in any woman with a history of early onset PE.

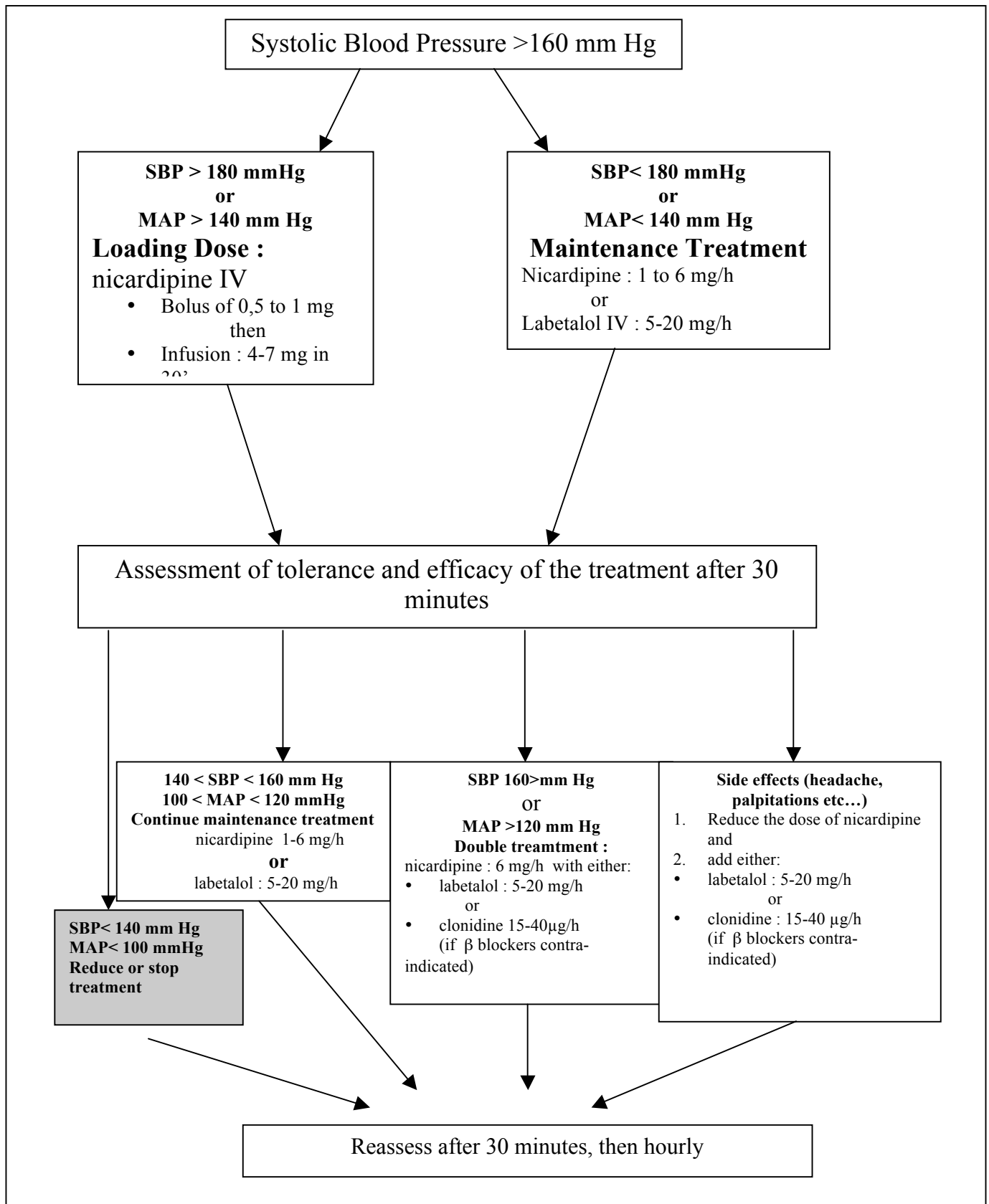
(G1+) It is recommended to monitor all the cardiovascular, renal & metabolic aspects in the long term following severe PE.

In essence, it appears that over the last eight years, even though the understanding of the pathophysiology of PE has made substantial progress, few changes in the management have proven effective.

The main advances have been made in the organization of the healthcare networks & the counselling of both mother and partner during the disease period.

This information is best provided in a prospective & collegial manner, in order to have both of the future parents participate in the therapeutic decision making process, as much as possible.

Figure 1: Flowchart for the prescription of anti-hypertensive treatment (MAP = Mean Arterial Pressure,  $[\text{Systolic BP} + 2 \times \text{Diastolic BP}] / 3$ )  
 SBP= Systolic Blood Pressure



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CIANE: Collectif interassociatif autour de la naissance

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