



THE CURRENT APPROACH TO PRECLAMPSIA

In Ancient Greece the believe was that the human body was made up of four types of humors, and any imbalances among them resulted in illness. Women were thought to be more vulnerable to disease because of an overproduction of fluids and due to the presence of a “wandering womb” that could invade her various organs and even cause seizures during pregnancy (1). Hippocrates, the father of medicine, thought that seizures during pregnancy were the result of blood congestion or depletion in the brain (2).

During the Middle Ages religious believes prevailed; charms, magical concoctions, and prayers for healing were used (1). In an attempt to reduce cerebral congestion and prevent eclampsia, Mauriceau recommended performing between two and three phlebotomies during pregnancy, and overstated in his writings the critical nature of the disease (3).

By the end of the 19th Century and early in the 20th Century, physicians in Germany and the Netherlands managed preeclampsia aggressively, delivering the fetus immediately, either vaginally or abdominally. This aggressive obstetric approach dramatically increased maternal mortality. Consequently, the conservative management of preeclampsia gained popularity (4). The pioneers of this method were Tweedy in Dublin and Stroganoff in Russia (1). The former considered that hastening of labor and delivery increased the occurrence of seizures due to reflex mechanisms. The physician should refrain from conducting any vaginal examinations, abdominal palpation, and cervical dilatation. The patient was sedated with high doses of morphine and if the patient went into labor, the application of forceps was permissible (5).

Stroganoff advocated in favor of medical and non-obstetric therapy for preeclampsia. Seizures could interrupt cardiac, liver, and pulmonary function. He treated eclampsia, ignoring pregnancy and waiting for the beginning of natural labor; Stroganoff recommended that the patient had to be in a silent and dark room, and administered analgesia and sedation with morphine and chloral hydrate. In order to restore the respiratory function, oxygen was administered, and to restore the myocardial function, digitalis agents were used. The artificial rupture of the membranes was recommended during labor, once a 6 cm dilatation was reached (6). This therapeutic approach that achieved the lowest maternal mortality rates at that time (5%), was called the Stroganoff Regimen, and in his last publication describing the use of low doses of magnesium sulfate, the method was called Extended and Improved Prophylactic Method for the Treatment of Eclampsia (7).

The 20th Century shed new light on the treatment of the disease. Professor Lazard of Los Angeles introduced in 1925 the systematic management with magnesium sulfate (8). As a result of the clinical experience of the North American School, several regimens were developed: Zuspan, 1964 (9); Pritchard, 1975 (10); Sibai, 1981 (11). At present, based on the work by Dr. Lelia Duley from Oxford, magnesium is the standard therapy for eclampsia (12) and the recommended approach to prevent the disease (13).

However, after the sixties, few new recommendations have been made for the treatment of preeclampsia (14). Once the diagnosis is made, management includes: hospitalization, rest, frequent blood pressure

and weight measurements, urinalyses, assessment of fetal wellbeing, and surveillance for compromise of several maternal organs that may lead to the suspicion of progression to severe preeclampsia, and the likelihood of developing eclampsia (15). The decision regarding the route of delivery depends on multiple factors, including gestational age, the cervical and the mother-fetus condition (16). The idea still prevails that a fundamental pillar to halt the progression of the severity of the disease is interruption of pregnancy (17).

At present, with the development of evidence-based medicine, clinical practice guidelines (18) and international consensus (19) have been published, with a view to establishing the best management, in accordance with the available information. Attempts have been made to identify a personalized medicine to approach the problem (20) and despite this illusion of progress, preeclampsia is still an old disease, treated with few recommendations based on levels of evidence A (21). There are many expert opinions that in their respective institutions represent individual management approaches and probably a number of subjective truths.

Current strong recommendations to be implemented include: the use of magnesium for the treatment and prevention of eclampsia, corticosteroid administration to promote lung maturity in preterm pregnancies with a satisfactory fetal status, parenteral antihypertensive drugs in hypertensive crisis, and not less important, a robust medical record, the identification of proteinuria, the risk-based approach of the illness, molecular and biochemical markers to establish multiple organ system involvement and ultrasound to determine the placental and fetal involvement (21).

Furthermore, certain options other than termination of pregnancy are now being evaluated for the management of preeclampsia far from term. One of these new options is the so called “expectant management” which is described in this issue of the journal in

a historical cohort of patients. Expectant management is based on considering that firstly in some patients the presentation of preeclampsia may be non-severe; in others, this “benign” form evolves into a severe form, and in other cases it is identified as severe preeclampsia from the very beginning. Secondly that the non-severe form may be subject to a contemplative management that enables increased fetal maturity without increasing the risk for the mother.

In order to consider the potential benefits and risks associated with expectant management, a number of concepts must be specified. First, if the disease is diagnosed prior to week 34—early preeclampsia—it is difficult to support the idea that the condition is evolving as a non-severe form, since it has been found that under the best circumstances, with the strictest follow-up, expectant management in these cases does not exceed 9 days in average (22). Hence, it is debatable to consider that the birth of a premature baby with low weight for gestational age as a result of abnormal placentation is a form of non-severe disease. Moreover, it could be argued that these 9 days in a premature baby could be beneficial in terms of pulmonary and metabolic maturation.

When the pregnant mother with this condition is between weeks 24 and 37, that is late onset preeclampsia (23). At this gestational age, all cases were individualized based on severity criteria (19), and women presenting with non-severe preeclampsia may be subject to expectant management. The severity criteria described by the American College of Obstetricians and Gynecologists (19) are expanded by the Canadian school that groups them into adverse conditions and severe complications of the disease (24). At this gestational age it is easier to decide when to induce labor, because of fetal maturity. Finally, there is preeclampsia diagnosed after week 37 that is usually the result of a prenatal control that failed to previously identify the preeclampsia. In these cases, the definitive management is immediate induction of labor (25). These cases should not occur if there is adequate prenatal control.

Based on the above, we believe that in the current obstetrics practice, one of the objectives of prenatal medical control is to prevent as far possible, eclampsia and to prevent maternal and perinatal mortality, extreme maternal morbidity, and perinatal morbidity associated with placental insufficiency; and to avoid any sequelae attributable to the disease, such as: irreversible neurological injury, maternal chronic renal damage, or neurological sequelae in the neonate associated with perinatal asphyxia.

In our opinion, mothers with early preeclampsia that meet the criteria for expectant management, shall be hospitalized and their management should never be ambulatory. The purpose of hospitalization is to ensure safe and high-quality care, for both the mother and the baby, in order to avoid as much as possible, any maternal and perinatal complications and potential sequelae from the disease. There must be a balance to maximize the perinatal benefits and minimize the risk for the mother. It is important to understand the multiple clinical expressions of an enigmatic disease, in which it is difficult to know exactly the extent of involvement of the various organs affected, and which exhibits broadly heterogeneous clinical phenotypes. Hence, it is advisable to make an adequate evaluation of new management proposals that go beyond the old guidelines (26).

We must strive to start a new era for an old disease. It is important to consider - in cases of early preeclampsia - the use of molecular and biochemical markers to select cases with a higher potential of complications, earlier during pregnancy, and with greater accuracy. A notable example is the risk of placental abruption inherent to early preeclampsia, which is difficult to predict (27). There is a current concept about early non-angiogenic preeclampsia, that uses the ratio sftl-1/PlGF (ratio between the soluble receptor of the Vascular Endothelial Growth Factor / Placental Growth Factor) as a biochemical marker, that apparently allows for a more precise diagnosis of the severity of the condition, than the classical severe PE criteria (28, 29). It is

important to undertake studies to assess the accuracy, the effectiveness and the safety of the new biochemical markers of the disease to objectively identify women at risk and to clearly define the cases where the aggressive interruption of pregnancy is imminent.

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