THE ROLE OF CLASSIFICATION ON THE MANAGEMENT OF SEVERE PREECLAMPSIA

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Preeclampsia occurs as a spectrum but is arbitrarily divided into mild and severe forms. This teminology is useful for descriptive purposes but does not indicate specific disease nor should it indicate arbitrary cut off points for therapy. The diagnosis of severe preeclampsia is confirmed when the following criteria are present:

1- Systolic blood pressure of 160 mm Hg or greater, or diastolic pressure of 110 mm Hg or greater.
2- Proteinuria of 2 g or more in 24 hours (2 or 3 plus on qualitative examination).
3- Increased serum creatinine (greater than 1-2 mg/dL unless known to be previously elevated)
4- Persistent headache or cerebral or visual disturbances
5- Persistant epigastric pain
6- Platelet count less than 100.000 / mm ^{3} and/or evidence of microangiopathic hemolytic anemia (with increased lactic acid dehydrogenase)

Edema has been abondoned as a marker in preeclampsia by the National High Blood Pressure Education Program (NHBPEP) (1).

The variable nature of pre-eclampsia mirrors the complexity of the pathophysiology of the condition. It is possible that pre-eclampsia is not a single entity, but only a final common pathway by which the woman reacts to pathological pregnancy. Clinicians seek to define pre-eclampsia to identify a group of women that have pregnancies at higher than average risk either to the women themselves or to their fetuses. By contrast, researchers seek to define preeclampsia so that workers can be as certain as possible that they are studying pre-eclampsia and not some other disease. Unlike the clinical definition, it does not matter if some who have the disease are omitted. What matters is that those who do not have the disease are excluded (2).

In developed and developing countries, preclampsia is still responsible for high maternal and fetal morbidity and mortality. In our country, the rate of maternal mortality is 49-132 per 100.000 live birth. Preeclampsia is account for 15,5 % of maternal mortality as a second reason after bleeding complications (Turkish Ministry of Health records).

The goal of classification for clinical management should be 1) Idendification of patients who have at risk having eclampsia and to provide these women adequate treatment for preventing seizures 2) to provide evaluation and management of severe preeclamsia at secondary or tertiary care hospitals with timely referal from primary care centers, 3) to define criteria for clinical desicion making between conservative management and expedited delivery of patients with severe preeclampsia. 4) preventing serious hypertension-related and low organ perfusion-related complications 5) to decrease perinatal morbidity and mortality.

Does the current classifications adequate for these purposes?

The problems with classification are as belows:

1- Preeclampsia has a clinical spectrum ranging from mild to severe forms and then potentially to eclampsia. Affected patients don't catch eclampsia or the severe forms of preeclampsia but rather progress through this spectrum.
2- In most cases, progression is slow, and the disorder may never proceed beyond mild preeclampsia. In others, the disease can progress more rapidly, changing from mild to

severe over days to weeks. In the most serious cases, progression can be fulminant, with mild preeclampsia evolving to severe preeclampsia over hours to days.(1)

In terms of proper clinical management, we must accept the fact that we are overdiagnosing the condition because, a major goal in managing preeclampsia is the prevention of the serious complications of preeclampsia, primarily through timing of delivery.

Preeclampsia is considered severe if blood pressure and proteinuria are increased substantially or symptoms of end-organ damage (including fetal growth restriction) occur. Management before the onset of labor includes close monitoring of maternal and fetal status, seizure prophylaxis with magnesium sulfate. Management during delivery includes seizure prophylaxis with magnesium sulfate and, if necessary, medical management of hypertension. Delivery remains the ultimate treatment. Access to prenatal care, early detection of the disorder, careful monitoring, and appropriate management are crucial elements in the prevention of preeclampsia-related deaths (3). But, identification and treatment of severe preeclampsia does not allow always to prevent the complications to mother and fetus.

Physicians now agree that the best medication for seizures with preeclampsia is magnesium sulfate. Some investigators are beginning to question whether all patients with preeclampsia should receive seizure prophylaxis. Physicians will often look the other way in cases of mild preeclampsia, relabeling the disease as “pregnancy-induced hypertension” to avoid the use of magnesium sulfate. Because, magnesium sulfate is not a benign drug. It is associated with complications, and although most studies have shown that it does not increase the duration of labor, maternal blood loss, or cesarean delivery rate, it does change intrapartum and postpartum care and does affect many maternal and fetal parameters (4, 5, 6). Some authors have suggested giving magnesium sulfate prophylaxis only to patients with severe preeclampsia. Unfortunately, most eclampsia occurs before patients reach the hospital and not primarily among women with severe preeclampsia. Randomized controlled trials and systematic reviews have demonstrated the efficacy of magnesium sulfate in preventing eclampsia in patients with preeclampsia or in patients with eclampsia (7). Whether magnesium sulfate should be administered only to patients with severe preeclampsia or to mild preeclampsia is controversial.

If hypertension is the hallmark of pre-eclampsia, then most would believe that it is proteinuria which distinguishes the hypertension of other causes (sinister or innocent) from the hypertension of pre-eclampsia. But, because of the variability of pre-eclampsia it is possible to have severe disease with all the other features of preeclampsia but without proteinuria. Proteinuria like hypertension and oedema might also be due to other conditions like kidney disease or urinary tract infection (8).

Given the current high expectations for the outcome of pregnancy, the definition should be as all encompassing as practical, even if it has a high false-positive rate—ie, women will be included where the excess risk is small, if there is any at all. For such a group a practical definition for pregnancy-induced hypertension would be: new hypertension with blood pressure of 140 mm Hg systolic or greater or 90 mm Hg diastolic or greater (phase V) arising after 20 weeks. This group does not necessarily have pre-eclampsia but is at risk of developing preeclampsia and must receive closer monitoring. The development of pre-eclampsia will usually depend on the appearance of new proteinuria (+ albuminuria on at least two occasions not in labour, urine protein concentration 500 mg/L, urine protein excretion 300 mg per 24 h) but other features such as fetal compromise symptoms, eclampsia, hyperuricaemia, thrombocytopenia, or other manifestations of HELLP (haemolysis, elevated liver enzymes, and low platelet count) syndrome could also be used to define the appearance of pre-eclampsia (8).

Two definitions are commonly cited in the literature (9,10). In general these definitions are advocated for epidemiological purposes—ie, to describe the incidence and prevalence of

hypertension in pregnancy in populations rather than to guide clinical management or to stringently characterise patients with pre-eclampsia for research purposes(8).
Davey and MacGillivray's classification (9) of pregnancy hypertension, is detailed and also considers several different forms of hypertension that could arise in pregnancy. Hypertension is diagnosed by a single diastolic blood pressure of 110 mm Hg or greater or consecutive readings of 90 mm Hg or greater on more than one occasion at least 4 h apart. Proteinuria is defined as a 24 h excretion of 300 mg or more, two clean-catch urine specimens at least 4 h apart with: 2+proteinuria by dipstick; 1+proteinuria if specific gravity less than 1030; and protein/creatinine index of 300 or more .
According to ACOG, although there have been changing definitions and language ambiguity, mild and severe preeclampsia are now defined clearly by ACOG, and these criteria should be used to make the best treatment decisions (10). ACOG criterias for mild and severe preeclampsia are as belows:

Mild preeclampsia
Hypertension withedema (≥ 1+), Proteinuria (≥0.3 gm/24 hr), or both after 20th week of gestation. Blood pressure ≥140/90 mm Hg on ≥ 2 occasions 6 hours apart

Severe preeclampsia
Blood pressure systolic, ≥160 mm Hg; blood pressure diastolic, ≥110 mm Hg (with patient at rest, 2 measurements at least 6 hours apart)
Proteinuria (≥ 5 g/24 hr or 3 + proteinuria) occurring for the first time in pregnancy and regressing after delivery
Increased serum creatinine level (≥1.2 mg/dL, unless known to be elevated previously)
Platelet count <100,000 (thrombocytopenia) or evidence of microangiopathic hemolytic anemia (with elevated lactate dehydrogenase)
Intrauterine growth retardation or oligohydramnios
Elevated hepatic enzymes (alanine aminotransferase, aspartate aminotransferase)
Microangiopathic hemolysis
Symptoms that suggest significant end-organ involvement: Headache, visual disturbances, epigastric or right upper quadrant pain, retinal hemorrhage, exudates, or papilledema
Pulmonary edema
Oliguria <500 mL/24 hr

Eclampsia
Mild or severe preeclampsia and seizures or coma

On the other hand, current model and management of eclampsia have developed from a reliance on the ancient Greek terminology. From the terminology the paradigm has been derived that preeclampsia evolves from mild disease to severe disease and then to eclampsia. This paradigm, in use today, assumes that the more severe the symptoms are, the more likely it is that a woman will have a seizure. A significant component of the management of severe preeclampsia is seizure prophylaxis (2).
Preeclampsia is a disease of endovascular damage. The endovascular damage leads to a loss of vascular autoregulation, significant vascular spasm, and vascular leakage. Disease severity varies not only from patient to patient but also from organ system to organ system within an individual. One woman may have oliguria but no change in liver functions, whereas another may have severe hypertension and minimal proteinuria. Logically, as the disease progresses,

organ systems become more susceptible to injury from vasospasm. Women with loss of cerebrovascular integrity may have seizures before the development of hypertension or proteinuria.

Katz et al. (2) questioned the tradition that eclampsia evolves in a fairly linear manner from mild preeclampsia to severe preeclampsia to seizures. It was also questioned the assumption that the seizures of eclampsia are predictable. Other than headache occurring shortly before the seizures, fewer than half of the patients had signs or symptoms of preeclampsia before seizure. In 32 of 53 (60%) seizures were the first signs of preeclampsia. Only patients could be considered to have signs of severe preeclampsia when one discounts the headache or visual changes that occurred immediately before the seizures. Among these 7, there were 4 who were receiving magnesium sulfate at the time of the seizure, and in 2 women magnesium sulfate was being readied by the nurse. Among the actual cases of eclampsia in this review only 9 were potentially preventable.

Is eclampsia really a predictable and potentially preventable disease? Eclampsia has not been found to be necessarily related to either the degree of proteinuria or the degree of hypertension (4,11). However, Yucesoy et al.(12) in 255 cases, 138 patients (54.11%) were found to have severe preeclampsia while 88 cases (34.50%) were diagnosed as mild preeclampsia. Of 138 severely preeclamptic cases, 28 cases (11%) had eclamptic convulsion and another 28 patients (11%) were demonstrated to have HELLP syndrome. Maternal mortality occured in 3 cases (1.2%) and all of those cases were complicated with HELLP syndrome. Intracranial bleeding was the cause of maternal death in one case while the other two cases were lost due to acute renal failure and disseminated intravascular coagulation, respectively. Intrauterine fetal demise was recorded in 24 cases on admission. Ten fetuses died during the intrapartum period. In these ten women, five cases were diagnosed as HELLP syndrome, two were severely preeclamptic and three were eclamptic. They concluded that the complications of severe preeclampsia and eclampsia could be prevented by more widespread use of prenatal care, education of primary medical care personnel, prompt diagnosis of high-risk patients and timely referral to tertiary medical centers .

Finally, the current management strategy is determined by classification of preeclampsia. Although, the current classification is based on the disease severity and allow us identifiying high risk patients and treat these women properly, it should not be forgotten that preeclampsia is a complex disease and serious complications such as eclampsia may also occur in mild preeclamsia. Physicians should take seriously all preeclamtic patients regardless of clinical classification and monitoring fetus and mother closely and treat them properly.

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