EXPECTANT MANAGEMENT OF PATIENTS WITH SEVERE PREECLAMPSIA-MATERNAL AND PERINATAL OUTCOME

Skrablin S and Banovic V

University department of Obstetrics and Gynecology, University of Zagreb, Petrova Hospital, Croatia

Preeclampsia (EI) still remains the leading cause of fetal and maternal morbidity and mortality. It is unpredictable in its onset and progression and thought to be incurable except by termination of pregnancy. The delivery is always appropriate therapy for the mother, but may not be so for the child if remote from term. So, in about two thirds of the patients, at least initially (1) conservative therapy is undertaken to achieve either some degreee of fetal pulmonal maturity or 34 weeks in gestation (2-4). Various treatment regimens have been advocated so far when trying to achieve this goal, but success rate reported was variable (2). The major obstacle to the advancement of our knowledge when and how to treat EI conservatively could be the publication of studies of mild cases, because the diagnosis is likely to be erroneous in about half of them (2), the inclusion of patients with exquisitely severe disease who biased all conservative approaches and the difficulties in understanding the underlying pathophysiology of the disease (3, 4).

The presence of severe disease mandates immediate hospitalization in labor and delivery suite and intravenous medication. To prevent convulsions, magnesium sulfate (5) is given frequently. Not all authors suggest magnesium treatment as the primary therapy, however. In the study of Haddad et al. (6), no magnesium therapy was given, yet no maternal death nor eclampsia developed. The aim of antihypertensive therapy is to keep systolic BP between 140 and 155 mm Hg and diastolic BP between 90 and 105 mm Hg. During the observation period maternal and fetal conditions are assessed and a decision is made regarding the need for delivery.

Patients with gestational ages of 24 -34 weeks are given corticosteroids to accelerate fetal lung maturity. In the past, it was believed that infants born prematurely to severely preeclamptic women had lower rates of neonatal mortality and morbidity than infants of similar gestational age from nonpreeclamptic women. This belief was based on the clinical impression that fetuses of preeclamptic women have accelerated lung and neurologic maturation as a result of stress in utero. This phenomenon, however, has never been documented in case-control studies (5). In contrast, several recent case-control studies have

demonstrated that premature infants born after severe preeclampsia have neonatal complications and mortality similar to those of other premature infants of similar gestational age and have higher rates of admission to neonatal intensive care units. In addition, case-control studies have revealed that fetuses of preeclamptic women do not exhibit accelerated lung or neurological maturation. In the past there was uncertainty regarding the efficacy and safety of corticosteroids in women with severe preeclampsia before 34 weeks' gestation. A prospective double blind, randomized trial of 218 women women with severe preeclampsia and gestational age between 26 and 3 4weeks receiving either betamethasone or a placebo reported a significant reduction in the rate of respiratory distress syndrome in the steroids group (7). Corticosteroid use also was associated with a reduction in the risks of neonatal intraventricular hemorrhage, neonatal infection, and neonatal death. Maternal evaluation includes monitoring of BP, urine output, cerebral status, and the presence of epigastric pain, tenderness, labor, or vaginal bleeding. Laboratory evaluation includes a platelet count and liver enzyme and serum creatinine testing. Fetal evaluation includes fetal heart monitoring, a BPP, and ultrasonographic assessment of fetal growth and amniotic fluid as well as Doppler flow velocimetry especially in the presence of suspected growth restriction. Patients with resistant severe hypertension despite maximum doses of labetalol (220 mg) plus nifedipine50 mg) or persistent cerebral symptoms while on magnesium sulfate deliver within 24-48 hours irrespective of fetal gestational age. Urapidylhydrochlorid can also be reccomended to treat severe hypertension (8). In addition, patients with either thrombocytopenia (platelet count less than 100,000) or elevated liver enzymes with epigastric pain and tender-ness or with serum creatinine of 2.0 mg/dL or more also deliver within 48 hours (9).

Patients with gestational ages of 33 to 34 weeks are given corticosteroids and could be delivered after 48 hours. Patients with gestational age below 23 weeks are offered termination of pregnancy. Patients at 23-32 weeks' gestation receive individualized treatment based on their clinical response during the 24-hour observation period. If BP is adequately controlled and fetal tests are reassuring, magnesium sulfate could be discontinued and the patients are then observed closely on the antepartum high-risk ward until 34 weeks' or development of a maternal or fetal indication for delivery. During hospitalization, they receive antihypertensive drugs if needed, usually oral nifedipine (40 -120 mg per day) plus labetalol (600-2400 mg per day), or urapidylhydrochlorid, alone or in combination with methyldopa (8) to keep systolic BP between 140 and 155 mm Hg and diastolic pressure between 90 and 105 mm Hg, The patients also receive daily assessment of maternal and fetal well-being (9). In general, most patients will require delivery within 2 weeks, but some patients may continue their

pregnancies for several weeks (4, 6, 10, 11) . It is important to emphasize that this therapy is appropriate only in a select group of patients and should be practiced only in a tertiary-care center with adequate maternal and neonatal intensive care facilities. In addition, once the decision is made for delivery, the patients should receive magnesium sulfate in labor and for at least 24 hours postpartum.

The goals of treatment of women with gestational hyper-tension-preeclampsia are early detection of fetal heart rate abnormalities, early detection of progression from mild to severe disease, and prevention of maternal complications. Pregnancies complicated by preeclampsia, particularly those with severe disease and/or fetal growth restriction, are at risk for reduced fetal reserve and abruptio placentae (4, 6, 10, 11). Therefore, all women with preeclampsia should receive continuous monitoring of fetal heart rate and uterine activity, with special attention to hyperstmulation and development of vaginal bleeding during labor. The presence of uterine irritability and/or recurrent variable or late decelerations may be the first sign of abruptio placentae in these women. Some women with mild hypertension-preeclampsia will progress to severe disease as a result of changes in cardiac output and stress hormones during labor. Maternal pain relief during labor and delivery can be provided by either systemic opioids or segmental epidural anesthesia. Epidural analgesia is considered the preferred method of pain relief in women with mild gestational hypertension and mild preeclampsia (12, 13). Either epidural, spinal, or combined techniques or regional anesthesia are considered by most obstetric anesthesiologists to be the method of choice during cesarean delivery. In women with severe preeclampsia general anesthesia increases the risk of aspiration and failed intubation due to airway edema and is associated with marked increases in systemic and cerebral pressures during intubation and extubation (13). It is important to emphasize that regional anesthesia is contraindicated in the presence of coagulopathy or severe thrombocytopenia (plate-let count less than 50,000/mm^3).

Magnesium sulfate is the drug of choice to prevent convulsions in women with preeclampsia. Two recent randomized trials showed that magnesium sulfate is superior to a placebo for prevention of convulsions in women with severe preeclampsia (14, 15). One of the largest randomized trials to date enrolled 10,141 women with preeclampsia in 33 nations in the ThirdWorld (15). Among all enrolled women, the rate of eclampsia was significantly lower in those assigned to magnesium sulfate. However, among the 1560 women enrolled in the Western world, the rates of eclampsia were 0.5% in the magnesium group and 0.8% in the placebo, a difference that was not significant. Our study comparing the 40 women treated primarily with magnesium sulphate and 47 women group treated with diazepam and urapidil, There are two randomized placebo-controlled trials evaluating the efficacy and safety of metildopa or nifedipine has proved magnesium sulphate therapy to be superior to magnesium sulfate in women with mild preeclampsia (16).There were no instances of conventional antihypertensive therapy in the management of severe preeclampsia (8).
eclampsia in either group in both of these trials. In addition, the findings of both studies revealed that magnesium sulfate does not efect the duration of labor or the rate of cesarean delivery. However, neither of these studies had an adequate sample size to determine the

efficacy of magnesium sulfate in preventing convulsions. Therefore, the benefit of magnesium sulfate in women with mild preeclampsia remains unclear. A randomized trial to answer this question is urgently needed.

There are no randomized trials comparing optimal methods of delivery in women with gestational hypertension-preeclampsia. Altgough almost half and even more pregnancies are delievered by cesarean section (4, 6, 10, 11), a plan for vaginal delivery should be attempted for all women with mild disease and for the majority of women with severe disease, particularly those beyond 30 weeks' gestation (17). The decision to perform cesarean delivery should be based on fetal gestational age, fetal condition, presence of labor, and cervical Bishop score. In general, the presence of severe preeclampsia is not an indication for cesarean delivery.

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