Severe preeclampsia: differences in the management according to gestational age

SEBASTIAN KWIAKOWSKI1, RAFAŁ RZEPKA1, ANDRZEJ TORBE1, ALEKSANDRA RAJEWSKA1, EWA KWIAKOWSKA2, WIOLETTA MIKOŁAJEJ-BEDNER1, JOANNA LEWANDOWSKA1, AGATA ŚWISZCZOWSKA1, MARTA ZAPAŁOWSKA-CHWYĆ1, RYSZARD CZAJKA1

Abstract

Severe preeclampsia is one of the serious complications of pregnancy. In literature occurs two different attitudes to severe preeclampsia depend on gestational age. We present our experience in diagnostic, monitoring and management, and try to evaluate perinatal results in two separate women groups with early and late onset severe preeclampsia.

Key words: early severe preeclampsia, late severe preeclampsia, gestational age

Introduction

Preeclampsia occurs in as many as 10% of pregnancies, usually in the second or third trimester. Some women experience preeclampsia as early as at 20 weeks of gestation, though this is a rare phenomenon. The only effective treatment for rapidly deteriorating preeclampsia or eclampsia is termination of pregnancy in the form of abortion or, in advanced stage of pregnancy, delivery performed in the manner of either vaginal labor induction or caesarean section [1].

At present early diagnosis and decision on delivery are crucial. But yet, this active management increases neonatal morbidity and mortality, caused by prematurity and by its adverse sequels. From another point of view, continuation of pregnancy increases the incidence of maternal secondary complications like eclampsia, HELLP syndrome and placental abruption. The management of preeclampsia depends on gestational age, clinical symptoms occurrence and maternal and fetal clinical state [2]. Questions arise, which kind of symptoms should play the essential role in decision making whether to deliver or to continue pregnancy, choosing expectant management.

The aim of our study was to evaluate the accuracy of diagnostics, monitoring and management in the pregnant with severe preeclampsia. Additionally, we analyzed delivery mode and perinatal outcomes in this group. Finally, we tried to pay attention for opportunities of different management pathways according to gestational age.

Materials and methods

The analysis was based on the group of 39 pregnant women admitted to our Department according to severe preeclampsia. The group included 11 multiparas, 10 primiparas and 18 primigravidas. There were 35 singleton and 4 twin pregnancies. Caesarean section was dominating delivery mode; it was performed in 35 women. Only 4 women gave birth by vaginal delivery.

The group was subsequently divided into two subgroups. Women suffering from severe preeclampsia diagnosed between 24th and 34th week of gestation were qualified to the first subgroup of Early Onset Severe Preeclampsia (EOSP). Preeclampsia diagnosed after 34th week of gestation was eligibility condition for second subgroup of Late Onset Severe Preeclampsia (LOSP). In these patients, clinical and biochemical parameters, as well as parity, maternal complications and delivery mode, were analyzed.

The diagnostic criteria were: blood pressure exceeding 160 mm Hg systolic and 110 mm Hg diastolic in two subsequent measurements with 6 hours interval accompanied by proteinuria higher than 2 g per 24 hours. In 15 women continuous blood pressure monitoring using Holter method was performed.

Every woman who was admitted before completed 34 weeks of gestation, received at least one dose of corticosteroids (12 mg of betamethasone). If the time left to delivery was longer than 48 hours, they had full-dose fetal lung maturation therapy completed. All patients

1 Department of Obstetrics and Gynecology, Pomeranian Medical University, Szczecin, Poland
2 Department of Nephrology, Transplantology and Internal Medicine, Pomeranian Medical University, Szczecin, Poland
were administered with oral hipotensive pharmacologic treatment with alpha-methyldopa, nifedipine, prazosine or dihydralazine which was matched according to hypertension severity and therapeutic effectiveness. 12 women required additional administration of intravenous hipotensive agents like dihydralazine or urapidil and 6 were given with prophylactic magnesium sulfate intravenous infusion.

We used Statistica 6 as adequate software for data processing. The distribution of variables was checked using non-parametric Shapiro-Wilk test and according to its results they were further analyzed. Values were presented as absolute numbers or as medians and range set. For nonparametric distributions U Mann-Whitney test was used, while for qualitative traits we used Chi square test. Level of significance (p) lower than 0.05 was considered significant.

**Results**

In 2 postpartum patients HELLP syndrome occurred. They presented hemolysis with lactate dehydrogenase (LDH) serum levels exceeding 600 U/l or total bilirubin level over 1.2 mg/dl, platelets count lower than $100 \times 10^9$/l and aspartate aminotransferase (AST) serum level over 70 U/l.

In all analyzed women NOTCH was observed in at least one uterine artery; in 23 of them NOTCH was present in both uterine arteries. Resistance index (RI) exceeding 0.58 in at least one uterine artery was found in 18 women. It is worth noting that none of analyzed women had bilateral NOTCH and increased RI in both uterine arteries simultaneously.

In 3 women pregnancy was complicated with threatened or overt eclampsia and in 2 placental abruption occurred. Four women developed oliguria with diuresis lower than 500 ml per 24 hours.

In 4 pregnancies oligohydramnios was found, 8 fetuses were diagnosed as suffering from intrauterine growth restriction (IUGR) and subsequently birth weight below $10^{th}$ percentile adequately to gestational age. In 3 fetuses Doppler test revealed the absence of end diastolic flow velocity (AEDFV) in umbilical arteries.

As shown in Table 1, there were not statistically significant differences neither in parity nor in delivery mode between compared EOSP and LOSP subgroups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EOSP (n = 16)</th>
<th>LOSP (n = 23)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age [weeks]</td>
<td>30 (26-34)</td>
<td>37 (35-38)</td>
<td>0.002</td>
</tr>
<tr>
<td>Systolic blood pressure [mm Hg]</td>
<td>180 (160-210)</td>
<td>170 (160-200)</td>
<td>ns</td>
</tr>
<tr>
<td>Diastolic blood pressure [mm Hg]</td>
<td>115 (110-140)</td>
<td>110 (110-130)</td>
<td>ns</td>
</tr>
<tr>
<td>Maternal body weight at delivery [kg]</td>
<td>75.3 (61-104)</td>
<td>82.5 (70-128)</td>
<td>ns</td>
</tr>
<tr>
<td>Maternal pregnancy weight gain [kg]</td>
<td>11 (7-19)</td>
<td>15 (5-25.5)</td>
<td>0.037</td>
</tr>
<tr>
<td>Neonatal birth weight [g]</td>
<td>1420 (745-1940)</td>
<td>3020 (1915-3750)</td>
<td>0.003</td>
</tr>
<tr>
<td>Maternal fluid income [ml]</td>
<td>2500 (1100-3500)</td>
<td>2600 (1500-3500)</td>
<td>ns</td>
</tr>
<tr>
<td>Maternal fluid outcome [ml]</td>
<td>1900 (200-3900)</td>
<td>2300 (700-4900)</td>
<td>ns</td>
</tr>
</tbody>
</table>

There were not statistically significant differences found neither in the highest systolic and diastolic blood pressure, nor in maternal fluid income and outcome, between compared EOSP and LOSP subgroups. Discreet difference in maternal body weight values at delivery was also insignificant. Significantly higher body weight gain in the course of gestation, obtained in women suffering from late preeclampsia was an obvious consequence of longer pregnancy duration in LOSP subgroup.

Analysis of biochemical parameters proved significantly higher proteinuria severity and serum uric acid elevation in EOSP compared with LOSP subgroup. However the differences in other studied parameters remained insignificant (Table 3).

Women qualified to EOSP subgroup were more prone to develop oliguria as a prodromal symptom of acute renal insufficiency. The analysis of uterine arteries...
blood flow evaluations with Doppler method also showed significantly higher frequency of increased RI in uterine arteries in the EOSP subgroup, however no statistically significant difference in NOTCH prevalence was found (Table 4).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EOSP (n = 16)</th>
<th>LOSP (n = 23)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria (g/24 h)</td>
<td>6.85 (2.24-17.2)</td>
<td>2.9 (2.76-17.2)</td>
<td>0.0181</td>
</tr>
<tr>
<td>Serum uric acid level (mg/dl)</td>
<td>7.4 (4.3-8.7)</td>
<td>6.05 (3.6-8.6)</td>
<td>0.0181</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>35.5 (28.7-43.7)</td>
<td>34.3 (22.2-45.4)</td>
<td>ns</td>
</tr>
<tr>
<td>Platelet count (100 x 10^9/l)</td>
<td>161 (58-393)</td>
<td>209 (79-523)</td>
<td>ns</td>
</tr>
<tr>
<td>Aspartate aminotransferase level (U/l)</td>
<td>24 (15-74)</td>
<td>26 (18-427)</td>
<td>ns</td>
</tr>
<tr>
<td>Alanine aminotransferase level (U/l)</td>
<td>21 (11-92)</td>
<td>18.5 (11-365)</td>
<td>ns</td>
</tr>
<tr>
<td>Lactate dehydrogenase level (U/L)</td>
<td>442 (102-789)</td>
<td>425 (230-1146)</td>
<td>ns</td>
</tr>
<tr>
<td>D-dimer serum concentration (ng/ml)</td>
<td>1251 (393-7325)</td>
<td>1682 (744-6110)</td>
<td>ns</td>
</tr>
<tr>
<td>Serum fibrinogen level (g/l)</td>
<td>3.99 (2.89-6.48)</td>
<td>4.1 (3.56-5.1)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Table 3. Biochemical parameters in the analyzed subgroups

The only statistically significant difference in respect of fetal complications was higher prevalence of AEDFV proven in EOSP subgroup. The differences in oligohydramnios and IUGR prevalence between EOSP and LOSP subgroups were found insignificant (tab. 5).

Table 4. Prevalence of maternal complications in the analyzed subgroups

<table>
<thead>
<tr>
<th>Complication characteristics</th>
<th>EOSP (n = 16)</th>
<th>LOSP (n = 23)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eclampsia prodromal symptoms</td>
<td>1 (6.25)</td>
<td>2 (8.69)</td>
<td>ns</td>
</tr>
<tr>
<td>Placental abruption</td>
<td>1 (6.25)</td>
<td>1 (4.35)</td>
<td>ns</td>
</tr>
<tr>
<td>Oliguria (&lt; 500 ml/24h)</td>
<td>4 (25)</td>
<td>0 (0)</td>
<td>0.024</td>
</tr>
<tr>
<td>Low platelet count (&lt;100 x 10^9/l)</td>
<td>5 (31.25)</td>
<td>2 (8.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Unilateral NOTCH</td>
<td>16 (100.0)</td>
<td>23 (100.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Bilateral NOTCH</td>
<td>12 (75.0)</td>
<td>11 (47.8)</td>
<td>ns</td>
</tr>
<tr>
<td>Resistance index &gt; 0.58</td>
<td>13 (81.25)</td>
<td>5 (21.74)</td>
<td>0.028</td>
</tr>
</tbody>
</table>

Table 5. Fetal complications in the analyzed subgroups

Duration of maternal hospitalization from admission to delivery was significantly longer in EOSP compared with LOSP subgroup. The only exception concerned one patient who delivered before 48 hours of hospitalization completed. In 81% of women from EOSP subgroup the time of pregnancy prolongation exceeded 3 days, while in 25% successful follow-up lasted over 10 days. Not surprisingly duration of patient’s stay in our Department, covering the period from delivery to discharge from hospital, was significantly longer in EOSP subgroup. In 16 women from LOSP subgroup the time of hospitalization was shorter than 4 days.

Discussion
Until recently typical management in severe preeclampsia was associated with the soonest possible delivery. Some reports published latterly suggest instead
that decision should depend on gestational age and occurrence of secondary complications [3].

As it is well known, preeclampsia typically affects primiparas. In our study group the percentage of primiparas and primigravidas together was 72, which is consistent with the literature.

In the current study in LOSP subgroup caesarian section was dominant and in EOSP subgroup – the only delivery mode; whereas in Alanis’ et al. research, based on the pregnant with preeclampsia diagnosed before 34 weeks of gestation successful vaginal delivery induction was achieved in 6.7% of women before 28th week of pregnancy, in 47.5% women between 28th and 32nd week of gestation and even in 68.8% of those between 32nd and 34th week of gestation [4].

We distinguished three categories of indications for caesarian delivery: severe, bad-controlled hypertension non-responsive for pharmacologic treatment, placental abruption and gradual deterioration in subsequent records of non-stress CTG tests. Most of women in analyzed group were primiparas and did not present signs nor symptoms of threatened preterm labor which significantly reduced probability of successful vaginal delivery induction. Analyzing delivery mode in women with severe preeclampsia. Loi et al. found the percentage of caesarian delivery as high as 90, which is consistent with our results [5]. Dissanayake et al. reported 78% of caesarian sections in analyzed group of preeclamptic women; the Authors avoided the distinction between mild and severe preeclampsia [6].

In his recommendations concerning the therapeutic pathways in preeclampsia Wagner et al. suggested vaginal delivery to be the proper way of parturition. As the Authors emphasized, it should be preferred if only possible, however the last condition was not clarified precisely [7].

Possibly high effectiveness of vaginal delivery inductions reported by Alanis et al. should be partly attributed to good availability of epidural analgesia, which in synergy with classic pharmacological hipotensive treatment allowed to lower excessive blood pressure.

In our research the pregnant from EOSP subgroup presented significantly lower weight gain than women qualified to LOSP subgroup, which was obviously due to shorter duration of their pregnancies. Despite of this maternal body mass at the time of delivery did not differ significantly between subgroups, which implies higher initial body mass in women developing early preeclampsia. All women in analyzed group demonstrated at least two episodes of blood pressure rise over 160/110 mm Hg during their hospital stay. As it is clear from the literature, pharmacologic treatment is the proper way of managing severe preeclampsia. Satisfactory response to hipotensive agents achieved within 48 hours, usually improves and stabilizes pregnant’s clinical state, which is crucial from the perspective of prolongation of pregnancy threatened with preterm birth [8]. In 8 cases in EOSP study group hipotensive pharmacologic treatment led to satisfactory blood pressure reduction. Analysis of biochemical parameters showed serum uric acid level to be increased significantly in EOSP subgroup. Koompans et al. emphasized high prognostic value of significantly increased serum uric acid level for such complications as HELLP syndrome and eclampsia in preeclamptic patients [9]. In contrary, Tangaratinam et al. concluding on the basis of Cochrane data analysis, adjudged serum uric acid level as a weak predictor of both maternal and neonatal complications [10]. Different conclusions reached by cited Authors impedes precise evaluation of this parameter, however our analysis’ results indicate on the connection between early onset of severe preeclampsia and high level of serum uric acid. Another biochemical factor found to be significantly increased in women included to EOSP subgroup was daily proteinuria. As Thornton et al. proved, blood pressure values in women with pregnancy induced hypertension and urine protein loss were significantly higher than in the pregnant without proteinuria. The first group was also at higher risk of preterm delivery and more prone to require caesarian delivery [11].

Still it is known, proteinuria can be absent in about 15% of the pregnant developing HELLP syndrome and even in 38% of women affected with eclampsia [12]. For that reason Haddad et al. do not consider it an adequate predictor of obstetric complications [8].

Results of our research suggest that severe proteinuria increases the risk of oliguria, which is in fact equivalent with acute renal insufficiency, as well as enhances probability of thrombotic complications. These conditions indicate the need of very careful monitoring of proteinuria severity in this group of pregnant women.

Noticeable in considered clinical data is high percentage of increased resistance index (RI) in uterine artery in the pregnant qualified to EOSP subgroup. Previous reports present adverse changes in uterine artery blood flow as connected with complications like fetal IUGR or preeclampsia [13]. Increased vascular resistance also predisposes to placental abruption.

We found higher prevalence of absence of AEDFV in umbilical arteries in fetuses of early preeclamptic mo-
such conditions can be the cause of IUGR occurrence and even lead to intrauterine fetal death [14]. Using adequate pharmacologic treatment as described above, we achieved significant prolongation of pregnancy in women affected with early severe preeclampsia. As it is reported longer duration of pregnancy in women with severe preeclampsia improves perinatal outcomes substantially, thus leads to reduction in percentage of neonatal complications [15]. Despite of this, increased risk of maternal complications like HELLP syndrome or acute renal insufficiency as possible consequence of expectant management of severe preeclampsia should be considered [8]. Crucial is that none of published randomized studies showed an increase in maternal mortality associated with the choice of conservative treatment. Still most Authors suggest to avoid continuing pregnancy in women affected with severe preeclampsia before 24 weeks of gestation, due to almost hundred percent neonatal mortality and high prevalence of maternal complications in this group [16]. Haddad et al. imply considering delivery in patients with severe preeclampsia beyond 34th week of gestation and Bombrlys et al. even suggest delivery right after completion of 32th week of gestation with previous corticosteroids administration [8, 17]. Results of randomized multicenter study, published in 2009 proved the advantage of delivery after 37 weeks of gestation complicated by pregnancy induced hypertension and mild preeclampsia [18]. In our observations we concluded significantly shorter duration of hospital stay in LOSP subgroup. Most of these women delivered before 4 days elapsed from admission to the hospital. Active management in such cases is usually motivated by our consciousness of significantly higher prevalence of maternal complications and the will to avoid them.

Conclusions

Caesarean section remains the dominant mode of delivery in women affected with severe preeclampsia, particularly in patients before 34 weeks of gestation.

High uric acid serum level and severe proteinuria are associated with earlier onset of severe preeclampsia; they can also relate to some kinds of secondary complications in the pregnant.

In the absence of complications like HELLP syndrome or eclampsia, particularly in women with severe preeclampsia before 34 weeks of gestation. Conservative management is acceptable and recommended.

Biophysical symptoms prodromal of maternal and fetal complications are more common in pregnancies affected with early severe preeclampsia which emphasizes the need for intensive perinatal surveillance in cases of conservative management.

References


