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Maternal and perinatal outcome of temporizing management in 254 consecutive patients with severe pre-eclampsia remote from term

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Abstract

Objective: To assess maternal and perinatal outcomes of expectant management with plasma volume expansion and pharmacologic vasodilatation in patients with severe pre-eclampsia remote from term. *Study design*: All women with severe pre-eclampsia between 20 and 32 weeks' gestation, not in labor and with a live, single fetus admitted to the University Hospital Rotterdam from 1985 to 1993 were managed with the intention to prolong gestation. Treatment consisted of correction of the maternal circulation with vasodilatation by means of dihydralazine and plasma volume expansion under central hemodynamic monitoring. Primary end-points of the study were prolongation of gestation, maternal antepartum and postpartum complications, and fetal and neonatal outcome. *Results*: Two-hundred fifty-four patients were included. The median prolongation of pregnancy was 14 (range 0–62) days. Hemodynamic treatment was associated with marked objective and subjective improvement in maternal condition. Complications of central hemodynamic monitoring were not observed. Perinatal mortality was 20.5%. *Conclusion*: Expectant management with plasma volume expansion and pharmacologic vasodilatation under central hemodynamic monitoring of the maternal circulation may delay delivery and enhance fetal maturity and does not appear to be associated with an increased risk of maternal morbidity and mortality.

Keywords: Pre-eclampsia; HELLP; Temporizing management; Perinatal outcome; Hemodynamics

1. Introduction

Pre-eclampsia complicates 5–10% of all pregnancies and is directly or indirectly responsible for a large proportion of maternal and perinatal mortality and morbidity [1]. Although the cause of pre-eclampsia is still unknown, the placenta is considered a key factor [2]. Therefore, delivery of fetus and placenta is the only effective treatment, which may benefit the mother but is often not in the interest of the second patient, the fetus, in particular remote from term. The decision to deliver must depend on the estimated balance of maternal and fetal-neonatal risks. In preterm pregnancy complicated by mild pre-eclampsia the balance of maternal and neonatal interests will usually lead to conservative management, in an attempt to postpone delivery in order to reduce neonatal morbidity and mortality [1,3]. On the other hand, in cases of severe pre-eclampsia or eclampsia most guidelines recommend expeditious delivery regardless of gestational age [1,4], in particular when pre-eclampsia is complicated by the HELLP syndrome [5,6]. In recent years, as methods for monitoring maternal and fetal wellbeing improved, these guidelines have been challenged and attempts have been made to postpone delivery also in women with severe pre-eclampsia remote from term [3,7,8]. However, recent reports of small series of patients indicate that such an approach could be associated with increased maternal morbidity [7].

In 1985 a protocol of temporizing management of severe pre-eclampsia remote from term was instituted in our department. The protocol is based on correction of the maternal circulation with plasma volume expansion and pharmacologic vasodilatation under central hemo-

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dynamic monitoring [9]. The purpose of this study is to assess the maternal and perinatal outcomes of 254 consecutive patients with severe pre-eclampsia before 32 weeks gestation managed according to this protocol.

2. Patients and methods

The study population consisted of all women with severe pre-eclampsia between 20 and 31 completed weeks of gestation, not in labor and with a live, single fetus, admitted to the antenatal wards of the University Hospital Rotterdam (AZR) between January 1, 1985 and December 31, 1993. The AZR serves as a perinatal tertiary care center for an area with approximately 35 000 deliveries per year.

Severe pre-eclampsia was defined as the occurrence after 20 weeks' gestation of a diastolic blood pressure, before treatment, of ≥ 110 mmHg (Korotkoff 4) and proteinuria of ≥ 0.3 g/l in a 24-h urine collection, or the occurrence of repetitive diastolic blood pressure values of ≥ 90 mmHg and proteinuria in combination with the HELLP syndrome or eclampsia. The HELLP syndrome was defined as the simultaneous occurrence of a platelet count of $< 100 \times 10^9$/l, serum aspartate aminotransferase (ASAT) and serum alanine aminotransferase (ALAT) concentrations > 30 U/l (2 S.D. above the mean in our hospital), and hemolysis defined by abnormal peripheral blood smear. Patients with known vascular, renal, hepatic or hematologic disease were excluded.

Gestational age was based on the last menstrual period and confirmed by early ultrasound in the majority of cases.

All patients were managed with the intention to prolong gestation in order to enhance fetal maturity. Temporizing treatment consisted of bed rest and correction of the maternal circulation to previously established normal hemodynamic values for the second half of gestation [10] by means of pharmacologic vasodilatation and plasma volume expansion under central hemodynamic monitoring. Each patient underwent pulmonary artery catheterization and radial arterial line placement in the obstetric intensive care unit as previously described in detail [9–11]. Briefly, a Swan-Ganz catheter was inserted in a median basilic vein and advanced into the pulmonary artery under continuous oscilloscopic monitoring. Baseline values of systemic and pulmonary arterial and venous pressures, and of cardiac output, were obtained after a stabilization period of approximately 1 h. Cardiac output was measured in triplicate in supine position at end-expiration by means of thermodilution, using 10 ml of chilled 5% dextrose solution. Patients with a pulmonary capillary wedge pressure (PCWP) of < 10 mmHg received intravenous infusion of pasteurized plasma at a rate of approximately 250 ml/h to reach and maintain PCWP values of 10–12 mmHg. If, after volume expansion, the cardiac index was still < 3.5 l.min^{-1}.m^{-2} and the systemic vascular resistance index was > 2000 dyne.s.cm^{-5}.m^2, patients received an intravenous infusion of dihydralazine at a rate of 1 mg/h followed by hourly increments of 1 mg, until the cardiac index had reached a value between 3.5 and 4.6 l.min^{-1}.m^{-2} and a systemic vascular resistance index of ≤ 2000 dyne.s.cm^{-5}.m^2 had been obtained. When cardiac index and systemic vascular resistance had reached normal values but diastolic blood pressure was still ≥ 100 mmHg, antihypertensive treatment with α-methyldopa was added. After a stable hemodynamic condition had been obtained and maintained for 1–2 days, the vascular catheters were removed and the patient was transferred to the antenatal ward. Antihypertensive treatment was continued under close monitoring of blood pressure, fluid balance, and laboratory values.

All patients kept bed rest and received an unrestricted diet. Maternal condition was assessed by monitoring blood pressures, fluid balance and pertinent laboratory values including protein in 24-h urine samples, complete blood counts, liver enzymes (ASAT, ALAT, gamma glutamyl transferase, serum lactic dehydrogenase) and total bilirubin, renal function tests (serum creatinine and uric acid) and tests for hemolysis (peripheral blood smear, serum haptoglobin). Coagulation tests (activated partial thromboplastin time, prothombin time, normotest, thrombotest, fibrinogen, fibrinogen degradation products, antithrombin III) were performed on admission in the majority of patients, and during treatment when indicated. Anticonvulsant treatment with intravenous diazepam was used in eclamptic patients and when eclampsia appeared to be imminent, as judged by hyperactive deep tendon reflexes with clonus. Platelet transfusions were given at the time of cesarean section when platelet counts were $\leq 30 \times 10^9$/l. Ultrasound examination was performed in all patients to detect fetal growth retardation and congenital abnormalities. Fetal condition was assessed by cardiotocography (non-stress CTG) on admission and at least daily thereafter. If labor occurred and delivery was still to be postponed, uterine activity was inhibited using intravenous fenoterol. Corticosteroids to accelerate fetal lung maturation were not used in patients with pre-eclampsia during the period of the study.

The decision to deliver was taken by the attending obstetrician in consultation with the neonatologist, weighing combined maternal and fetal risks against the risks of neonatal mortality and morbidity. The mode of delivery was individualized and mainly determined by fetal condition. Neonates requiring intensive care were transferred to our neonatal intensive care unit. Pulmonary surfactant therapy was used after 1991.

The study protocol was approved by the University and Hospital Ethics Committee. The primary endpoints of the study were the number of days of prolongation of gestation after admission, predefined maternal antepartum and postpartum complications (mortality, HELLP syndrome, eclampsia, abruptio placentae, postpartum hemorrhage, pulmonary edema), and specified measures of fetal and neonatal outcome (birthweight, perinatal mortality, neonatal morbidity as judged by Apgar score, artifical ventilation, bronchopulmonary dysplasia, cerebral bleeding).

Birthweight is presented as actual weight at birth and related to the Dutch reference curve, corrected for gestational age, parity and fetal sex [12]. Data on perinatal mortality comprise all stillbirths and neonatal deaths occurring within 28 days of birth; infant mortality includes all deaths between 28 days and 1 year after birth. Bronchopulmonary dysplasia is defined as a requirement for oxygen at 28 days of life, irrespective of gestational age at birth.

Data analysis was based on intention to treat and included all patients, also when they were delivered before the actual start of temporizing treatment. Data are presented as median (range) unless stated otherwise. Hemodynamic and laboratory values were examined by non-parametric one-way analysis of variance for repeated measurements and Wilcoxon's rank sign test as appropriate. Categorical variables were assessed with the χ^2-test. A P-value of < 0.05 (two-tailed) was considered significant.

3. Results

During the period of the study 254 patients with severe pre-eclampsia before 32 weeks' gestation who met the inclusion criteria were delivered at this center. General characteristics on admission are summarized in Table 1. The majority of the patients (94%) were referred from regional hospitals, usually because of complications such as the HELLP syndrome (33%), eclampsia (5%), or severe fetal growth retardation (20%); half the number of patients had already received antihypertensive treatment because of a diastolic blood pressure of ≥ 110 mmHg.

Table 1
General characteristics on admission of 254 patients with severe pre-eclampsia

Age (years)	27 (18–44)
Nulliparous	188 (74%)
Gestational age (weeks)	29.3 (21.7–31.9)
Diastolic blood pressure (mmHg)	110 (90–170)
Antihypertensive treatment before admission	138 (54.3%)
Eclampsia before admission	12 (4.7%)
HELLP before admission	85 (33.5%)
Upper abdominal pain	116 (45.7%)
Severe fetal growth retardation	50 (19.7%)

Values are median (range) or numbers (percentage) as appropriate.

Table 2
Laboratory data on admission

Proteinuria (g/l)	2.8 (0.3–35.9)
≥ 5 g/l	80
Creatinine (μmol/l)	72 (40–165)
Uric acid (mmol/l)	0.41 (0.16–0.84)
Hemoglobin (mmol/l)	7.7 (4.9–10.7)
Hematocrit (l/l)	0.37 (0.23–0.51)
Platelets ($\times 10^9$/l)	145 (14–436)
50–100	73
<50	22
Bilirubin (μmol/l)	8 (2–75)
ASAT (U/l)	27 (7–779)
ALAT (U/l)	20 (3–780)
LDH (U/l)	356 (168–3219)
Haptoglobin (g/l)	0.2 (<0.1–2.8)

Values are median (range) or numbers as appropriate.

Baseline hemodynamic measurements showed patterns similar to those previously observed in untreated and treated pre-eclamptic patients [10] and will be reported elsewhere. The total amount of plasma expander administered during treatment varied between 1 and 4 liters, mainly administered during the first 3 days after admission. All patients received dihydralazine in doses varying between 1 and 15 mg/h; 40% of the patients also required α-methyldopa in doses between 750 mg and 4 g/24h. The relevant laboratory data on admission are shown in Table 2. During treatment proteinuria increased significantly ($P < 0.001$) from a median value of 2.8 g/l to 4.9 g/l, without changes in plasma creatinine levels. None of the patients developed a creatinine level > 200 μmol/l. Between admission and delivery the hemoglobin concentration showed a significant fall from 7.7 to 7.0 mmol/l ($P < 0.001$).

Table 3 summarizes maternal outcome. There were no maternal complications associated with the introduction or maintenance of the radial artery or Swan-Ganz catheter. Pregnancy was terminated within 48 h after admission in 13% of patients because of fetal distress as judged by the non-stress fetal CTG ($n = 29$), or fetal death ($n = 3$). When patients delivered within 48 h are omitted from the calculation, the median prolongation of pregnancy was 17 days with a prolongation of ≥ 14 days in 51% of the patients.

Eclampsia occurred in one patient shortly after admission, before the start of treatment, followed by cortical blindness; normal vision returned 1 day after cesarean section for fetal distress. Visual disturbances were observed in two other patients. One severely hypertensive patient developed cortical blindness 1 day after the start of treatment; normal vision returned within 2 days, and pregnancy was prolonged by 6 days. In the second patient temporary visual problems after

delivery were due to retinal edema. Bleeding problems observed in 6% of patients were not severe and consisted of abdominal hematoma following cesarean section ($n = 12$), postpartum uterine bleeding ($n = 1$), hematemesis ($n = 1$) and a hematoma of the vulva ($n = 1$). Renal failure or disseminated coagulopathy was not observed.

In all patients with the HELLP syndrome the upper abdominal pain abated and usually disappeared within 2–3 h after the start of treatment. In 42 of 75 patients who were admitted with HELLP and who were not delivered within 48 h because of fetal distress, all signs and symptoms disappeared before delivery. On the other hand, 20 women developed a complete antepartum HELLP syndrome during treatment, which resolved in six patients before delivery. All four patients with pulmonary edema were admitted with the HELLP syndrome. Two women developed antepartum pulmonary edema; the first one during induction of labor with prostaglandin E_2 after fetal death, the second one during tocolysis with fenoterol. Both patients were treated successfully with diuretics. In the two patients with pulmonary edema after delivery, a diagnosis of cardiomyopathy was made by ultrasound; one of these patients had received prostaglandin E_2 after delivery. Both patients needed artificial ventilation for 2–3 days and recovered completely.

Perinatal outcome is shown in Table 4. The high proportion of very small-for-gestational age ($< 2.3^{rd}$ percentile) infants is mainly caused by the 73 women admitted at a gestational age of ≤ 27 weeks, of whom 25% were delivered of very small-for-gestational age infants compared with 10.5% in women admitted between 27 and 32 weeks' gestation ($P < 0.01$). Total perinatal loss was 20.5%, with a 95% confidence interval of 15–26%. Of the 52 cases of perinatal loss, 60% were due to fetal death. All stillbirths, except one caused by complete abruptio placentae at 34 weeks' gestation, occurred in cases with severe fetal growth retardation at gestational ages < 30 weeks. Although fetal distress was recognized, it was decided not to deliver because of low estimated birthweight, small chance of survival, or high estimated risk of serious morbidity and later handicap. The majority of neonatal deaths (76%) were due to respiratory distress associated with very preterm birth. One of the two infants with a cerebral bleeding grade III had a ruptured cerebral aneurysma and died 1 day after birth, the other infant survived and showed a minor delay in speech development at the age of 1 year. No correlation could be demonstrated between the last maternal platelet count before delivery and neonatal platelet count. Eight infants died in their first year of life, in all cases due to severe bronchopulmonary dysplasia.

Table 3
Maternal outcome

Prolongation of pregnancy (days)	14 (0–62)
Termination within 48 h	32 (12.6%)
Prolongation in remaining patients (days)	17 (3–62)
Antepartum resolution of HELLP	48 (45.7%)
Prolongation of pregnancy (days)	22 (8–62)
Maternal mortality	0
Maternal morbidity	
Eclampsia	1
Visual disturbances	3
Abruptio placentae	
Complete	1
Partial	12
Hemorrhagic problems	15
HELLP syndrome	
Antepartum	20
Postpartum	4
Pulmonary edema	4
Termination of pregnancy	
Vaginal delivery	43 (16.9%)
Spontaneous labor	9
Induced labor	34
Cesarean section	211 (83.1%)
Fetal indication	181
Maternal indication	22
Combined indication	8

Values are median (range) or numbers (percentage) as appropriate.

Table 4
Perinatal and neonatal outcome

Gestational age at delivery (weeks)	31.2 (22.3–37.7)
Birthweight (g)	1102 (180–2370)
Below 10^{th} percentile	149 (58.7%)
Below 2.3^{rd} percentile	37 (14.6%)
Perinatal mortality	52 (20.5%)
Fetal deaths	31
Gestational age (weeks)	27.1 (22.3–34.4)
Birthweight (g)	680 (180–2370)
Neonatal deaths	21
Gestational age (weeks)	30.0 (26.6–33.7)
Birthweight (g)	990 (480–1510)
Infant deaths	8
Primary cause of neonatal death	
Respiratory insufficiency	16
Sepsis	3
Ruptured cerebral aneurysm	1
Lethal congenital abnormality	1
Neonatal morbidity	
Apgar score at 5 min < 7	25
Platelet count $< 100 \times 10^9/l$	30
Cerebral bleeding	
Grade I–II	8
Grade III	2
Artificial ventilation	115
Duration (days)	5 (0.1–61)
Bronchopulmonary dysplasia	25

Values are median (range) or numbers (percentage) as appropriate.

Table 5
Perinatal outcome by gestational age on admission

Gestational age (weeks)	Number	Prolongation (days)	Birthweight (g)	Birthweight percentile		Fetal deaths (n)	Neonatal deaths (n)	Perinatal mortality	
				$< 10^{th}$ (n)	$< 2.3^{rd}$ (n)			%	95% CI
< 26	25	16 (2–42)	650 (180–990)	16	9	16	5	84	64–95
26	18	15 (0–60)	900 (480–1785)	11	3	5	3	44	22–69
27	30	18 (3–61)	1027 (675–1800)	22	6	5	4	30	15–49
28	42	12 (0–62)	965 (640–2130)	25	4	1	6	17	7–31
29	44	13 (0–46)	1115 (625–2140)	27	8	3	1	9	3–22
30	47	12 (1–50)	1290 (610–1860)	25	2	0	2	4	1–15
31	48	13 (0–39)	1527 (955–2370)	23	5	1	0	2	1–11

Values are numbers or medians (ranges) as appropriate. CI, confidence interval.

Table 5 shows perinatal outcome related to gestational age on admission and prolongation of pregnancy. Of the 25 pregnancies with an onset of pre-eclampsia before 26 weeks' gestation, only four babies survived and did well, after a median prolongation of pregnancy of 16 (2–42) days. Perinatal survival improved significantly with gestational age, with reductions in perinatal mortality of approximately 50% per week between 27 and 32 weeks' gestation on admission.

4. Discussion

Severe pre-eclampsia < 32 weeks' gestation is an infrequent complication of pregnancy and published experience in managing such patients is limited. In this report we present our experience with temporizing management in what is, to the best of our knowledge, the largest consecutive series of patients with severe pre-eclampsia remote from term treated in one center. Our treatment is based on the assumption that symptomatic correction of maternal hemodynamics may improve perfusion of maternal tissues and organs and could thus benefit the mother and perhaps also the fetus [13,14]. Whereas hemodynamics in untreated pre-eclamptic women are characterized by a reduced cardiac output and circulating volume and a high peripheral vascular resistance, patients receiving antihypertensive drugs and intravenous fluids show hemodynamic patterns that are variable and unpredictable [10]. For that reason we consider central hemodynamic monitoring an indispensable tool to assess the hemodynamic balance of flow, pressure and resistance in the systemic and in particular the pulmonary circulations in treated pre-eclamptic patients referred from other hospitals, and to monitor antihypertensive treatment and plasma volume expansion [13]. Based on the results of the present study and on previously reported experience [10,11], the maternal risks of the invasive hemodynamic monitoring applied in the first 1–3 days of treatment appear to be small in our hands. This may, at least in part, be attributed to the small number of skilled operators involved, and to the presence in the obstetric intensive care unit of an experienced medical and nursing staff, 24 h per day and 7 days per week.

In contrast to other reports on conservative management in which patients with the HELLP syndrome [7,8,15–17], with eclampsia [4,7,8,16–18], with severe fetal growth retardation [8,17], and with fetal distress [8,15–17] were excluded, our study includes all patients with early onset pre-eclampsia and a live fetus on admission. Despite the presence of eclampsia, HELLP, and fetal compromise, in more than 40% of cases, the mean prolongation of pregnancy of 16 (range 0–62) days is similar [4,8,15,17,19] or better [7,16,18,20] than that reported in comparable studies in selected patients.

In contrast to the results of a recent study [7], suggesting that expectant management without hemodynamic correction in patients with severe pre-eclampsia may increase maternal morbidity, in our study hemodynamic treatment was associated with marked objective and subjective improvement in maternal condition. We did not observe maternal mortality [6,18] and severe complications such as ruptured liver hematoma [4,6], intracerebral hemorrhage [4] and renal failure [4,6,7,18]. In our study four (1.6%) patients developed pulmonary edema, which compares favorably with the reported incidence of 2.9% among pre-eclamptic patients [21]. Two of these patients were treated with prostaglandin E_2, and one with fenoterol, drugs that have been reported to cause [22] or exacerbate pulmonary edema [23]. The observation of complete resolution of the HELLP syndrome before delivery in 51% of the patients in whom pregnancy could be prolonged for > 48 h, supports our earlier report on the beneficial maternal effects of temporizing hemodynamic treatment in patients with HELLP [11]. Although it is said that the natural history of the HELLP syndrome is that of a deteriorating postpartum process [24], HELLP recurred post partum in only two patients.

Table 6
Comparison between maternal and perinatal outcome of temporizing management in patients with severe pre-eclampsia remote from term in the University Hospital Rotterdam (AZR) 1985–1993, and as published in the literature

	This study ($n = 254$)	Oláh et al. 1993 [7] ($n = 28$)	Sibai et al. 1995 [8] ($n = 49$)
Gestational age on admission (weeks)	28.9 (21–31)	29.2 (24–32)	30.7 (28–32)
Platelets $< 100 \times 10^9$/l before admission	95 (37.4%)	0	0
HELLP before admission	85 (33.5%)	0	0
Eclampsia before admission	12 (4.7%)	0	0
Fetal exclusion criteria		+	+
Prolongation of pregnancy (days)	16.2 (0–62)	9.5 (2–26)	15.4 (4–36)
Maternal mortality	0	0	0
Gestational age at delivery (weeks)	31.2 ± 2.6	30.6 ± 4.7	32.9 ± 1.5
Birthweight (g)	1160 ± 390	1480 ± 450	1622 ± 360
Below 10th percentile	149 (58.7%)	?	15 (30.1%)
Perinatal mortality (%)	20.5	7.1	0
Fetal deaths	31	0	0
Neonatal deaths	21	2	0

Values are mean ± S.D. (range), or numbers (percentages), as appropriate.

The rise in protein excretion observed in the majority of the pre-eclamptic patients during temporizing treatment may be due to the plasma volume expansion, which is known to magnify proteinuria in patients with the nephrotic syndrome [25].

As shown in Table 5, a gain in pregnancy of 1 week appears to improve perinatal outcome considerably in pregnancies with a gestational age below 32 weeks, which agrees with previous studies [26,27]. However, assessment of the perinatal results of prolongation of pregnancy in our observational study is hampered by the absence of an appropriate control group, and comparison with the perinatal results of expectant management in pre-eclamptic patients reported in the literature is difficult because gestational age on admission is often not comparable [4,15–17,19,20,28]. In addition, in many reports patients are excluded for various reasons, including fetal growth retardation and fetal distress [4,7,8,15–19]. Finally, because of recent advances in perinatal care, results obtained in recent years cannot be compared with those of earlier studies. Two studies [7,8] on expectant management in pre-eclamptic patients with a mean gestational age on admission that is comparable with our study are summarized in Table 6. Oláh et al. [7] reported a perinatal mortality of only 7.1% in a retrospective analysis of 28 selected patients with severe pre-eclampsia in whom pregnancy was prolonged by 9.5 days. In that study patients were treated with nifedipine and methyldopa and were only selected for conservative treatment if hypertension could be satisfactorily controlled. Only patients without an unspecified maternal or fetal indication for immediate delivery were included. Sibai et al. [8] reported a randomized trial of aggressive ($n = 46$) vs. expectant ($n = 49$) management in pre-eclamptic patients between 28 and 32 weeks gestation. Expectant management was begun after a stable maternal condition was obtained during a 24-h observation period using magnesium sulfate, hydralazine or nifedipine. In that study no perinatal mortality occurred in both groups, but patients with fetal growth retardation and fetal distress were excluded. In the study by Sibai et al. [8], as well as in the study of Oláh et al. [7], corticosteroids to accelerate fetal lung maturation were used, which may be an important advantage of prolongation of pregnancy for at least 48 h [29,30]. During the study period corticosteroids were not used in patients with pre-eclampsia in our center. Our reluctance to administer corticosteroids to hypertensive patients was based on the results of the first randomized trial of antenatal corticosteroid therapy [31]. That trial included 90 pre-eclamptic women, and 12 fetal deaths were observed in 47 treated patients compared with three fetal deaths among 43 non-treated patients. Later observational studies, although small, have failed to confirm an excess risk of fetal death associated with the use of antenatal corticosteroids in hypertensive patients [30] and because of convincing evidence of its efficacy in the prevention of the neonatal respiratory distress syndrome, antenatal corticosteroid therapy was introduced in the management of pre-eclamptic patients in our department in 1994. The perinatal mortality of 20.5% in our patients compares favorably with that of 62% in the 50 patients reported by Moodley et al. [18], in which study patients with impending or evident eclampsia were excluded. Also in this study corticosteroids were used. The study of Moodley et al. [18] is omitted from Table 6, because of too many unreported data.

Our study confirms findings of earlier studies that perinatal outcome in patients with an onset of pre-eclampsia before 26 weeks is generally poor [4,15,18,28] and cannot be markedly improved by prolongation of

pregnancy. The high incidence of fetal growth retardation in our study is consistent with earlier reports [19,32,33] and suggests that the fetal-placental impact of severe pre-eclampsia has preceded overt clinical disease by a considerable period of time.

In conclusion, our experience obtained in a large number of patients with severe early-onset pre-eclampsia shows that expectant management with plasma volume expansion and pharmacologic vasodilatation under invasive monitoring of the maternal circulation and with careful surveillance of maternal and fetal condition may delay delivery and does not appear to be associated with an increased risk of maternal morbidity and mortality. Such treatment should only be practiced in tertiary care centers with adequate facilities for mother and infant. Controlled studies are needed to further define the value of temporizing hemodynamic treatment in patients with severe early onset pre-eclampsia.

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