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THE IMPLEMENTATION OF NEW ALGORITHM OF THE MANAGEMENT OF SEVERE PRE-ECLAMPSIA (CLINICAL CASE REPORT)

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ИМПЛЕМЕНТАЦИЯ НОВОГО АЛГОРИТМА ЛЕЧЕНИЯ ТЯЖЕЛОЙ ПРЕЭКЛАМПСИИ (КЛИНИЧЕСКИЙ СЛУЧАЙ)

Преэклампсия является потенциально серьезным осложнением беременности с прогрессирующей тенденцией и причиной 9–26 % материнской смертности, значительной части преждевременных родов, а также материнской и неонатальной заболеваемости.

Мы приводим случай с серьезными осложнениями во время беременности из-за тяжелой преэклампсии, который закончился смертью пациентки. Несмотря на своевременную диагностику и лечение, пациентка умерла через 62 ч после родов путем кесарева сечения. Раннее выявление, оптимальная профилактика и алгоритм "CALM DOWN" действий медицинского персонала в случае тяжелой преэклампсии на всех уровнях здравоохранения необходимы для лучших материнских и перинатальных результатов.

Мы надеемся, что наш клинический случай сделает более понятными конкретные аспекты неотложной помощи в акушерстве. Как и во всех клинических случаях, существует ряд подходов, которые могут быть использованы, и ни один подход в конкретном случае не является обобщающим.

Ключевые слова: тяжелая преэклампсия, алгоритм "CALM DOWN", командная работа, отек легких.

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Pre-eclampsia is a potentially serious complication of pregnancy with increasing significance worldwide. Pre-eclampsia is the cause of 9–26% of global maternal mortality and a significant proportion of preterm delivery, and maternal and neonatal morbidity.

We present the case, which has had serious complications during pregnancy due to severe pre-eclampsia, and that ended with the death of the patient. Despite the management with the timely diagnosis and therapy, patient died 62 hours after caesarean delivery. Early detection, optimal prevention, and algorithm "CALM DOWN" of medical personnel actions of severe PE at all levels of health care are required for better maternal as well as perinatal outcome.

We hope our clinical case will complement the understanding of specific areas of obstetric emergency care. As in all clinical cases there are often a number of approaches that can be taken and the way each case is ultimately managed, does not necessarily represent the only management strategy.

Key words: severe pre-eclampsia, algorithm "CALM DOWN", teamwork, pulmonary edema.

The pre-eclampsia (PE) is defined as the presence of a systolic blood pressure (SBP) greater than or equal to 140 mm Hg or a diastolic blood pressure (DBP) greater than or equal to 90 mm Hg or higher, on two occasions at least 4 hours apart in a previously normotensive patient, or an SBP greater than or equal to 160 mm Hg or a DBP greater than or equal to 110 mm Hg or higher [7]. In addition to the blood pressure criteria, proteinuria of greater than or equal to 0.3 grams in a 24-hour urine specimen, a albumin (mg/dL)/creatinine (mg/dL) ratio of 0.3 or higher, or a urine dipstick protein of 1+ (if a quantitative measurement is unavailable) is required to diagnose preeclampsia [7].

The incidences of PE are 5 to 14% of all pregnancies in the world, contributes to 15% of preterm deliveries, and between 9% and 26% of maternal deaths worldwide, while severe PE can develop to about 25 percent of all cases of preeclampsia. Severe pre-eclampsia may lead to liver and renal failure, disseminated intravascular coagulopathy (DIC), and central nervous system (CNS) abnormalities. In world, preeclampsia and eclampsia is responsible for approximately 14 percent of maternal deaths per year (50,000–75,000) [10]. According to WHO the incidence is 7 times greater in developing countries compared to developed countries. PE is a risk to health not only in the immediate peripartum period — women who have suffered from preeclampsia are at increased risk of cardiovascular disease throughout life, and children born from pregnancies affected by PE are more likely to suffer from metabolic syndrome, cardiovascular disease, and hypertension at earlier ages [6; 8; 14].

The main problem is the systematization in the provision of emergency care by medical personnel with severe preeclampsia. It is the coordinated teamwork of the personnel of the medical institution/department that should become the guarantee of the optimality of medical care for severe preeclampsia. Optimizing management of PE is a major step toward improving population health worldwide.

We would like to present the clinical case of inadequate clinical management of a severe PE, which has had serious complications and that ended with the death of the patient.

Material and methods

Mrs. S. is a previously well 35-year-old woman, gravida 1 para 0, with 28 weeks' gestation. She reported a severe headaches, abdominal pain, and facial, hand and bilateral lower limb edema, she was admitted to the district hospital secondary to elevated blood pressure of 220/110 mm Hg. The facial, hand and bilateral lower limb edema started 2 weeks before. The headaches had occurred in the past six hours and were worse when lying down.

Mrs. S. is a primagravida. Patient had her menarche at 17 years of age, her menses were irregular ranging from 28 to 40 days. She was never on the oral contraceptive pill or on any other formulation of contraception. She hadn't a history of infertility. Her last menstrual period was 28 weeks ago. Mrs. KG did not have any problems during the first trimester. The first visit in antenatal clinic was at term 24 weeks of gestational age. Data from the history show that the patient was low risk factors for preeclampsia (family history of early-onset cardiovascular disease, first ongoing pregnancy). The assessments using abdominal imaging (ultrasound/CT scan) and hematology profiles during the second trimester showed no abnormality. All routine investigations (complete blood count; Syphilis, Hepatitis B and C, HIV screen, blood glucose) were reported within the normal ranges, also. Her blood group was B Rhesus positive.

At the admission department, she had a blood pressure of 280/120 mm Hg; pulse of 105 beats per minute, oxygen saturation was 95, respiratory rates — 20 per minute. Fetal heart beats — 118 per minute. Skin and mucous membranes were pale and dry. On auscultation, the chest was clear. There was adequate air entry on both sides of the chest without any crackles. On abdominal examination, the abdomen was distended compatible with pregnancy. The fetus was palpable in a longitudinal lie and the presentation was cephalic. No pain was elicited in the right upper quadrant and epigastric region. A facial, hand and bilateral lower limb edema were noted. From the neurological examination, the patient was noted to have hyperreflexia with sustained clonus which was most marked in the knee jerk on both sides. The diagnosis of severe preeclampsia was supported.

Initial antihypertensive therapy was started from nifedipine — 10 mg, 25% magnesium sulphate given as a 4 g loading dose (diluted in normal saline — 20 minutes), and oxygen by the mask.

Laboratory assessment on admission showed normal levels of liver enzymes and platelets, and urinalysis with +2 proteinuria, hemoglobin was normal. Coagulation profile was normal too. Abdominal ultrasound showed oligohydramnios and a healthy fetus with an estimated fetal weight at the 25th percentile.

In 20 minutes blood pressure of 260/110 mm Hg; pulse of 110 beats per minute, oxygen saturation was 97, respiratory rates — 22 per minute. Fetal heart beats — 112 per minute.

Antihypertensive medication as bolus dose of urapidil was given 25 mg (5 ml) i/v during 5 minutes. Magnesium sulphate (25%) given as a 7.5 g in (supporting dose 2 g/h). Donation of oxygen was prolong.

In 10 minutes blood pressure of 200/100 mm Hg; pulse of 110 beats per minute, oxygen saturation was 97, respiratory rates — 22 per minute. Fetal heart beats — 132 per minute. Urapidil was 25 mg (5 ml) i/v repeat during 5 minutes. Magnesium sulphate (25%) given as a 7.5 g in (supporting dose 2 g/h) was prolong. Donation of oxygen was prolong.

In 10 minutes blood pressure of 140/100 mm Hg; pulse of 90 beats per minute, oxygen saturation was 96, respiratory rates — 20 per minute. Fetal heart beats — 132 per minute. It followed by a continuous infusion of urapidil and her BP started to stabilise and her diastolic fallen to 100 mm Hg.

Patient was transferred to intensive care unit, where she was intubated and connected to the respiratory apparatus. Laboratory assessment was showed normal levels of liver enzymes and platelets, coagulation profile was normal, total protein — 52 g/L, urinalysis with +2 proteinuria. The cardiotocogram done was normal. Ophthalmologic assess-

ment showed macular edema and hypertensive retinopathy. She was given dexamethasone to accelerate fetal lung maturation. The ultimate diagnosis: The first pregnancy 28 weeks' gestation, severe preeclampsia.

After stabilization of vital parameters for one hour, it was decided about cesarean delivery after a written consent of the patient. A Pfannenstiel incision was made and a female fetus was delivered weighing 775 grams with APGAR score of 3 in the first minute and 7 in the fifth minute. The patient was treated with supplementary oxygen, crystalloid, antibiotics, H_2-blockers, LMWH, frozen plasma, diuretic, analgesic, antihypertensive and magnesium sulphate under monitoring of cardiologist, and anaesthesiologist.

In 2 days of treatment in intensive care unit, the patient's condition was nonstable. Blood pressure was 140–160/100–110 mm Hg; pulse of 80–110 beats per minute, oxygen saturation was 94, respiratory rates — 24 per minute. After consultations with a cardiologist, anesthesiologist and pulmonologist were suspected hemorrhagic stroke. DIC, and pulmonary edema, and therefore patient was shifted to the intensive care unit in the Vinnitsa Regional Clinical Hospital.

In 8 hours after transfer, patient's condition rapidly deteriorated. Despite the resuscitation measures taken, it unfortunately ended up in her death after 62 hours of cesarean delivery postpartum.

Discussion

PE is a major cause of maternal mortality throughout the world with 60,000 maternal deaths attributed to hypertensive disorders of pregnancy. PE also results in fetal morbidity due to prematurity and fetal growth restriction. The precise etiology of PE remains an enigma with multiple theories including a combination of environmental, immunological and genetic factors. The conventional and leading hypotheses for the initial insult in PE is inadequate trophoblast invasion which is thought to result in incomplete remodelling of uterine spiral arteries leading to placental ischaemia, hypoxia and thus oxidative stress. The significant heterogeneity observed in pre-eclampsia cannot be solely explained by the placental model alone. Herein we critically evaluate the clinical (risk factors, placental blood flow and biomarkers) and pathological (genetic, molecular, histological) correlates for PE. Furthermore, we discuss the role played by the (dysfunctional) maternal cardiovascular system in the etiology of PE [15].

The early detection/diagnosis and appropriate management is extremely important in patients with preeclampsia, for better maternal as well as perinatal outcome. Early onset and late onset preeclampia have different implications for fetuses and neonates, with perinatal mortality rising about 10-fold higher on early onset, and doubling in late-onset. Early onset preeclampsia is a severe pregnancy complication characterized by elevated blood pressure, metabolic and inflammatory changes leading to generalized endothelial dysfunction and end-organ damage due to vascular disorders. Early onset preeclampsia is a potentially life-threatening disease for both mother and baby [13; 14]. Early onset preeclampsia is the most severe clinical variant of disease occurring 5–20% of all cases of preeclampsia and is associated with impaired fetal growth, fetal pathology and uterine blood circulation, small size of the placenta, preterm delivery, neonatal morbidity and mortality. Early onset preeclampsia developments are associated with impaired trophoblast invasion, complete transformation of the uterine spiral artery, immune maladaptation and increased markers of endothelial dysfunction. Preeclampsia late onset is about 75–80% of all cases of preeclampsia, which are associated with maternal morbidity (meta-

bolic syndrome, impaired glucose tolerance, obesity, dyslipidemia, chronic hypertension), normal birth weight and normal placental volume [13].

Women at increased risk of pre-eclampsia are recommended to take calcium supplementation (1–2.5 g/d) if they have low calcium intake by three guidelines. Five guidelines recommended low-dose aspirin (75–150 mg/d) with initiation in early pregnancy, and three guidelines recommend that it continue until delivery. In women identified as at increased risk of pre-eclampsia based on clinical characteristics, low-dose aspirin results in a small decrease in pre-eclampsia (RR 0.75, 95% CI 0.66–0.85; 18 trials; 4121 women for this outcome), preterm delivery < 37 weeks' gestation (RR 0.89, 95% CI 0.81–0.97; I2 32%; 10 trials, 3252 women for this outcome), perinatal death (RR 0.69, 95% CI 0.53–0.9; 17 trials, 4443 women for this outcome) (40 trials, 33,098 women overall), and intrauterine growth restriction (RR 0.80, 95% CI 0.65–0.99; I2 36.9%, 13 trials, 12,504 women for this outcome). There is low level evidence that low-dose aspirin may help to prevent pre-eclampsia (RR 0.67, 95% CI 0.48–0.94; 5 trials, 898 women) in multiple gestations. The ASPRE trial is doing so for aspirin (150 mg/d at bedtime) started in the first-trimester in women identified as being at increased risk. Aspirin does not increase or decrease miscarriage risk. There is no evidence of short- or long-term adverse effects on the mother or newborn. Who should receive aspirin, in what dose, and when are unclear. Subgroup analyses in meta-analyses suggest a number of important considerations. First, aspirin is more effective in decreasing pre-eclampsia among women at high risk (NNT 19, 95% CI 13–34) compared with those at moderate risk (NNT 119, 95% CI 73–333), though a recent meta-analysis did not show any effect of preconceptionally started aspirin in reducing hypertensive pregnancy complications in IVF women. Second, aspirin may be more effective at decreasing the following outcomes when it is initiated before 16 weeks' gestation (optimal after 12 weeks' gestation): severe pre-eclampsia, preterm pre-eclampsia, preterm delivery, perinatal death and SGA infants. Preconception-initiated low-dose aspirin was associated with the outcome of higher live birth rates in women with a single documented loss at less than 20 weeks' gestation during the previous year [1; 11; 14].

All clinical guidelines recommends antihypertensive treatment for pregnant women with blood pressure more than or equal to 160 mm Hg systolic or 110 mm Hg diastolic. Severe hypertension requiring urgent treatment is defined as a systolic blood pressure greater than or equal to 170 mm Hg with or without diastolic blood pressure greater than or equal to 110 mm Hg. This represents a level of blood pressure above which the risk of maternal morbidity and mortality is increased. This degree of hypertension requires urgent assessment and management. Increasing evidence exists that cerebral perfusion pressure is altered in pregnant women making them more susceptible to cerebral haemorrhage, posterior reversible encephalopathy syndrome and hypertensive encephalopathy [8].

Preeclampsia with severe features is defined as the presence of one of the following symptoms or signs in the presence of preeclampsia [7]:

SBP of 160 mm Hg or higher or DBP of 110 mm Hg or higher, on two occasions at least 4 hours apart while the patient is on bed rest (unless antihypertensive therapy has previously been initiated).

Impaired hepatic function as indicated by abnormally elevated blood concentrations of liver enzymes (to double the normal concentration), severe persistent upper quadrant or epigastric pain that does not respond to pharmacotherapy and is not accounted for by alternative diagnoses, or both.

Progressive renal insufficiency (serum creatinine concentration > 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease);

New onset cerebral or visual disturbances;

Pulmonary edema;

Thrombocytopenia (platelet count < 100,000/мL).

In a patient with new-onset hypertension without proteinuria, the new onset of any of the following is diagnostic of preeclampsia:

Platelet count below 100,000/мL;

Serum creatinine level above 1.1 mg/dL or doubling of serum creatinine in the absence of other renal disease;

Liver transaminase levels at least twice the normal concentrations;

Pulmonary edema;

Cerebral or visual symptoms.

Edema is not included in the diagnostic features of preeclampsia. It is a common feature of normal pregnancy and severe preeclampsia may be present in the absence of any edema. Nevertheless rapid development of generalised edema should alert the clinician to screen for preeclampsia [14].

Accurate blood pressure measurement is important as the level of blood pressure may result in changes in clinical management [3]. The woman should be seated comfortably with her legs resting on a flat surface and her arm resting at the level of her heart. The woman should not talk, read, look at her phone/computer, or watch television. The woman's arm should be resting at the level of her heart. This may require use of a pillow. Supine posture should be avoided because of the supine hypotension syndrome. The variation in blood pressure between arms is usually less than 10 mm Hg, with 8% and 2% of pregnant women having an inter-arm difference of at least 10 mm Hg for systolic and diastolic blood pressure, respectively. The systolic blood pressure is accepted as the first sound heard (K1) and the diastolic blood pressure the disappearance of sounds completely (K5). Where K5 is absent, K4 (muffling) should be accepted [6; 14].

The measurement and interpretation of proteinuria in hypertensive disorders of pregnancy has been recently reviewed. Dipstick testing is not accurate to confirm or exclude significant proteinuria (≥ 300 mg/24 hours): sensitivities of 22–82% have been reported. This is improved slightly with automated dipstick testing but even this will miss more than half the patients with significant proteinuria. The presence of 2+ or 3+ proteinuria or repeated +1 dipstick testing increases both sensitivity and specificity and, therefore, should be assumed to represent significant proteinuria until proven otherwise by confirmatory tests. Twenty four hour urine protein has been the historic gold standard for quantifying proteinuria in pregnancy although its accuracy is affected by numerous factors such as adequacy and accuracy of collection and variations in protein excretion. A spot urine protein/creatinine cut-off level of 30 mg/mmol equates to a 24-h urine protein > 300 mg per day and at this level has adequate sensitivity and specificity to be used as a 'rule out' value below which true proteinuria is unlikely to be present. This is the recommended method and cut-off for diagnosing proteinuria in pregnancy. Proteinuria testing does not need to be repeated once significant proteinuria of preeclampsia has been confirmed. [6; 8].

In the WHO Prevention and Treatment of Pre-eclampsia and Eclampsia recommendations, antihypertensive treatment of severe hypertension during pregnancy was strongly recommended. This seems very reasonable despite the fact that the quality of evidence on which the recommendation was based was graded as 'very low'. First, there are no relevant placebo-controlled randomised controlled trials that prove that women randomised to antihypertensive therapy more frequently have their blood pressure lowered

compared with those randomised to placebo; however, such randomised controlled trials would be unethical and will never be done. Second, severe systolic hypertension is a independent risk marker for stroke in pregnancy. Third, an individual short-acting antihypertensive agent is successful at lowering maternal blood pressure in at least 80% of women, based on randomised controlled trials of one antihypertensive drug versus another (as discussed below). Finally, a recent report of the Confidential Enquiries into Maternal Deaths in the UK that covered the hypertensive disorders of pregnancy (2005–2008) identified the failure to treat the severe (particularly systolic) hypertension of pre-eclampsia as the single most serious failing in the clinical care of the women who died. It is of note that concerted efforts in the UK to address treatment of severe hypertension have been associated with a fall in the contribution of the hypertensive disorders of pregnancy to maternal mortality, based on 2009–2012 data. Similarly, in South Africa that has a legislated Confidential Enquiries into Maternal Deaths process, maternal deaths owing to complications of hypertension have featured prominently, and recommendations for antihypertensive therapy have been associated with a reduction of deaths in this category. In deciding on the need for treatment and the urgency with which blood pressure should be lowered, both the absolute level of blood pressure (i. e., severe or non-severe) and the rate with which it has risen should be considered. Experimental evidence from cats suggests that an abrupt (versus step-wise) increase in blood pressure is associated with more permeability of the cerebral vessels, taken as a measure of vascular injury. Presumably, abrupt increases in intraluminal pressure may result in mechanical distension of the cerebral vessel wall which may adapt better to gradual or step-wise increases. Women with a hypertensive 'urgency' (i. e., acute rise in blood pressure that is not associated with end-organ dysfunction) may be treated with oral antihypertensive agents that have peak drug effects in 1–2 hours (e. g., oral labetalol), recognising that gastric emptying may be delayed or unreliable among women in active labour. Choice of agents is discussed below [14].

There is a general appreciation that the goal of antihypertensive therapy for severe hypertension is not normalisation of blood pressure, but rather, lowering of blood pressure to a non-severe level of hypertension that decreases the risk of stroke. Also, there is recognition that lowering of blood pressure, even to levels that remain outside the hypertensive range has the potential to precipitate fetal distress and fetal heart rate monitoring (FHR) monitoring is advised. Based on extrapolation of the approach outside pregnancy, hypertensive emergencies should be treated with short-acting antihypertensive agents and an arterial line when possible aimed at lowering mean arterial blood pressure by no more than 25% over minutes to hours; this is equivalent to taking a blood pressure of 220/130 mm Hg to 165/98 over 1–2 hours, and then further lowering blood pressure below 160/100 mm Hg over the next 2 hours [4].

Sudden and severe increases in blood pressure may be the presenting feature of hypertensive disease in pregnancy, intrapartum or in the postnatal period. Blood pressure greater than or equal to 160 mm Hg systolic or 100 mm Hg diastolic constitute severe hypertension requiring urgent treatment (Table 1).

Whilst there is no controlled trial to determine how long severe hypertension may be left untreated, it is recommended that treatment be administered promptly aiming for a gradual and sustained lowering of blood pressure. Most guidelines recommend a blood pressure goal of < 160/110 mm Hg (SOGC, ACOG, QLD), but a goal of < 150/80–100 mm Hg is recommended in the UK (NICE), < 160/100 mm Hg in Australasia (SOMANZ), and ACOG makes a specific recommendation for women with chronic hypertension for whom blood pressure should be < 160/105 mm Hg [14].

Table 1

Agents used most commonly for treatment of a blood pressure ≥ 160/110 mm Hg

Agent	Mechanism of action	Dosage	Onset	Peak	Duration	Comments
Nifedipine	Calcium channel blocker (vasodilator)	5–10 mg to swallow without biting Repeat after 30 min	5–10 min	30–45 min	6 h	Headache, flushing
Labetalol	Peripheral alpha-1 and (non-selective) beta-1 and 2 receptor antagonist	Start with 20 mg IV over 2 min. Repeat with 40 mg then 80 mg IV (each over 2 min) q 30 min. Continuous infusion 1–2 mg/min (max dosage 300 mg)	5 min	30 min	4 h	Best avoided in women with asthma or heart failure, may cause neonatal bradycardia
Hydralazine	Direct-acting vasodilator	Intermittent dosing 5 mg IV Repeat 5–10 mg IV every 30 min Continuous infusion 0.5–10 mg/h IV (max dosage 45 mg)	5 min	20–30 min	3-8 h	May increase the risk of maternal hypotension
Urapidil	α_1-adrenoceptor antagonist and 5-HT_{1A} receptor agonist	Initially 5–10 mg slow IV (over 2 min) followed by 3–24 mg/h (via syringe driver). Continue with a maintenance infusion of 6–9 mg/hr once BP is reduced sufficiently	2–3 min	5–15 min	3 h	Dizziness, nausea, headache, fatigue, orthostatic hypotension, palpitations, pruritus nervousness, allergic skin reactions
Clonidine	Centrally acting alpha-2 receptor agonist	0.1–0.2 mg orally (max dosage 0.8 mg)	10–30 min	2–4 h	6–10 h	Not recommended during breastfeeding
Nitroglycerin infusion	Direct vasodilators that has its affects veins more than arterioles	5 μg/min, increased every 5 min (max rate 100 μg/min)	2–5 min	5 min	5–10 min	Main side-effects are headache (direct vasodilation) and tachycardia (sympathetic activation)
Captopril *only post-partum*	Angiotensin-converting enzyme inhibitor	6.25–12.5 mg orally. Repeat in 1 h (max dosage 75 mg)	30 min	60–90 min	≥ 8 h	Captopril must NOT be administered before delivery

There is concern that a precipitous fall in blood pressure after antihypertensive treatment, particularly intravenous hydralazine, may impair placental perfusion resulting in fetal distress. The medication available in Germany, nifedipine and urapidil, can both be used without preference for the initial treatment of severe hypertension. However, the off-label use of nifedipine and urapidil must be observed [12]. Alternative antihypertensive medications include a nitroglycerin infusion, oral clonidine, or postpartum, oral captopril. Sodium nitroprusside should be reserved for extreme emergencies and used for the shortest amount of time possible because of concerns about cyanide and thiocyanate toxicity in the woman and fetus or newborn, and increased intracranial pressure with potential worsening of cerebral edema in the woman. Once the hypertensive emergency is treated, a complete and detailed evaluation of maternal and fetal well-being is needed with consideration of, among many issues, the need for subsequent pharmacotherapy and the appropriate timing of delivery [5]. Atenolol and prazosin are not recommended prior to delivery. Magnesium sulphate is not recommended solely as an antihypertensive agent. Continuous CTG monitoring should be considered in these situations, particularly when there is evidence of existing fetal compromise. However, fetal distress as a result of such treatment is rare [6].

Magnesium sulphate ($MgSO_4$) is listed on the WHO Model List of Essential Medicines (2015) for treatment of severe pre-eclampsia. The treatment of choice for the prevention of eclampsia is the intravenous administration of magnesium sulphate which is indicated in severe preeclampsia, especially where there are central nervous system symptoms, as a significant reduction in the risk if eclampsia can be achieved with magnesium sulphate. Intravenous therapy is with a loading dose of 4 g of diluted magnesium sulphate (in 50 ml) administered over 10–15 min via syringe driver or short infusion and continued with a maintenance dose of 1 g/h [5; 6; 14].

Multiple guidelines recommend against plasma volume expansion (SOGC, NICE, SOMANZ). Fluid restriction in pre-eclampsia is recommended by two guidelines (SOGC, NICE), one of which recommends administration of no more than 60–80 mL/h of IV fluids (NICE). Although maternal plasma volume is often reduced in women with preeclampsia, there is no maternal or fetal benefit to maintenance fluid therapy. The choice between colloid and crystalloid remains controversial as previous trials generally excluded pregnant women. Fluid should not be routinely administered to treat oliguria (< 15 mL/hr for 6 consecutive hours). Administration of fluid at a rate greater than normal requirements should only be considered for:

1. Women with severe preeclampsia immediately prior to regional anaesthesia or immediate delivery: 250 mL bolus.

2. Initial management in women with oliguria where there is a suspected or confirmed deficit in intravascular volume: 300 mL challenge, repeat with careful assessment.

As vascular permeability is increased in women with preeclampsia, administration of large volumes of intravenous fluid before or after delivery may cause pulmonary edema and worsen peripheral edema. This tendency is further aggravated by hypoalbuminemia. Appropriate blood product replacement is necessary when there has been haemorrhage, as in cases of placental abruption. Post-partum oliguria is a regular accompaniment of preeclampsia and care must be taken to avoid its' overtreatment. Persistent oliguria beyond 24 hours post-partum with rising plasma creatinine suggests the possibility of post partum renal failure. There is no evidence that fluid manipulation is able to prevent this rare complication [8].

Monitoring in a high dependency care unit is ideal for these cases because of the risk of pulmonary edema as mentioned above. Invasive monitoring should only be consid-

ered when there is developing renal failure or pulmonary edema. In view of the reduced plasma volume in most women with preeclampsia, diuretics should not be used in the absence of pulmonary edema.

Delivery is the only intervention that initiates resolution of preeclampsia, and women with gestational hypertension or pre-existing hypertension may develop preeclampsia. Consultation with an obstetrician is mandatory in women with severe preeclampsia. There is general consensus that women with pre-eclampsia should be delivered if pre-eclampsia is 'severe' or gestational age is either prior to fetal viability (WHO, ACOG, SOGC, SOMANZ 2014) or term (NICE, WHO, ACOG, SOGC, SOMANZ 2014). Definitions of severe pre-eclampsia vary, but none of the guidelines that have gestational age < 34 weeks as a severity criterion indicate that women at < 34 weeks with pre-eclampsia must be delivered (WHO, ASH 2008, AOM 2012). It should be noted that of 14 guidelines, only four indicate that 'heavy proteinuria' is a pre-eclampsia severity criterion; if applied strictly, it would mean that women with pre-eclampsia and heavy proteinuria should be delivered (WHO, ASH 2008, NVOG 2011, AOM 2012). There is consensus that women with pre-eclampsia should be considered for expectant management if they are at a gestational age associated with fetal viability and < 34 weeks (WHO, NICE, ACOG, SOGC, SOMANZ 2014) [14].

All women with severe preeclampsia should be delivered immediately (either vaginally or by Caesarean), regardless of gestational age. For women with non-severe preeclampsia complicated by hemolysis, elevated liver enzymes, low platelets syndrome at 24+0 to 34+6 weeks' gestation, consider delaying delivery long enough to administer antenatal corticosteroids for acceleration of fetal pulmonary maturity if there is temporary improvement in maternal laboratory testing. For women with any hypertensive disorder of pregnancy, vaginal delivery should be considered unless a Caesarean delivery is required for the usual obstetric indications [6].

The anaesthesiologist should be informed when a woman with preeclampsia is admitted to the delivery suite. Early insertion of an epidural catheter (in the absence of contraindications) is recommended for control of labour pain. In the absence of contraindications, all of the following are acceptable methods of anaesthesia for women undergoing Caesarean delivery: epidural, spinal, combined spinal-epidural, and general anaesthesia. A routine fixed intravenous fluid bolus should not be administered prior to neuraxialanaesthesia. Central venous pressure monitoring is not routinely recommended, and if a central venous catheter is inserted, it should be used to monitor trends and not absolute values. Pulmonary artery catheterization is not recommended unless there is a specific associated indication, and then only in an intensive care unit setting [6].

Blood pressure should be measured during the time of peak postpartum blood pressure, at days 3 to 6 after delivery. Women with postpartum hypertension should be evaluated for preeclampsia (either arising de novo or worsening from the antenatal period). Consideration should be given to continuing antihypertensive therapy postpartum, particularly in women with antenatal preeclampsia and those who delivered preterm. Severe postpartum hypertension must be treated with antihypertensive therapy to keep systolic blood pressure < 160 mm Hg and diastolic blood pressure < 110 mm Hg. In women without co-morbidities, antihypertensive therapy should be considered to treat non-severe postpartum hypertension to keep blood pressure < 140/90 mm Hg. Women with co-morbidities other than pre-gestational diabetes mellitus should be treated to keep blood pressure < 140/90 mm Hg. Antihypertensive agents generally acceptable for use in breastfeeding include the following: nifedipine XL, labetalol, methyldopa, captopril, and enalapril [6; 14].

The occurrence of acute pulmonary edema in a hypertensive pregnant or recently pregnant woman is a medical emergency and should trigger an emergency response. Treatment aimed at rapidly assembling an experienced team of staff. Further deterioration may occur, leading to cardiac arrest, and staff should be prepared to institute advanced life support and consider peri-mortem caesarean section. Transthoracic echocardiography can assist in differentiating a low cardiac output from a high cardiac output state, as well as exclude other important causes of acute pulmonary edema. Despite the risks of aspiration, non-invasive ventilation should be tried as the initial technique before tracheal intubation, as it provides increased inspired oxygen concentration, displaces fluid from the alveoli into the pulmonary and subsequently systemic circulation, decreases the work of breathing, and decreases the need for tracheal intubation. The use of non-invasive ventilation also avoids the complications associated with tracheal intubation in pregnant or recently pregnant women who are hypertensive, such as intracerebral haemorrhage. Mechanical ventilation strategies incorporating the known cardiorespiratory and metabolic changes of pregnancy need to be considered when ventilating the lungs of a pregnant or recently pregnant woman, as well as the lung protective strategies of low tidal volumes and low peak pressures. Avoidance of aortocaval compression is essential. Urgent reduction of critically high blood pressure with an intravenous antihypertensive agent is necessary. Nitroglycerin (glyceryl trinitrate) is recommended as the drug of choice in pre-eclampsia associated with pulmonary edema. Reduction in systolic and diastolic blood pressure should occur at a rate of approximately 30 mm Hg over 3–5 min followed by slower reductions to blood pressures of approximately 140/90 mm Hg. Intravenous furosemide (bolus 20–40 mg over 2 min) is used to promote venodilation and diuresis, with repeated doses of 40–60 mg after approximately 30 min if there is an inadequate diuretic response (maximum dose 120 mg. h^{-1}) [2].

New tools for early detection, prevention, and management of preeclampsia have the potential to revolutionize practice in the coming years. The purpose of clinical implementation of the new algorithm of the management of severe pre-eclampsia (CALM DOWN) for medical personnel will to reduce maternal and perinatal mortality as a result of complex teamwork (Table 2).

Our algorithm for the actions of medical personnel "CALM DOWN" in the cases of severe pre-eclampsia, offers to systematize and optimize the participation of each member of the team in the provision of emergency care [9]. The sequence of actions also depends on the number of medical staff in various health care facilities. That is why the indicated CALM DOWN algorithm should be implemented in clinical practice based on the peculiarities of the specifics of work, resources, functioning and localization of the maternity facilities when forming the route of the patient.

Conclusion

The clinical case report of patient who presented with 28 weeks of pregnancy, headache, and epigastric pain to our district hospital. She developed complications associated with severe pre-eclampsia and unfortunately ended up with fatal outcome after 62 hours of cesarean delivery post-partum, despite of timely diagnosis and clinical management.

Pre-eclampsia is associated with substantial maternal complications, both acute and long-term. Early detection, optimal prevention, and algorithm of medical personnel actions of severe PE at all levels of health care are required for better maternal as well as perinatal outcome.

Table 2

The algorithm of medical personnel actions in the cases of severe preeclampsia "CALM DOWN" [9]

Mnemonic	Definition	Action of personnel	Time, min
C	**C**alling for help	Calling on duty doctors, an anesthesiologist at the onset of symptoms of severe preeclampsia, with fixation of actual time	1–3
A	**A**ssessment	Check the airway, auscultation of the lungs, re-measure blood pressure, heart rate, assess the oxygen saturation, fetal heart beats, assess the patient's consciousness	3–5
L	**L**ow blood pressure	Antihypertensive therapy: nifedipine 10 mg p. o., urapidil 10 mg IV or labetalol 20 mg IV or hydralazine 5 mg IV	5–10
M	**M**agnesium sulfate	Intravenous therapy is with a loading dose of 4 g of diluted magnesium sulphate (in 50 ml)	10–15
	Pause	Evaluate the effectiveness of prescribed medications. A goal of < 150–160/90–100 mm Hg is recommended	5–10
D	Decision	Decide about further management. Transfer to the intensive care unit or operating theatre or delivery room, depending on gestational age and patient' condition	5–10
O	**O**liguria	Women with severe preeclampsia immediately prior to regional anaesthesia or immediate delivery: 250 mL bolus. Fluid restriction in pre-eclampsia is recommended no more than 60–80 mL/h of IV fluids	5–10
W	Fetal **W**ell being	Monitor fetal well-being with NST and ultrasonographic assessment	10–30
N	Parturitio**N**	All women with severe pre-eclampsia or eclampsia should be delivered within 24 hours, regardless of gestational age	

Consent. We had obtained the necessary consent from the patient' relative in case history for use of data pertaining to his case in this study.

Conflict of interest: None declared.

Ethical approval: The study was approved by the Ethics Committee of the Vinnytsya Pirogov Memorial National Medical University.

Ключові слова: тяжка прееклампсія, алгоритм "CALM DOWN", командна робота, набряк легень.

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