



Pharmacological Management of Arterial Hypertension and Clinical Outcome of a Retrospective Cohort of Patients with Eclampsia

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Authors' contributions

This work was carried out in collaboration among all authors. Author JGVR designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors JGVR, MOC and CISP managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: The best therapeutic measures in patients with eclampsia are termination of pregnancy, administration of anticonvulsant drugs, control of blood pressure with antihypertensive drugs, and critical care to improve outcome. This study aimed to analyze the pharmacological management of arterial hypertension and clinical outcome of a retrospective cohort of patients with eclampsia.

Methods: This is a retrospective cohort of 37 patients with eclampsia from the intensive care unit (ICU). The files were consulted to know their general data, the characteristics of the seizures and blood pressure. Changes in blood pressure at admission vs. discharge were compared, as well as antihypertensive management and outcome. Descriptive statistics and the Student's t-test with the SPSS version 20 program were used. $P=0.05$ was significant.

Results: Mean age 25.86 ± 7.82 years and gestation 33.48 ± 3.97 weeks. Patients with pregnancy 56.76% and puerperium 43.24%. Anticonvulsant drugs was administered in 100% (magnesium sulfate, sodium phenytoin, diazepam). Systolic blood pressure: admission vs discharge 143.08 ± 22.10 vs 125.7 ± 11.26 mmHg ($P=0.06$) and diastolic blood pressure: admission vs

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discharge 88.69 ± 14.15 vs 76.6 ± 9.56 mmHg ($P=0.76$). It was found that 91.89% received antihypertensive drugs and 8.11% none. Indeed, a group of patients with severe preeclampsia convulsed in the ICU 21.63% ($n=8/37$) when they were already receiving anticonvulsant drugs. In them, pre-seizure blood pressure increased compared to admission pressure (systolic 13.53%, $P=0.05$, diastolic 22.46%, $P=0.05$), one patient did not have antihypertensive management and seven patients received only oral antihypertensive drugs. ICU stay was similar to that of the group ($P=0.20$). Mortality was 0%.

Conclusion: The evolution of the patients was not satisfactory, but without maternal deaths. Eight new cases of eclampsia occurred in the ICU with uncontrolled hypertension, probably due to insufficient pharmacological management. The data suggest not discontinuing antihypertensive agents despite blood pressure remaining controlled. Deviations from the handling guidelines should be avoided.

Keywords: Eclampsia; antihypertensive management; hypertension and pregnancy; intensive care in obstetrics; high risk pregnancy.

1. INTRODUCTION

Eclampsia is defined as the presence of generalized tonic-clonic seizures in patients with preeclampsia during pregnancy, labor, or the puerperium and that are not caused by epilepsy or other seizure disorders. It appears more frequently in patients with severe preeclampsia (SP), but can also occur in women with mild preeclampsia, and occasionally in patients without full criteria for the diagnosis of preeclampsia [1].

Most patients with eclampsia have high blood pressure (blood pressure $>140/90$ mmHg). Severe headache unresponsive to common analgesics is the classic manifestation of early central nervous system involvement. Visual disorders such as scotomas, amaurosis, blurred vision, homonymous hemianopsia, irritability, hyperreflexia and clonus, as well as pain in the epigastrium or right hypochondrium, nausea, vomiting, and respiratory symptoms are the findings of severity that must be treated immediately because they announce the imminence of eclampsia [2].

In eclampsia, perfusion pressure rather than blood flow favors brain injury. Therefore, women with uncontrolled hypertension are at increased risk of developing seizures. Arterial hypertension affects the autoregulation mechanism of cerebral arteries producing endothelial barotrauma, vasogenic edema, and ischemia. If high blood pressure is not corrected, then the mechanism of injury may continue [3,4]. In particular, systolic arterial hypertension (systolic pressure >140 mmHg) has been the subject of research, for two decades it has been considered one of the triggering factors of seizures in eclampsia [5-7].

Systolic blood pressure (SBP) is the relationship between the stroke volume during left ventricular systole and the elasticity of the larger systemic arteries [7]. In this regard, in 2005 Martin et al. [6] studied the relationship between cerebral hemorrhage and increased SBP in 28 patients with eclampsia and found greater probabilities of neurological complications when SBP was between 155 and 160 mmHg. Based on all these antecedents, it has been insisted that the pharmacological control of arterial hypertension in patients with SP is absolutely necessary to prevent progression to eclampsia and other widely known serious cerebral complications such as extensive edema, parenchymal hemorrhage, intracranial hypertension, posterior reversible encephalopathy syndrome (PRES) and long-term sequelae [5,8].

The therapeutic goal that has been recommended is to maintain SBP <160 mmHg (usually between 140 and 150 mmHg) and diastolic blood pressure (DBP) <110 mmHg (generally between 90 and 100 mmHg) [1,9-11]. The results of each specialized care center should be subject to continuous review to generate evidence and establish new pharmacological management strategies. The aim of the research was to analyze the pharmacological management of arterial hypertension and clinical outcome of a retrospective cohort of patients with eclampsia.

2. MATERIALS AND METHODS

This is a retrospective cohort of cases with eclampsia from the Intensive Care Unit (ICU) of a High Specialty Medical Unit in Mexico City (Gynecology-Obstetrics Hospital No. 3. National Medical Center "La Raza", Mexican Institute of

Social Security) who were treated from January 1, 2018 to January 31, 2021. Patients with prepartum, intrapartum or puerperium eclampsia were included, of all ages and parity, any morbidity, findings of severity of preeclampsia and with the available clinical file. All cases met the inclusion criteria and had complete records, therefore no patient was excluded from the study. It was not necessary to calculate the sample size because the cases were selected for convenience.

Thirty-seven patients who met all the selection criteria were studied. All the patients came from external hospitals because they were referred to the host hospital to receive intensive care. The files were consulted to document their general data (maternal age, gestational age, morbidities, pregnancy or puerperium condition, mode of delivery, anesthetic technique, length of stay in the ICU, reasons for ICU discharge, mortality), as well as signs and symptoms, the characteristics of the seizures (onset, number of episodes, whether they were present in the ICU (face to face) or not, duration time), imaging studies, and anticonvulsant drugs. SBP and DBP values measured at ICU admission were compared with discharge measurements to identify changes. The pharmacological management of arterial hypertension in the patients was also recorded.

2.1 Data Analysis

The data were analyzed with descriptive statistics (mean, median, standard deviation, range). Continuous variables were analyzed by Student's test. Kolmogorov-Smirnov test was used to confirm normal distribution and homogeneity of variance for continuous variables. Categorical variables were analyzed by the Chi-squared test or Fisher's exact test as appropriate. A value $P=0.05$ was considered to be statistically significant. The SPSS statistical program (Windows version 20.0, IBM Corp. Armonk, New York, United States) was used for data entry and analysis.

3. RESULTS

The mean of maternal age, gestational age, morbidities, pregnancy or postpartum condition, mode of delivery, anesthetic technique, length of stay in ICU, reasons for ICU discharge, and mortality are shown in Table 1.

The most frequent symptom was intense headache 51.35% (19 cases) and the most

frequent sign was hyperreflexia 40.54% (15 cases). The distribution and frequency of symptoms and signs is shown in Table 2.

Most of the patients presented seizures in the prepartum stage and were followed by postpartum seizures, a small group of patients presented antepartum and postpartum seizures. The most frequent was a single episode of seizures, but patients with two, three, four seizures and one case with status epilepticus were documented. Most were non-face-to-face episodes, but in 21.63% (8 cases) the seizures were face-to-face in the ICU lasting from 20 seconds to 20 minutes Table 3.

The search for structural brain lesions with imaging studies was performed only in 54.05% (20 cases), the most frequent studies were cranial tomography (CT) and magnetic resonance imaging (MRI). Two patients were studied with an electroencephalogram as a complement to imaging studies, it was not performed as a solitary study Table 3. In the 20 imaging studies performed, all the findings were considered as serious brain injuries Table 4.

The thirty-seven patients studied, without exception, received anticonvulsant drugs, the most used agents were intravenous magnesium sulfate (an initial dose of 4 g infused over 30 min followed by 1 g/hour infused as a maintenance dose), intravenous phenytoin sodium (an initial dose of 15 mg/K of weight infused over 30 min followed by 125 mg bolus every 8 hours as a maintenance dose) and intravenous diazepam. The most frequent regimen was the initial administration of magnesium sulfate, which was later replaced by sodium phenytoin to avoid its toxicity because urinary volumes were reduced (oliguria, urine ≤ 30 ml/hour; anuria, urine ≤ 5 ml/hour) in the first hours of stay in the ICU. Other schemes had a lower selection frequency Table 3. Intravenous diazepam (5 to 10 mg bolus, dose-response) was the only drug used to control seizures that presented in the ICU. After delivery, in all cases sodium phenytoin was administered with the same maintenance dose already mentioned. Measurement of anticonvulsant blood concentrations was not requested.

The mean SBP of the thirty-seven patients when they were admitted to the ICU was 143.08 ± 22.11 mmHg (limits 100 to 200). It was found that in 43.24% (16 cases) the SBP values were normal

(≤ 140 mmHg) and in 56.76% (21 cases) the values corresponded to systolic arterial hypertension (>140 mmHg). The mean SBP at the time of ICU discharge was 125.7 ± 11.26 mmHg (limits 100 to 200), the statistical comparison (admission SBP vs. discharge SBP) did not show a significant difference ($P=0.06$). Fig. 1 (Panel a).

The mean DBP of the thirty-seven patients when they were admitted to the ICU was 88.69 ± 14.15 mmHg (limits 60 to 120). It was found that in 72.98% (27 cases) the measurement were normal (≤ 90 mmHg) and in 27.02% (10 cases) the measurement corresponded to diastolic arterial hypertension (>90 mmHg). The mean DBP at the time of ICU discharge was 76.60 ± 9.56 mmHg (limits 54 to 95), the statistical comparison (admission DBP vs. discharge DBP) did not show a significant difference ($P=0.76$). Fig. 1 (Panel b).

Initial antihypertensive drugs (before convulsions): it was found that 91.89% of the patients (34 cases) received antihypertensive drugs, but 8.11% (3 cases) did not receive treatment. The most frequent scheme was the simultaneous administration of oral agents with intravenous drugs in 54.06% (20 cases) followed by the prescription only with combined oral drugs 37.84% (14 cases). The most used oral antihypertensive agents were methyldopa 51.35%, metoprolol 51.35%, nifedipine 51.35% and hydralazine 48.65% followed by prazosin, enalapril, losartan and captopril, the latter three were administered to postpartum patients Table 5. The most popular parenteral antihypertensive drug was hydralazine administered as intravenous boluses in 45.95% (17 cases), followed by nimodipine and isosorbide dinitrate administered as intravenous infusion Table 5. Intravenous labetalol was not used because it is not available in the hospital.

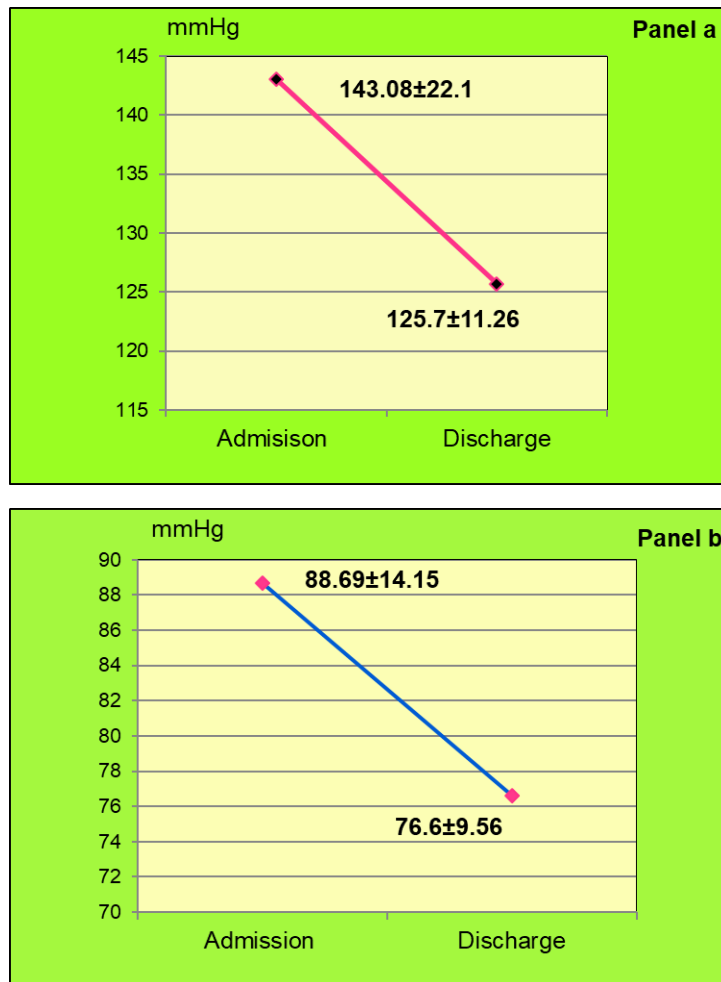


Fig. 1. Comparison of blood pressure on admission and discharge from the Intensive Care Unit (n=37). Panel a: Changes in systolic blood pressure ($P=0.06$). Panel b: Changes in diastolic blood pressure ($P=0.76$)

Table 1. General data of thirty-seven patients with eclampsia

Parameters	Data
Maternal age (years)	25.86 ± 7.82
Gestational age	33.48 ± 3.97
Premature labor (<37 weeks)	67.56% n=25
Term newborns	32.44% n=12
Morbidities	21.63% n=8 Chronic kidney failure without dialysis n=2 Chronic kidney disease without insufficiency n=1 Chronic arterial hypertension n=1 SLE inactive n=1 SLE inactive with APS controlled n=1 APS with primary hypothyroidism n=1 Carbohydrate intolerance n=1
Obstetric condition	Preeclamptic patients with pregnancy 56.76% n=21 immediate surgical postpartum 43.24% n=16
HELLP syndrome class I (Mississippi classification)	18.91% n=7
Mode of delivery	Cesarean section 100% n=37
Anesthesia technique	Neuraxial block 91.90% n=34 General anesthesia 5.4% n=2 Combined anesthesia 2.70% n=1
ICU stay (days)	3.02 ± 1.68 limits 0.83 to 7
Reasons for ICU discharge	Improvement 89.19% n=33 Transfer to the Neurology department of a high specialty hospital due to neurological complications 10.81% n=4
Mortality	0%

SLE: Systemic Lupus Erythematosus; APS: Antiphospholipid Syndrome; ICU: Intensive Care Unit

Table 2. Distribution and frequency of symptoms and signs in 37 patients with eclampsia

Symptoms	Number of cases	Percentage
Severe headache	19	51.35
Nausea and vomiting	11	29.72
Tinnitus	8	21.62
Amaurosis	5	13.51
Epigastric pain	5	13.51
Right hypochondrium pain	4	10.80
Dizziness	4	10.80
Drowsiness	4	10.80
Blurry vision	3	8.10
Fever	2	5.40
Asthenia and adynamia	2	5.40
Fainting	1	2.70
Insomnia	1	2.70
Dysarthria	1	2.70
Signs		
Hyperreflexia	15	40.54
Nystagmus	1	2.70
Disorientation	1	2.70
Anuria (urine ≤ 5 ml/hour)	1	2.70
Oliguria (urine ≤30 ml/hour)	1	2.70
Hematuria	1	2.70

Table 3. Characteristics of seizures, imaging studies and drug management of 37 patients with eclampsia

Onset of seizures	<48 hours prepartum 51.35% n=19 >48 hours postpartum 37.83% n=14 prepartum and postpartum 10.82% n=4
Number of seizures	One, n=21 Recurrent (two, n=11, three, n=2, four n=2) Status epilepticus n=1
Seizures in the ICU (Face-to-face or not)	no 78.37% n=29 yes 21.63% n=8 *
Duration time	Seizures prior to admission to the ICU: irregularly specified duration in files or no reported. Seizures in the ICU: 20 seconds to 20 minutes (status epilepticus)
Imaging studies	None 45.95% (n=17) CT 48.65% (n=18) CT with electroencephalogram 2.7% (n=1) CT, MRI and electroencephalogram 2.7% (n=1) *
Anticonvulsant drugs	Magnesium sulfate and then phenytoin sodium 43.24% (n=16) Phenytoin sodium 21.62% (n=8) Phenytoin sodium with Diazepam 16.22% (n=6) Magnesium sulfate 10.81% (n=4) Phenytoin sodium with magnesium sulfate and Diazepam 8.11% (n=3)*

* Includes one case with status epilepticus; CT = Cranial Tomography; MRI = Magnetic Resonance Imaging

Table 4. Findings of brain imaging studies performed on 20 of 37 patients with eclampsia

Findings	Number of cases	Percentage
Severe diffuse cerebral edema	6	30
Thrombosis of the superior longitudinal venous sinus	5	30
Ischemic infarction	4	20
Subarachnoid hemorrhage	2	10
Parenchymal hematoma	2	10
Cortical vein thrombosis	1	5
Total	20	100

Table 5. Antihypertensive drugs on admission to the Intensive Care Unit of 37 patients with eclampsia

Drugs	Percentage	Number of cases
Oral agents		
Methyldopa	51.35	19
Metoprolol	51.35	19
Long-acting nifedipine	51.35	19
Hydralazine	48.65	18
Prazosin	18.92	7
Enalapril *	16.22	6
Losartan *	10.82	4
Captopril *	2.7	1
Intravenous agents		
Hydralazine bolus	49.95	17
Nimodipine infusion	10.82	4
Isosorbide dinitrate infusion	5.4	2

* Drugs administered to postpartum patients

In addition, blood pressure, antihypertensive management, hypertensive complications and the outcome of preeclamptic pregnant patients who presented seizures in the ICU were studied, represented 21.63% (8/37 cases). When they were admitted to the ICU, the mean SBP was 135.75 ± 19.46 mmHg (limits 100 to 160) and before the seizures 175 ± 45 mmHg (limits 140 to 240). The comparison of the values (SBP admission vs SBP pre-seizure) showed a borderline statistical difference ($P=0.050$). The mean increase in SBP before seizures was 19.36 ± 6.02 mmHg, which represented 13.53% higher than the values at admission Table 6. When they were discharged from the ICU, the mean SBP was 119.75 ± 11.04 mmHg (limits 100 to 140), comparatively a reduction of 55.25 mmHg was found, that is, 31.57% lower than its pre-seizure value ($P=0.006$). and 16 mmHg, that is, 11.78% compared to the measurement of his admission to the ICU ($P=0.062$).

Mean DBP on admission to the ICU was 84.71 ± 10.75 mmHg (limits 70 to 100) and prior to seizures 109.25 ± 27.48 mmHg (limits 90 to 150). The comparison of the measurements (admission DBP vs pre-seizure DBP) did not show a significant difference ($P=0.059$). The pre-seizure increase was 24.54 ± 16.73 mmHg, which represented 22.46% higher than their ICU admission values Table 6. When they were discharged from the ICU, the mean DBP was 76.37 ± 10.51 (limits 59 to 90), comparatively, a reduction of 32.88 mmHg was found, that is, 30.09% lower compared to the pre-seizure value ($P=0.011$) and of 8.36 mmHg, that is, 9.86% compared to the measurement of his admission to the ICU ($P=0.15$).

Antihypertensive management and imaging study findings are shown in Table 7.

Mean ICU stay was 2.22 ± 1.06 days (limits 0.83 to 4), when compared to the stay of the 37 patients studied (3.02 ± 1.68 days) no significant difference was found ($P=0.20$). Mortality was 0%.

4. DISCUSSION

For decades it has been known that the best therapeutic measures in patients with eclampsia are termination of pregnancy, administration of anticonvulsant drugs, control of blood pressure with antihypertensive drugs, and critical care to improve outcome [12]. The recommendation is that antihypertensive management should continue in the prepartum, intrapartum, and

postpartum periods, mainly in preeclampsia with severe neurological findings, HELLP syndrome, and in cases that have already progressed to eclampsia [13-15]. Blood pressure control improves the maternal condition for pregnancy termination (vaginal, cesarean section) because it reduces the possibility of hypertensive complications of the heart, lungs, kidneys, liver, coagulation mechanism and placenta. It also decreases the risk of serious brain injuries such as the severe edema that characterizes PRES, cerebral hemorrhage, the onset or recurrence of seizures due to eclampsia, and long-term sequelae [8,16-18].

Management with antihypertensive drugs is constantly changing, so the data from each specialized care center should be subject to periodic review to learn about the strengths and weaknesses of antihypertensive pharmacological management of patients with preeclampsia and eclampsia and to establish new strategies [17].

In this research, thirty-seven patients with eclampsia admitted to the ICU of a High Specialty Medical Unit in Mexico City were studied in order to analyze the clinical outcome, the characteristics of the seizures and, mainly, the antihypertensive management. The retrospective cohort included patients with prepartum and/or postpartum eclampsia and pregnant women with SP who progressed to eclampsia in the ICU. Chronic and acute morbidities that the current literature has already fully identified as risk factors for eclampsia, such as chronic kidney disease, chronic arterial hypertension, systemic lupus erythematosus, antiphospholipid antibody syndrome, and HELLP syndrome, were documented [13-15]. The morbidities of the patients possibly contributed to the development of hypertensive disease during the second and third trimesters of pregnancy (mean 33.48 ± 3.97 weeks) with a high frequency of preterm labor (67.56%) Table 1. In addition, the signs and symptoms reflected the aggressiveness of the maternal disease, thus justifying the need for admission to the ICU. Table 2.

All patients received intensive care and anticonvulsant drugs according to the recommendations of international experts [1,10,11] Table 3. However, eight new cases of eclampsia occurred in the ICU and their imaging studies showed severe brain lesions, but with 0% mortality Table 4. In theory, intensive care, management with anticonvulsant, and

antihypertensive drugs should have stabilized the neurological condition and blood pressure of the thirty-seven studied patients to prevent new cases of eclampsia or to avoid recurrence, but in the practice did not happen like that. In this regard, at least four points of analysis should be considered: the natural history of preeclampsia, sub-therapeutic doses of anticonvulsant drugs, inadequate coverage of antihypertensive agents, and the presence of serious brain lesions that can cause seizures.

First, it has been documented that preeclamptic patients can convulse despite anticonvulsant

management and with blood pressure values in the safe range recommended by experts because the activity of preeclampsia can take an aggressive course in an unpredictable manner. This situation could have occurred in the studied patients because chronic and acute morbidities that favor a poor prognosis, were documented [19].

Second, the blood concentration of magnesium sulfate and sodium phenytoin was not requested in the patients, therefore, the possibility of sub-therapeutic doses is feasible.

Table 6. Blood pressure of 8 new cases of eclampsia in the ICU

Blood pressure mmHg	ICU admission	Prior to seizures	Value p	Change	
				mmHg	Percentage
Systolic	135.75 ± 19.46	175 ± 45	0.050	19.36 ± 6.02	↑13.53
Diastolic	84.71 ± 10.75	109.25 ± 27.48	0.0592	24.54 ± 16.73	↑22.46

ICU: Intensive Care Unit

Table 7. Data, antihypertensive drugs and imaging study findings of the 8 new cases of eclampsia in the ICU

Case	Gestational Weeks	Number of seizures *	Antihypertensive drugs		Findings in the imaging studies
			Oral	Intravenous	
1	35	2	Methyldopa, Hydralazine, Metoprolol	None	Diffuse cerebral edema
2	30	4	None	None	Diffuse cerebral edema
3	34	1	Methyldopa, Hydralazine, Metoprolol	Hydralazine bolus	Diffuse cerebral edema
4	38	3	Nifedipine, Metoprolol, Prazosin, Losartan**	None	Superior longitudinal sinus thrombosis and cortical infarcts
5***	39	2	Methyldopa, Hydralazine, Nifedipine, Metoprolol	Nimodipine infusion	Hypodense frontal image and possible ischemic lesion
6***	38	1	Metoprolol, Nifedipine, Enalapril **	None	Parenchymal hematoma and Fisher class IV subarachnoid hemorrhage
7	31	2	Methyldopa	None	Superior longitudinal sinus thrombosis
8	30	2	Prazosin, Hydralazine, Losartan **, Metoprolol, Nifedipine	Hydralazine bolus, Isosorbide dinitrate infusion	Diffuse cerebral edema

ICU = Intensive Care Unit; * Median = 2; ** Drugs administered to postpartum patients; *** Cases with class I HELLP syndrome

Third, to study the possibility of inadequate coverage, the antihypertensive regimen of the thirty-seven patients was reviewed when they were admitted to the ICU. It was found that only 91.89% of the cases were administered antihypertensive drugs and 8.11% did not receive them because the SBP and DBP measurements were interpreted by the medical team as "permissible". The first line regimen was oral agents, the most common were methyldopa, metoprolol, nifedipine and hydralazine followed by prazosin, enalapril, losartan and captopril, the last three were administered in postpartum patients. Table 5. Oral drugs have the drawbacks of tolerance to the oral route, intestinal absorption time that can increase, and absorption that can become irregular and unpredictable, as in all critically ill patients. Also, methyldopa should not be used when it comes to urgently lowering blood pressure [11]. Prazosin, an α adrenergic receptor blocking agent, has not been accredited as an eligible antihypertensive agent in preeclampsia-eclampsia, and captopril, enalapril and losartan are not recommended during pregnancy. In addition, their usefulness for blood pressure control in peripartum stage has not been documented [1,10,11]. The intravenous antihypertensive drugs administered to control hypertensive crises were bolus hydralazine, nimodipine, and intravenous infusion of isosorbide dinitrate. Intravenous labetalol was not used because it is not available in the hospital. Only hydralazine has sufficient evidence for the recommendation of international experts, but not nimodipine and isosorbide dinitrate [1,10,11]. Nimodipine has not been considered as a therapeutic option, despite the fact that its lipid solubility characteristics and its cerebral vasodilator effect put it at an advantage over intravenous nitrates, whose action on arterial and venous vascular tone is exerted rather in the pulmonary and systemic vasculature and not in the territory. cerebral. In 2006, Vázquez [20] studied the effect of intravenous nimodipine as a third antihypertensive in the treatment of patients with SP. It was found that intravenous nimodipine in continuous infusion at a fixed dose of 1 mg per hour for 24 consecutive hours added to conventional oral management (methyldopa with hydralazine) does not confer advantages for blood pressure control nor does it modify the clinical evolution of patients. At the host hospital, nimodipine continues to be administered to patients with SP and hypertensive crises with brain involvement, with severe systolic hypertension, or with eclampsia as an unofficial option in an attempt to improve

their critical condition and the possibility of maternal death. The same occurs with the use of oral (prazosin) or intravenous (isosorbide dinitrate) medications that are outside the recommended regimens [21].

Numerous clinical trials have compared various short-acting antihypertensive agents for the management of severe hypertension or hypertensive crisis during pregnancy. The most commonly screened drugs are parenteral hydralazine, parenteral labetalol, and oral nifedipine (short-acting, intermediate-acting, or long-acting). A Cochrane review in 2013 [22] concluded that these drugs are comparable with respect to safety and efficacy. The recommendation was that professionals can choose them based on their experience and familiarity with a particular drug. The possibility of using little-studied drugs, but with a proven effect on uncontrolled hypertension based on the experience of the medical team or protocols recommended by professional societies, was also considered. 22 In our country, therapeutic limitations (labetalol) have forced uncontrolled clinical trials. This trend is not exclusive to one region, nor is it a fashion of recent times. This situation has been occurring for several decades, mainly in the developing countries of the five continents [21].

Uncontrolled systolic hypertension was not documented in this investigation, as has been described in previous publications. [6,15] SBP and DBP were found to be equally increased prior to seizures in the 8 new cases of eclampsia in the ICU. Changes from admission measurements were similar ($P=0.050$ and $P=0.59$) Table 6. Highlighted that one patient did not have antihypertensive management, one patient only received methyldopa, three patients received three oral agents, two cases were managed with four medications and one more with five oral drugs, none was managed with intravenous agents Table 7. Thus, the use of unaccredited drugs and incomplete coverage of antihypertensive management may have participated in the uncontrolled blood pressure and seizures in new cases of eclampsia in the ICU.

Fourth, the case series was characterized by the development of serious maternal complications at the cerebral level. Imaging studies were useful to demonstrate a variety of severe neurological injuries that put the lives of patients at risk. Imaging studies were not part of any study

protocol nor were they performed before and after the seizures. For this reason, it cannot be established whether uncontrolled arterial hypertension generated the seizures and then the lesions or whether the lesions were generated first and then the seizures. Fortunately, at the end of the study, no cases of maternal death occurred, but there is the possibility of serious long-term sequelae as described in the literature [8,16-18].

Based on the data of this investigation, the following recommendations can be established:

- a) Neurological signs and symptoms should always be considered to imply the extreme severity of preeclampsia and that eclampsia can occur at any time.
- b) The frequency of new cases of eclampsia despite receiving conventional management was high. For this reason, eclampsia should not be ruled out in a hemodynamically stable patient with adequate anticonvulsant coverage.
- c) New cases of eclampsia should not be interpreted as therapeutic failure because it should be taken into account that the course of the disease includes unpredictable hypertensive crises.
- d) Cerebrovascular injuries should be investigated in all patients with eclampsia through special imaging studies because their frequency is high and they are extremely serious.
- e) In patients with signs and symptoms of cortical irritation identified in the initial evaluation, conventional oral antihypertensive agents should be started accompanied by an intravenous drug [23].
- f) The data indicate the need to establish a consensus on antihypertensive management to reduce the possibility of new cases of eclampsia in the ICU related to uncontrolled blood pressure. The therapeutic goal that international experts have recommended should be reviewed [1,9-11]. Deviations from the handling guidelines should be avoided.

Finally, the analysis of the data of the present cohort was sufficient to know their clinical characteristics, seizures, management with anticonvulsant agents and hypertensive drugs. A group of new cases of eclampsia in the ICU with severe brain injuries and deviations in antihypertensive management were also identified, which should require a review of

management to improve results. These are considered to be the main strengths of the research. Its weaknesses lie in its design, since it is a retrospective study of a small number of cases with regional results, but which may be occurring in other regions of the world for various reasons, including limitations in the availability of drugs recommended by experts and international organizations.

5. CONCLUSION

The evolution of the patients was not satisfactory, but without maternal deaths. Despite the fact that all patients received intensive care, anticonvulsant drugs, and interruption of pregnancy, eight new cases of eclampsia were recorded in the ICU with uncontrolled blood pressure, probably due to insufficient pharmacological management. The data suggest that coverage of antihypertensive agents should not be discontinued despite blood pressure remaining controlled. Deviations from the handling guidelines should be avoided

CONSENT

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The study was previously approved by the local health research committee no. 3504 and Ethics in Health committee of the host hospital (Registration: R-2021-3504-46).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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