Achievement of the therapeutic blood pressure goal in pregnant patients with eclampsia

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Original Article

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Background:
Objective: Determine the percentage of achievement of the therapeutic goal of blood pressure in pregnant patients with eclampsia.
Material and methods: A retrospective cohort of 32 pregnant patients with eclampsia admitted to the Intensive Care Unit (ICU) was studied. Their general data, ICU stay, mortality, and average blood pressure in the antepartum, intrapartum, and postpartum stages were documented. The percentage of cases in which the therapeutic goal of systolic (<160 mmHg) and diastolic (<110 mmHg) pressure was achieved in each stage and management with antihypertensive agents were calculated. The data were analyzed with descriptive statistics, Student's t test, Mann-Whitney U test, and chi square with the statistical program SPSS™ version 20.0. The value p <0.05 was significant.
Results: Maternal age 26.43±6.34 years, pregnancy 34.55±3.08 weeks, morbidities 21.87%, cesarean section in 96.87%, intrapartum complications 0%, reinterventions 0%, ICU stay 3.31 ± 2.41 days and mortality 3.12%. Achievement of the therapeutic goal: antepartum systolic blood pressure 37.5%, intrapartum 75% and postpartum 81.25%; diastolic blood pressure antepartum 68.75%, intrapartum 87.5% and postpartum 87.5%. Management: oral medications: three agents (methyldopa-hydralazine-metoprolol) 65.64%, two agents (methyldopa-hydralazine) 15.62%, single agent (methyldopa) 15.62%, and four agents (methyldopa-hydralazine-metoprolol-long acting nifedipine) 3.12%. Intravenous drugs: hydralazine boluses 12.5%, nimodipine infusion 6.25% and isosorbide dinitrate infusion 3.12%.
Conclusions: The percentage of achieving the therapeutic goal of antepartum, intrapartum and postpartum blood pressure in pregnant patients with eclampsia was acceptable.

Keywords: Eclampsia; Antihypertensive management; Hypertension and pregnancy; Obstetric intensive care; High risk pregnancy.

Eclampsia is the convulsive manifestation of preeclampsia, it is defined as the appearance of generalized tonic-clonic seizures in a patient with preeclampsia that cannot be explained by other causes. [1] It can occur during pregnancy (>20 weeks or earlier), childbirth, or in the postpartum period. At all times, blood pressure control is a fundamental measure of the medical management of patients. [2,3]

The World Health Organization (WHO), international associations and expert groups periodically review the antihypertensive management of preeclampsia-eclampsia with disagreements and points of consensus. [1-4] In the North American region (Canada, United States of America, Mexico) the topic is also reviewed periodically based on the evidence of the most recent research.

The Canadian guideline for the diagnosis, evaluation and management of hypertensive disorders of pregnancy issued in 2014 [5] recommends that systolic blood pressure should be reduced to <160 mmHg and diastolic blood pressure <110 mmHg. The guideline mentions that initial antihypertensive treatment in the hospital should be with short-acting nifedipine capsules, intravenous hydralazine, or intravenous labetalol. Alternative antihypertensive medications include nitroglycerin infusion, oral methyldopa, oral labetalol, oral clonidine, or oral postpartum captopril. Intravenous sodium nitroprusside is recommended for the management of refractory hypertension.

The guideline for the clinical management of gestational hypertension and preeclampsia of the American College of Obstetricians and Gynecologists (ACOG) of the United States of America published in 2020 [1] describes that the goals of the treatment of severe hypertension are to prevent heart congestive failure, myocardial ischemia, renal injury or failure,

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Characteristics	Results
Maternal age years mean (limits)	26.43±6.34 (19 to 39)
Parity median (limits)	1 (1 to 4)
Morbidities % (n)	
chronic hypertension	15.62 (5)
gestational diabetes	6.25 (2)
Weeks of pregnancy mean	34.55±3.08
prematurity (< 37 weeks % (n)	71.87 (23)
term pregnancy % (n)	28.13 (9)
Medical complications % (n)	25 (8)
acute kidney injury without dialysis	12.5 (4)
HELLP syndrome class I	6.25 (2)
cerebral hemorrhage	3.12 (1)
multiorgan failure	3.12 (1)
New medical complications in the ICU %	0
Admission-delivery time hours (limits)	15.76±1.73 (1 to 72)
Termination of pregnancy % (n)	
cesarean section	96.87 (31)
vaginal birth	3.13 (1)
Fetal status % (n)	
in utero mortality	28.13 (9)
live newborns	71.87 (23)
Apgar score median	
minute 1	8
minute 5	9
Anesthetic technique % (n)	
neuraxial block	84.37 (27)
intravenous general anesthesia	15.63 (5)
Intrapartum bleeding ml (limits)	380.76±203.65 (200 to 1,100)
Obstetric hemorrhage (> 1,000 ml) % (n)	3.12 (1)
Intrapartum complications %	0
Surgical reintervention %	0
ICU stay days mean (limits)	3.31±2.41 (0.8 to 6)
Mortality	3.12% (n=1)
cause	Multiorgan failure

ICU = Intensive Care Unit
HELLP = hemolysis, elevated liver enzymes, and low platelet count

Table 1. General data.

and ischemic or hemorrhagic stroke. The recommendation is to initiate antihypertensive treatment once severe acute-onset hypertension has been identified (systolic blood pressure ≥160 mmHg, diastolic blood pressure ≥110 mmHg, or both) once its persistence for 15 minutes or more is confirmed. The three recommended antihypertensive agents are intravenous hydralazine, intravenous labetalol, and short-acting oral nifedipine. To cover expectant management, the guide recommends oral drugs such as labetalol and short-acting nifedipine. As a therapeutic goal, it is recommended that systolic blood pressure should be reduced to <160 mmHg and diastolic blood pressure <110 mmHg.

In Mexico, the technical guideline for the prevention, diagnosis and management of preeclampsia-eclampsia issued in 2007 [6] recommends intravenous hydralazine, intravenous labetalol and oral short-acting nifedipine for the management of hypertensive crises and oral methyldopa, hydralazine and labetalol for the maintenance management. The guideline does not establish the recommended therapeutic blood pressure goal. The Clinical Practice Guideline (CPG) of the Mexican Ministry of Health for the prevention, diagnosis and treatment of preeclampsia in the second and third level of care updated in 2017 [7] recommends antihypertensive management in all patients with severe preeclampsia and pressure blood >160/110 mmHg starting with oral agents as the first line of therapy (methyldopa 250-500 mg every 8 hours, hydralazine 25-50 mg every 6 hours, metoprolol 100-200 mg every 8-12 hours, long-acting nifedipine 20-60 mg every 24 hours, labetalol 100-400 mg every 8 hours). The second line of drugs to control hypertensive crises includes labetalol (20 mg intravenous boluses up to 40 mg every 10 to 15 minutes, or infusion 1 to 2 mg/minute, maximum dose: 220 mg), hydralazine (5-10 mg as an intravenous boluses or infusion at 0.5-10 mg per hour, maximum dose 30 mg) and short-acting nifedipine (10 mg oral every 10-15 minutes, maximum dose 50 mg). The recommended therapeutic goal is to maintain blood pressure <160/110 mmHg, preferably systolic blood pressure between 130 and 155 mmHg and diastolic blood pressure between 80 and 105 mmHg.

In the Intensive Care Unit (ICU) of the hospital where this research is carried out, the study protocol, drug therapy, obstetric conduct and life support of the mother and fetus are governed according to the recommendations of the technical guideline [6] and CPG [7] of the Mexican health sector with the pertinent modifications related to the characteristics of the patients, the availability of drugs and the preference of the medical team based on evidence.

International and national reports on the results of alternative antihypertensive management in pregnant patients with eclampsia are scarce. With this panorama, the **objective** of the research was to determine the percentage of achievement of the therapeutic goal of blood pressure in pregnant patients with eclampsia managed in the highly specialized ICU.

Methods

An observational, longitudinal, retrospective, descriptive and analytical study was carried out in pregnant patients with eclampsia admitted to the ICU of the High Specialty Medical Unit Hospital of Gynecology and Obstetrics No. 3 of the National Medical Center "La Raza" belonging to the Mexican

Blood pressure mmHg	Measurements antepartum	intrapartum	pospartum
systolic	156.93±29.64	140.57±15.98	130.46±27.72
diastolic	94.53±23.89	88.42±7.29	78.2±16.04

Table 2. Average blood pressure in 32 pregnant patients with eclampsia

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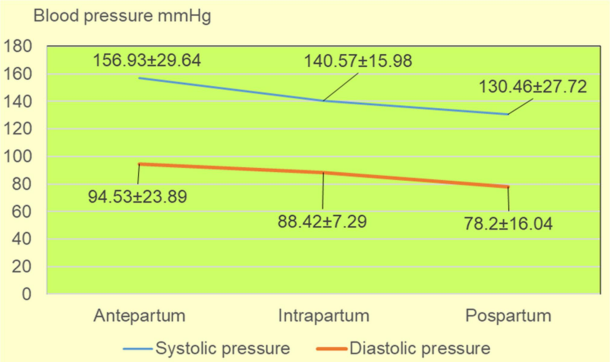

Figure 1. Averages of systolic and diastolic blood pressure in the three measurements of the study.Systolic blood pressure: Antepartum vs intrapartum p=0.009, intrapartum vs postpartum p=0.289 and antepartum vs postpartum p=0.019. Diastolic blood pressure: antepartum vs intrapartum p=0.191, intrapartum vs postpartum p=0.041 and antepartum vs postpartum p=0.045.

Institute of Social Security (IMSS), Mexico City.

The registry of patients admitted to the ICU in the period from January 2019 to December 2023 was reviewed to identify possible candidates to participate in the research. Patients over 18 years of age with any parity and morbidities, with pregnancy ≥20 weeks complicated by eclampsia diagnosed according to ACOG recommendations issued in 2020 [1] and with available clinical records were included. Patients with a history of epilepsy, brain tumors, neuroinfection, neuroparasitosis, brain surgery, old or recent head trauma, or any chronic condition with potential brain complications were excluded.

Thirty-two patients who met the selection criteria were identified. In all cases, the seizures due to eclampsia occurred at home or in the hospitals where their medical management began and were then transferred to the Emergency Department of the hospital where this research was conducted. They were examined by an intensive care physician who decided on their admission to the ICU. When the ICU medical team considered that the best possible conditions of maternal and fetal stability had been achieved, the scheduled termination of the pregnancy was carried out in the Toco-Surgery Unit of the same hospital through cesarean section or vaginal delivery using a

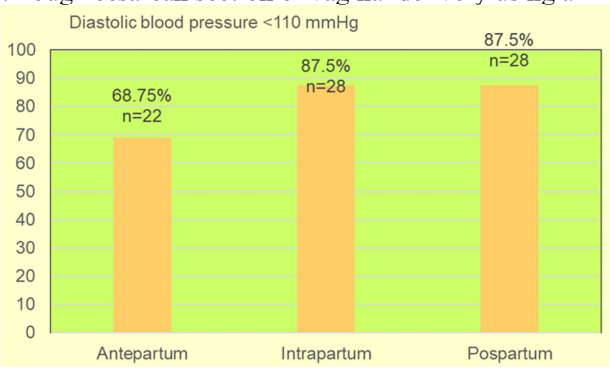

Figure 2. Percentage of patients with average systolic blood pressure <160 mmHg as a therapeutic goal in the three stages.

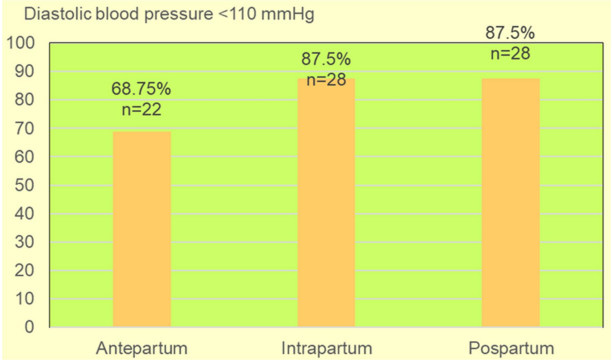

Figure 3. Percentage of patients with average diastolic blood pressure <110 mmHg as a therapeutic goal in the three stages.

block. neuraxial or general intravenous anesthesia. After delivery care, the patients were transferred back to the ICU to continue their medical management under clinical, hemodynamic and biochemical monitoring. The research period began from the moment the patients were admitted to the ICU and concluded when they were discharged.

The records of the thirty-two patients were consulted to obtain the data necessary for the investigation. All records were available so none of them were eliminated from the study. Age, parity, morbidities, weeks of gestation, acute medical complications accompanying eclampsia, type of delivery care, anesthetic technique, intrapartum bleeding, obstetric hemorrhage (loss >1,000 ml), intrapartum complications, surgical reinterventions, time of stay in the ICU, mortality and its causes were documented.

For the purposes of the research, the average of the blood pressure readings recorded in the ICU of the antepartum, intrapartum and postpartum stages was calculated to know the percentage of cases in which the therapeutic goal of systolic (<160 mmHg) and diastolic (<110 mmHg) blood pressure was achieved in accordance with the ACOG recommendations issued in 2020 and the IMSS CPG in force since 2017. [1,7] Pharmacological management

Number of drugs	Percentage (n)
Oral drugs	
One methyldopa	15.62 (5)
Two methyldopa-hydralazine	15.62 (5)
Three methyldopa-hydralazine-metoprolol	65.64 (21)
Four methyldopa-hydralazine-metoprolol-long acting nifedipine	3.12 (1)
Intravenous drugs	
hydralazine boluses	12.5 (4)
nimodipine infusion	6.25 (2)
isosorbide dinitrate infusion	3.12% (1)

Table 3. Antihypertensive drugs

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Oral drugs	
Methyldopa	500 mg every 8 hours
Hydralazine	50 mg every 6 hours
Metoprolol	100 mg every 12 hours
Long-acting nifedipine	30 mg every 8 hours
Intravenous drugs	
Hydralazine boluses	10 mg every 30 minutes, dose-response
Nimodipine infusion	2 mg/hour, dose-response
Isosorbide dinitrate infusion	2 to 10 mg/hour, dose-response

Table 4. Doses of antihypertensive drugs.

with antihypertensive agents in the antepartum, intrapartum, and postpartum stages was also reviewed. To carry out the research, prior authorization was obtained from the Local Health Research Committee and the Local Health Research Ethics Committee of the host hospital (Registration: R-2023-3504-4). The data were **analyzed** with descriptive statistical measures (mean, median, standard deviation, range), and inferential statistical tests. The continuous variables were analyzed with the Kolmogorov-Smirnov test to determine their distribution, the Student T test was used for continuous variables with normal distribution and the Mann-Whitney U test was used as a non-parametric test. Categorical variables were analyzed with the chi-square test. The value of p <0.05 was considered statistically significant. The statistical program SPSS™ Windows version 20.0 (IBM Corp. Armonk, New York, United States) was used to record and analyze the data.

Results

General data

The general characteristics of the thirty-two patients in the study are shown in **Table 1**. It was found that no patient breastfed the newborn during the study period.

Blood pressure measurements

We had access to the records of non-invasive measurements of systolic and diastolic blood pressure from the antepartum, intrapartum and postpartum stages of all patients. The averages are shown in **Table 2**.

When the data were analyzed comparatively, it was found that systolic and diastolic blood pressure had a tendency to reduce. Changes in systolic blood pressure had statistical significance when comparing antepartum vs intrapartum (p=0.009) and antepartum vs postpartum (p=0.019) measurements while changes in diastolic blood pressure were significant when comparing antepartum vs postpartum (p=0.045) and intrapartum vs postpartum measurements (p=0.041).

Goals of blood pressure management

When the percentage of patients with average systolic blood pressure <160 mmHg as a therapeutic goal was calculated, an increase in the percentage of patients under control was found in the intrapartum and postpartum stages compared to the antepartum average. The distribution is shown in **Figure 2.**

When the percentage of patients with average diastolic blood pressure <110 mmHg as a therapeutic goal was calculated, an increase in the percentage of patients under control was found in the intrapartum and postpartum stages compared to the antepartum average. The distribution is shown in **Figure 3**.

Management with antihypertensive agents

It was found that in all the patients, management with oral antihypertensive drugs had already begun in their places of origin, but in an irregular manner and there was no precise record. In the ICU, the most frequently used oral medications in the antepartum stage were methyldopa, hydralazine, metoprolol and long-acting nifedipine. No oral medications were used during delivery. In the postpartum stage, the established schemes were continued. Thus, the most frequent was the administration of three oral antihypertensive drugs. **Table 3** The doses are shown in **Table 4**. In the antepartum stage it was necessary to add an intravenous antihypertensive agent to the oral regimen in 21.88% (7 patients) with the following distribution: hydralazine in boluses 4 cases, nimodipine infusion 2 cases, and isosorbide dinitrate infusion 1 case. Intrapartum and postpartum stages, intravenous antihypertensive agents were not used. **Table 3** The doses are shown in **Table 4** Labetalol, an alpha and beta adrenergic receptor blocking agent, was not used because the host hospital does not have this drug.

Discussion

Not all primary care centers and second and tertiary hospitals can carry out the recommendations for antihypertensive management of preeclampsia-eclampsia issued by the WHO, international associations and expert groups. This is a global reality. Countries with low and middle income are mainly affected by costs, lack of infrastructure, medical resources, and drug shortages. [8]

This situation of inequity has led to the innovation of therapeutic schemes being necessary for the management of patients using the available medications with a proven effect during pregnancy,

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considering data based on scientific evidence and the experience of the medical team at each site. The problem has been considered for several years by the WHO [4] and also by technical guideline [6] and CPG [7] of Mexico. Experts have opened the possibility of antihypertensive management with modifications or alternatives aimed at controlling blood pressure, avoiding deterioration. maternal and adverse fetal effects attributed to in utero exposure to drugs.

In this context, data from a retrospective cohort of thirty-two patients with pregnancy and eclampsia were analyzed to determine the percentage of achievement of the antihypertensive therapeutic goal with pharmacological management of the ICU of a highly specialized center in Mexico City. In this place, the first-line antihypertensive agents are oral medications, the second line of therapy includes intravenous drugs. **Tables 3 and 4** This is a therapeutic scheme with which the ICU medical team has generated its own experience over the years; the data have been shared in national and international literature. [9-14]

The therapeutic goal of systolic blood pressure (<160 mmHg) was achieved in 37.5% (12 cases) in the antepartum stage and increased to 75% (24 cases) in the intrapartum stage, reaching 81.25% (26 cases) in the postpartum stage. **Figure 2** On the other hand, the therapeutic goal of diastolic blood pressure (<110 mmHg) was achieved in higher percentages: antepartum stages 68.75% (22 cases), intrapartum 87.5% (28 cases) and postpartum 87.5% (28 cases). The data is encouraging. However, a small number of patients had hypertension resistant to management during the antepartum stage with the need to use intravenous agents. **Table 3** No new medical complications of preeclampsia-eclampsia occurred during their stay in the ICU or new episodes of seizures. This information becomes important once systolic hypertension has been associated with the onset and recurrence of seizures due to eclampsia. [15]

The characteristics of the fetal state at birth (prematurity, fetal death, Apgar score) cannot be attributed to the effect of antihypertensive drugs since the in utero exposure was relatively short because the termination of the pregnancy occurred in a matter of hours (15.76±1.73 hours). **Table 1** Furthermore, no cases were reported with maternal hypotension or tachycardia or deterioration in fetal reactivity, bradycardia or arrhythmias at birth. No newborn was breastfed.

Caesarean section as the most common method for terminating pregnancy is not new in our environment. In this investigation, caesarean section was a resolute and safe surgery once the amount of intrapartum bleeding did not exceed the range established as normal, obstetric hemorrhage occurred only in 3.2% (1 case) and no reinterventions were needed. The anesthetic technique with neuraxial blockade was not accompanied by complications, hypertensive uncontrol or hypotension during delivery and there was no need to administer intravenous drugs. The average stay in the ICU was 3.31±2.41 days, which is within the range recommended by the IMSS (≤ 5 days) for patients receiving critical care in the ICU of the host hospital. [16] The longest stay in the ICU did not exceed 6 days and was due to the waiting time for recovery from the complications of preeclampsia-eclampsia that the patients had already suffered since their admission to the ICU, such as HELLP syndrome and acute kidney injury. and not exactly to the failure of antihypertensive management. Maternal mortality of 3.12% (1 case) was considered acceptable; the death of a patient with multiorgan failure occurred, a very complex complication in which critical care did not modify the outcome.

High blood pressure in preeclampsia-eclampsia directly affects the anatomy of the maternal vasculature and cerebral hemodynamics causing very serious organic complications in a short time such as cerebral edema, posterior reversible encephalopathy syndrome, eclampsia and cerebral hemorrhage. [17-19] Intravenous labetalol, intravenous hydralazine, methyldopa and short-acting nifedipine are widely recommended pharmacological agents based on the results of randomized clinical trials and the conclusions of meta-analysis. [20-23] The medications in the alternative scheme used in the ICU of the host hospital are considered useful because they controlled high blood pressure in the majority of patients, but the scheme does not have sufficient solid bases for scientific scrutiny by experts and its inclusion as safe options. In any case, the report of its results is valuable because the therapeutic scheme resolves the medical obligation of pharmacological intervention to reduce complications, maternal and fetal mortality and late sequelae in all possible cases. The design of placebo studies is restricted in our country because severe preeclampsia and eclampsia are potentially lethal and legal action may occur that is difficult to overcome. This situation may be happening in other nations.

The description of successful maternal outcomes from an alternative pharmacological regimen is the main strength of the present investigation. The retrospective design, the small number of patients, the limitation of the study to analyze the data of the patients only during their stay in the ICU and the lack of similar works for comparison are the main weaknesses of the study. All these inconveniences are the common denominator of many reports and are considered the main methodological challenges for the investigation of hypertension during pregnancy. [24]

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Conclusion

The percentage of achievement of the therapeutic goal of systolic and diastolic blood pressure was satisfactory in the patients in the study. No maternal adverse effects attributed to drugs or new medical complications of preeclampsia-eclampsia were documented. The ICU stay resulted in the established institutional limit and a single case of maternal death occurred.

Conflicts of interest

The authors have no conflicts of interests to declare.

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