

## **Hemodynamic Evaluation and Anti-Hypertensive Schemes Used in Puerperal Women Following Pre-Eclampsia**

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Pre-eclampsia is still a very prevalent disease with critical hemodynamic changes. This study was evaluated the major anti-hypertensive schemes used at the Materno Perinatal Hospital "Monica Pretelini" (HMPMP) hospitalized at the Obstetric Intensive Care Unit (OICU) for at least seven days. In other group of patients we compared hemodynamic monitoring with Swan-Ganz catheter versus transthoracic electrical bioimpedance (TEB) and gasometric formulas. Statistical analysis was done using the Statistical Package for Social Science (SPSS) software, version 17. Amlodipine + temisartan + prazosin was the preferred anti-hypertensive drug combination used in our intensive care unit. Sodium nitroprusside is required in 25% of patients until reaching control. There was no statistically significant difference in cardiac output calculated with gasometric formulas compared to thermodilution with Swan-Ganz catheter. Calcium antagonists + angiotensin II receptor blocker (ARB) +  $\alpha$ -blockers offer the best option to control hypertension in puerperal women that followed pre-eclampsia, but oral and IV drugs to control hypertension is required in 20% of cases, in a Mexican Intensive Care Unit specialized in obstetrical patients. Hemodynamic monitoring with gasometric formulas is still useful in this set of patients, without discarding TEB with a correction factor due to the accumulated extravascular water in these patients.

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**Key words:** Anti-hypertensive drugs, Bioimpedance, Pre-eclampsia, Swan-Ganz

### **Introduction**

**P**re-eclampsia is one of the most common complications of pregnancy that may threaten the mother and fetal survival. It is generally defined as a new hypertension and proteinuria and the progress to eclampsia is marked by the onset of seizures. Women with pre-eclampsia have a significantly elevated long-term risk of developing cardiovascular diseases in later life<sup>1</sup>.

The treatment goal for women with pre-eclampsia is to lower the blood pressure to prevent cerebral hemorrhage, the leading cause of maternal death from pre-eclampsia-eclampsia. Despite interruption of gestation hypertension can last several days and some women become chronically hypertensive. Once in puerperium we can offer the next options to lower blood pressure: angiotensin II receptor blocker (ARB), angiotensin-converting enzyme inhibitors (ACEI),  $\alpha$ -blockers,  $\beta$ -blockers, calcium antagonists, diuretics and sodium nitroprusside.

During normal pregnancy, the cardiac output (CO) and the plasma volume are raised, (1L/min/m<sup>2</sup>) and (600 ml) respectively. Although these changes may elevate the blood pressure in non-pregnant woman, the adaptive hemodynamic factors such as the

elevation of vasodilator systems (kallikrein kinin, prostaglandins and L-arginine-nitrous oxide) preserve the good function in this new hyperkinetic heart. On the other hand, the placental spiral arteries must suffer a remodeling in order to allow a correct blood supply and nutriment exchange. Pre-eclamptic women lack this remodeling, obtaining, as a consequence, a reduced cardiac output with hemoconcentration. There is general agreement that plasma volume is reduced in these patients<sup>2</sup>.

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### Original Contribution

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The proper interpretation of hemodynamic data is predicated on knowledge of normal values during pregnancy and immediate postpartum. Alternatives to cardiac function monitoring, such as the oxygen saturation of mixed venous blood, have been reevaluated, which according to several studies are well correlated with the values of cardiac output<sup>3,4,5</sup>.

Transthoracic electrical bioimpedance (TEB) is a non invasive procedure to measure cardiac output<sup>6</sup>. This system monitors haemodynamic parameters using methods of impedance cardiography (ICG) and impedance plethysmography (IPG). The volume and velocity of blood in the aorta changes with each beat of the heart, this produces a change in the electrical resistance (impedance) of the thorax to electrical alternating current.

Despite the fact that TEB is a useful tool, when the pathophysiology of critically ill obstetric patients cannot be explained by noninvasive hemodynamic monitoring and the patient fails to respond to conservative medical management, invasive hemodynamic monitoring may be helpful in guiding treatment. Pulmonary artery catheterization has been used in the obstetric population, particularly in patients with severe pre-eclampsia associated with pulmonary edema and renal failure<sup>7</sup>. By using this approach, Hjertberg et al., used the Swan-Ganz Catheter to monitor 10 severe preeclamptic women<sup>8</sup>.

The objective of our study was to evaluate the blood pressure in pre-eclamptic and eclamptic women along seven days in the Obstetric Intensive Care Unit (OICU). We also wanted to establish a comparison between three methods to measure cardiac output in critically ill obstetric patients.

#### Methods

This was a descriptive, prospective clinical and longitudinal study. Women attended in the OICU of the Materno Perinatal Hospital "Monica Pretelini" (HMPMP) from January 2011 to July 2011. Patients were not included in this study if they were expected to have a short-term (<24 hours) intensive care hospitalization. Patient data, clinical information, and blood samples were collected prospectively.

*Two sets of patients were analyzed to cover different objectives:*

i) Evaluation of the major anti-hypertensive schemes used at the HMPMP: Women hospitalized at the OICU for at least seven days. Blood pressure was measured each hour and the anti-hypertensive drugs were registered, ii) Comparison of hemodynamic monitoring: Critical patients who were monitored with a Swan-Ganz Catheter and who results were compared to TEB and gasometric formulas.

#### *Anthropometric measures*

Height with a measuring tape and weight with an electric bed (Hill-Rom, Total Care), were uniformly recorded at the OICU. Blood pressure was measured with an electronic monitor (Infinity Delta XL, Dräger, USA.).

During each day of hospitalization, with a fasting period of eight hours blood samples were collected into Vacutainer tubes and centrifuged to separate serum from plasma. We measured albumin (mg/dl), cholesterol (mg/dl), creatinine (mg/dl), glucose (mg/dl), triglycerides (mg/dl), uric acid (mg/dl) (Dimension Rx L Max, Dade Behring) and hemoglobin (g/dl) (Advia 120, Bayer Health). All these tests were measured in the HMPMP according to standardized procedures recommended by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

#### *Hemodynamics*

Gasometric formulas: Gasometric analysis of arterial and venous samples were practiced in the Gem® Premier 3000 (Instrumentation Laboratory). The elected formulas were: i) Cardiac Output (CO) (L/min) =  $[(CF \times BSA) / \text{Dif a-v O}_2] / 10$ . CF: cardiac frequency in pulse per min, BSA: body surface area, Dif a-v O<sub>2</sub>: arterial-venous oxygen difference = CaO<sub>2</sub> - CvO<sub>2</sub>. CaO<sub>2</sub>: arterial oxygen concentration =  $[(1.34 \times Hb \times SaO_2) + (0.0031 \times PaO_2)] / 100$ , CvO<sub>2</sub>: venous oxygen concentration =  $[(1.34 \times Hb \times SvO_2) + (0.0031 \times PvO_2)] / 100$ . SaO<sub>2</sub>: arterial oxygen concentration, PaO<sub>2</sub>: partial pressure of arterial oxygen, SvO<sub>2</sub>: venous oxygen concentration, PvO<sub>2</sub>: partial pressure of venous oxygen, Hb: hemoglobin (g/dl). The value 1.39 represents the amount of oxygen in ml that can be delivered by one gram of hemoglobin, and 0.0031 is the solubility of oxygen in the plasma, ii) Cardiac Index (CI) (L/min/m<sup>2</sup>) = CO/BSA, iii)

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Oxygen delivery ( $DO_2$ ) ( $ml\ O_2/min$ ) =  $CO \times CaO_2 \times 10$ . iv) Systemic Vascular Resistance (SVR) ( $dynes \times s/cm^5$ ) =  $[(MAP-CVP)/CO] \times 80$ . MAP: Mean Arterial Pressure (mmHg), CVP: Central Venous Pressure, v) Systemic Vascular Resistance Index (SVRI) ( $dynes \times s/cm^5/m^2$ ) =  $[(MAP-CVP)/CI] \times 80$ , vi) Stroke Index (SI) ( $ml/m^2/beat$ ) =  $[(CO \times 1000)/CF]/BSA$ .

*TEB:* We used the non-invasive monitoring Niccom<sup>TM</sup> equipment (Medis, GmbH IImenou, Germany), that measures or calculates stroke volume and several other important hemodynamic parameters based on the change in impedance over time.

*Invasive monitoring:* Swan Ganz Catheter (Arrow International, Inc. USA.) was inserted in the pulmonary artery with the use of a C-arm fluoroscope (BV Pulsera, Phillips). Cardiac output was measured with the Infinity HemoMed (Dräger, Medical Systems, Inc. USA.). The values were showed in a monitor (Infinity Delta XL, Dräger, USA.).

Measures with the three alternatives (gasometric formulas, Niccom<sup>TM</sup> and Swan Ganz catheter) were practiced at the same time.

The present study was approved by the Ethical Committee of the HMPMP, conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Written informed

consent was obtained from the patient, her spouse, or the appointed legal guardian.

Statistical analysis was done using the Statistical Package for Social Science (SPSS) software, version 17 (SPSS Inc., Chicago, United States). Due to the skewed distribution of most of the parameters, data are given as media (range). Differences between two groups were assessed by Mann-Whitney-U-test.

**Results**

We included 15 severe preeclamptic and 6 eclamptic patients, age (media, range) of 29 (16-38) and 21.5 (16-36) respectively.

*Anti-hypertensive treatment*

In our work, as in others<sup>9</sup>, the different anti-hypertensive therapeutic options have been detailed, as well as the evolution for seven days (Figure 1). To treat pre-eclampsia the most common oral drugs were amlodipine (26%), telmisartan (22%), prazosin (12%), metoprolol (10%), furosemide (10%), nifedipine (7%), hydrochlorothiazide (7%), carvedilol (3%) and several other drugs with scarce percentage. Exact 90% of all patients received at least three drugs for at least 48 hours. The preferred antihypertensive drug combination was amlodipine + temisartan + prazosin in seven cases (46.6%). Sodium nitroprusside was used in 3 (20%) patients.

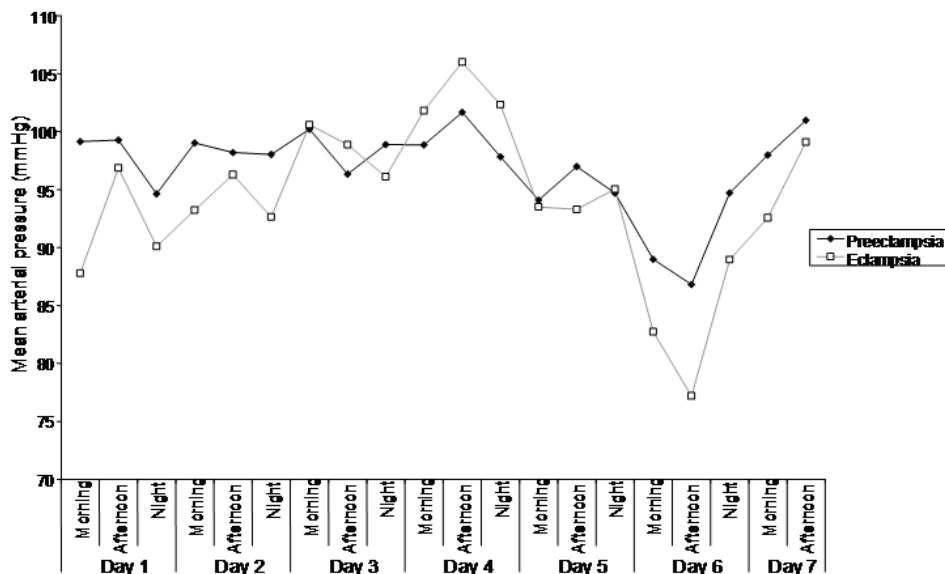


Figure 1: Evolution of different anti-hypertensive therapeutic options for seven days

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In eclampsia the most common oral drugs used were amlodipine, telmisartan and furosemide (22% each other), prazosin and carvedilol (11% each) and metoprolol and nifedipine (6% each).

In relation to the mean arterial pressure, there were no statistical differences within each group attributed to the workday (morning, afternoon, evening). The values were 96.7, 96.5 and 96.4 mmHg for pre-eclampsia and 93.2, 94.7 and 94.1 mmHg for eclampsia respectively.

#### *Hemodynamics*

Six patients required invasive hemodynamic monitoring, their anthropometric characteristics

(mean, range) were: age 33(18-39) years, weight 62.7(58.2-82.6) kg, body mass index (BMI) 25.4(23.1-33.9) kg/m<sup>2</sup>. The diagnosis of the patients, all in immediate puerperium were: case 1: severe craneo-encephalic trauma, left parieto-occipital parenchymal hemorrhage; case 2: eclampsia; case 3: hyperthyroidism; case 4: cardiac congestive failure, rheumatic valvulopathy, severe pre-eclampsia, acute pulmonary edema; case 5: septic shock, uterine perforation; case 6: sepsis, pneumonia, hyperthyroidism, superimposed pre-eclampsia in chronic hypertension.

Table I: Hemodynamic values

	Swan-Ganz	TEB	Gasometric formulas
Cardiac output (L/min)*	7.8 (4.8-10.9)	3.7 (1.6-4.6)	9 (2.9-11.1)
Cardiac index (L/min/m <sup>2</sup> )	-	2.3 (1-3.1)	5.1 (1.7-8.8)
DO <sup>2</sup> (ml O <sub>2</sub> /min)	-	430 (241-489)	687 (283-1222)
SVR (dynes×s/cm <sup>5</sup> )	-	1672 (1253-3627)	688 (452-2359)
SVRI (dynes×s/cm <sup>5</sup> /m <sup>2</sup> )	-	2819 (1674-5697)	1237 (568-3948)
SI (ml/m <sup>2</sup> /beat)	-	23.5 (13-32)	42.8 (24.4-85.1)

TEB: transthoracic electrical bioimpedance, DO<sub>2</sub>: oxygen delivery, SVR: systemic vascular resistance, SVRI: systemic vascular resistance index, SI: Stroke Index.

\*p<0.05

The hemodynamic variables are listed in Table I. In CO there was statistical significant difference between TEB and Swan-Ganz catheter, but not between Swan-Ganz and gasometric formulas.

#### **Discussion**

Obstetric management of severe pre-eclampsia focuses on medical management of blood pressure and prevention of seizures using magnesium sulphate, but the ultimate cure remains delivery of the fetus and placenta<sup>10</sup>.

We conclude that the combination of amlodipine + telmisartan + prazosin is highly used in our hospital and offers good results. Another observation was that the blood pressure increase cannot be considered as a prelude to eclampsia.

The blood pressure control in pre-eclampsia/eclampsia must be intensive irrespective of the drug election as the benefit to impede potential complications (cerebrovascular disease) are greater than the risk of the drugs by themselves,

even more, as we know that the pregnant preeclamptic woman only has as a treatment the gestational interruption and the damage for the fetus due to oral drugs is minimum.

Reported central hemodynamics obtained with a Swan-Ganz pulmonary artery thermodilution catheter in pre-eclamptic patients show marked disparity, which has been interpreted to indicate a variable hemodynamic expression of the disease. However, the variability also may be due, at least in part, to the pharmacological treatment that most of the women studied received during Swan-Ganz measurements<sup>11</sup>. We wanted to determine the clinical usefulness of invasive and non-invasive hemodynamic assessment in pre-eclampsia. Previous published data are available illustrating

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the correlation between echocardiographic techniques and pulmonary artery catheterization<sup>12</sup>. Cardiac output measurements by thermodilution and TEB have been compared in several studies with varying results<sup>13,14</sup>. Also, several formulas have been compared to evaluate the hemodynamic state in critically ill patients<sup>15,16,17,18</sup>. In our study the gasometric formulas were more approached to the Swan-Ganz measures than the impedance study, with the latter method the values are underestimated by a factor of approximately 2.5. It is important to note that the more narrow the SO<sub>2</sub> difference between arterial and venous gasometries, the accurate of the hemodynamic parameters by gasometric formulas is poorer. We did not evaluate electric transesophageic bioimpedance that seems to be superior to other options of hemodynamic monitoring.

#### Conclusion

In obstetric critically ill patients, the hypertension is a hard to control problem, requiring high doses of several drugs, including I.V. sodium nitroprusside all of which have to be administered to avoid a cerebrovascular damage. Hemodynamic formulas based on gasometric results are still useful to evaluate the hemodynamic state of puerperal women, being a valuable tool to take therapeutic decisions. When using bioimpedance equipment we must consider an adjustment for puerperal women due to the water retention.

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