Central Hemodynamic Observations in Untreated Preeclamptic Patients

Willy Visser and Henk C.S. Wallenburg

Reported central hemodynamics obtained with a Swan-Ganz pulmonary artery thermodilution catheter in preeclamptic 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. To evaluate the effects of treatment on hemodynamics, we compared the results of Swan-Ganz measurements in 87 preeclamptic women who had received no treatment at all with those obtained in 47 preeclamptic women who had received various drugs and intravenous fluids. Control values were obtained in 10 normotensive pregnant volunteers. Measurements were performed between 25 and 34 weeks of gestation. The median (range) cardiac index in the untreated patients of 3.3 (2.0–5.3) l·min⁻¹·m⁻² was significantly lower than that in the treated patients of 4.3 (2.4–7.6) l·min⁻¹·m⁻² and in the normotensive pregnant women of 4.2 (3.5–4.6) l·min⁻¹·m⁻². The systemic vascular resistance index in the untreated group of 3,003 (1,771–5,225) dyn·sec·cm⁻²·m⁻² was significantly higher than that of 2,212 (1,057–3,688) in the treated and of 1,560 (1,430–2,019) dyn·sec·cm⁻²·m⁻² in the normotensive control group. The median (range) pulmonary capillary wedge pressure in the untreated group was 7 (1–20) mm Hg and did not differ from that of 7 (0–25) mm Hg in the treated group. Variability of all hemodynamic variables was much lower in untreated than in treated patients. These results indicate that untreated preeclamptic patients show a rather uniform pattern of a low cardiac index, a high systemic vascular resistance index, and normal filling pressures. The reported extremes of the hemodynamic profile in preeclampsia are artifacts due to treatment. (Hypertension 1991;17:1072–1077)

Over the past 10 years, at least eight reports have been published in the English literature on the results of central hemodynamic measurements obtained in preeclamptic patients with the flow-directed, thermistor-tipped Swan-Ganz pulmonary artery catheter.¹⁻⁸ The reports show marked disparity with regard to cardiac output, peripheral vascular resistance, and left ventricular filling pressures, with values covering a wide spectrum between the extremes of a high-output, low-resistance and a low-output, high-resistance hemodynamic state. The observed hemodynamic variability usually is attributed to a variable pathophysiological expression of the pregnancy-induced hypertensive disorder.¹⁻⁴,⁶⁻⁷

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Supported in part by grant 28-1133 from the Dutch Praveentiefonds.

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Close examination reveals that, with a single exception,⁵ all studies were carried out during or after pharmacological treatment consisting of magnesium sulfate, antihypertensive medication, and intravenous fluids. In addition, variables that may modulate the hemodynamic state—such as parity; labor; underlying cardiac, renal, or hypertensive disease; and the severity of the hypertensive disorder—were not taken into account in the majority of published studies.

The present study was done to test the hypothesis that the reported hemodynamic variability in preeclampsia mainly is secondary to treatment rather than reflecting a variable pathophysiological state. We compared the results of central hemodynamic measurements in patients with untreated severe antepartum preeclampsia in the second or early third trimester of pregnancy with those obtained in patients with preeclampsia of similar severity in the same gestational period who already had received pharmacological treatment.

Methods

Selection of Patients

A group of 134 consecutive pregnant patients with severe preeclampsia was studied. All patients were
managed between 1985 and 1990 at the University Hospital Rotterdam Dijkzigt and all met the following inclusion criteria: 1) gestational age less than 34 weeks, 2) singleton pregnancy with a live fetus, 3) no obstetric indication for immediate delivery, 4) unrestricted diet, 5) not in labor, 6) no signs of pulmonary edema, and 7) no known preexisting hypertensive, cardiac, or renal disease. Severe preeclampsia was defined as the occurrence of a diastolic blood pressure of 100 mm Hg or more on two occasions at least 4 hours apart and proteinuria of 0.5 g/l or more. All patients developed preeclampsia after the 20th week of gestation and became normotensive and nonproteinuric after delivery.

Before the start of hemodynamic investigations, patients who had not received any kind of pharmacological treatment, including parenteral administration of fluids, were labeled untreated. Patients who already had received intravenous fluids or any kind of antihypertensive or anticonvulsive treatment were labeled treated. The study protocol as approved by the University and Hospital Ethics Committee was explained in detail, and informed consent was obtained in all cases.

**Catheterization Procedures**

A normal baseline electrocardiogram was obtained from all patients. A 7F triple-lumen Swan-Ganz catheter was inserted percutaneously through an 8F introducer placed in a median basilic vein. The catheter was advanced under continuous electrocardiographic and oscillographic pressure waveform monitoring. The correct position of the catheter tip was confirmed by a single chest radiograph. A radial artery was cannulated with a 2-inch, 20-gauge catheter for intra-arterial blood pressure measurement. The catheterizations were performed without the use of analgesics or sedatives. All patients received intravenous heparin at a rate of 10,000 IU per 24 hours as long as the catheters were in place.

**Hemodynamic Measurements**

Pressures were measured with appropriate disposable strain-gauge pressure transducers (model UTAH, Baxter Healthcare Corp., Bentley Laboratories Europe, Uden, The Netherlands), with zero reference 5 cm below the third intercostal space; transducers were rezeroed after each change of position. Heart rate and systemic and pulmonary arterial pressures were monitored continuously with a multichannel scope (model 78354A, Hewlett-Packard, Böblingen, FRG). Measurements were begun at least 1 hour, usually longer, after catheterization, when heart rate and systemic arterial blood pressure had reached a steady state. Cardiac output was determined by means of the thermodilution method using a cardiac output analog computer (Edwards Laboratories, Irvine, Calif.). For each measurement, 10 ml of a chilled (5–7°C) 5% dextrose solution was injected with a closed injectate delivery system (model 93-5002, Baxter Healthcare, Edwards Critical Care Div., Santa Ana, Calif.). Cardiac output measurements were performed in triplicate at end expiration, and the arithmetic mean was taken as the final value. Pulmonary capillary wedge pressure was measured at end expiration. Right atrial and pulmonary pressures were determined with the patient in a supine position; cardiac output was determined with the patient in a supine and in a left lateral position.

**Study Protocol**

At least four measurements of cardiac output and pulmonary capillary wedge pressure were performed in each patient, and the arithmetic mean was taken as the representative value of each hemodynamic variable. Patients were pharmacologically treated or delivered after the hemodynamic measurements. The Swan-Ganz catheter was removed within 72 hours of insertion in all cases.

**Data Analysis**

All hemodynamic variables are expressed in centimeter gram second (metric) units, except for blood pressures, which are presented in millimeters of mercury. Resistances and indexes of left ventricular stroke work were calculated as described previously. Body surface area was calculated from the Dubois body surface area chart with the use of the actual height and weight of the patient. Data are presented as median and range, unless otherwise stated. Differences were statistically analyzed with the Wilcoxon test, and the significance of correlations was tested with the Spearman test. A value of p < 0.05 was taken as the level of significance.

**Results**

Right ventricular catheterization was successful and uncomplicated in all patients.

**Clinical Characteristics**

Clinical characteristics of the 134 preeclamptic patients included in the study are summarized in Table 1. The majority of the 47 treated patients were maternal transfers from other hospitals who had received dihydralazine, magnesium sulfate, diazepam, or a variety of other drugs and intravenous fluids. There were no significant differences between groups with regard to any of the maternal characteristics, gestational age, or severity of the hypertensive disorder. Also presented in Table 1 are the clinical characteristics of 10 normotensive parous women with uncomplicated pregnancies from whom reference values for central hemodynamic variables were obtained by means of pulmonary artery catheterization as part of an ongoing and as yet unpublished study. Maternal variables and gestational age in these normotensive pregnant women were comparable with those in the preeclamptic patients.

**Hemodynamic Findings**

The hemodynamic findings in untreated and treated preeclamptic patients are shown in Table 2.
TABLE 1. Clinical Characteristics of 134 Preeclamptic Patients and 10 Normotensive Pregnant Women at Measurement of Central Hemodynamics

<table>
<thead>
<tr>
<th></th>
<th>Preeclamptic untreated</th>
<th>Preeclamptic treated</th>
<th>Normotensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>26 (18-42)</td>
<td>26 (19-41)</td>
<td>30 (24-37)</td>
</tr>
<tr>
<td>Gestational age (wk)</td>
<td>30.4 (25.3-33.6)</td>
<td>29.1 (26.1-33.9)</td>
<td>28.9 (28.0-30.4)*</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>31.3 (25.1-33.9)</td>
<td>1.77 (1.55-2.20)</td>
<td>1.85 (1.54-2.05)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>110 (100-140)</td>
<td>1.86 (1.57-2.03)</td>
<td>115 (100-150)</td>
</tr>
<tr>
<td>Proteinuria (g/l²)</td>
<td>3.0 (0.5-25.3)</td>
<td>3.0 (0.5-39.3)</td>
<td>3.8 (0.5-23.1)</td>
</tr>
</tbody>
</table>

Values given are median (range).
*p<0.05 vs. untreated parous patients.
†p<0.05 vs. preeclamptic patients.

There were no differences between cardiac output values measured with patients in a supine and left lateral position. There was no significant difference in hemodynamic variables within groups between nulliparous and parous patients, except for the median stroke volume index, which was 27% lower in parous than in nulliparous untreated patients. We found no significant correlations between arterial pressures and cardiac index. Comparison between treated and untreated preeclamptic women showed a significantly lower cardiac index and stroke volume index and a higher systemic vascular resistance index in untreated patients. Also, pulmonary vascular resistance was higher in untreated than in treated patients, although the difference between parous patients did not reach significance. Left ventricular filling pressures were not different between groups.

Hemodynamic reference values obtained in our study in 10 normotensive parous women with an uncomplicated pregnancy between 28 and 31 weeks duration are shown in Table 3 in comparison with the hemodynamic variables observed in untreated and treated preeclamptic patients. In untreated preeclamptic patients, cardiac index and heart rate are significantly lower, and systemic and pulmonary vascular resistance was higher in untreated than in treated patients, although the difference between parous patients did not reach significance. Left ventricular filling pressures were not different between groups.

TABLE 2. Hemodynamic Profile in Untreated and Treated Patients With Severe Preeclampsia

<table>
<thead>
<tr>
<th></th>
<th>Untreated</th>
<th>Parous</th>
<th>Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nulliparous (n=74)</td>
<td>Parous (n=13)</td>
<td>Nulliparous (n=32)</td>
</tr>
<tr>
<td>Systemic circulation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min⁻¹)</td>
<td>74 (57-110)</td>
<td>78 (51-95)</td>
<td>84 (64-131)*</td>
</tr>
<tr>
<td>Mean intra-arterial pressure (mm Hg)</td>
<td>125 (92-156)</td>
<td>123 (96-143)</td>
<td>120 (80-138)*</td>
</tr>
<tr>
<td>Cardiac index (l/min⁻¹·m²)</td>
<td>3.4 (2.1-5.3)</td>
<td>3.1 (2.0-4.2)</td>
<td>4.3 (3.0-7.6)*</td>
</tr>
<tr>
<td>Stroke volume index (m³·beat⁻¹·m⁻²)</td>
<td>48 (25-75)</td>
<td>&lt;0.05</td>
<td>35 (29-56)</td>
</tr>
<tr>
<td>Systemic vascular resistance index (dyne·sec·cm⁻²·m³)</td>
<td>2,951 (1,771-5,225)</td>
<td>3,331 (1,827-4,753)</td>
<td>2,162 (1,057-3,325)*</td>
</tr>
<tr>
<td>Left ventricular stroke work index (J·beat⁻¹·m⁻²)</td>
<td>0.71 (0.40-1.16)</td>
<td>0.63 (0.45-0.85)</td>
<td>0.81 (0.48-1.27)</td>
</tr>
<tr>
<td>Pulmonary circulation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean pulmonary arterial pressure (mm Hg)</td>
<td>12 (3-26)</td>
<td>12 (3-18)</td>
<td>13 (5-29)</td>
</tr>
<tr>
<td>Pulmonary capillary wedge pressure (mm Hg)</td>
<td>7 (–1-20)</td>
<td>5 (0-13)</td>
<td>7 (1-20)</td>
</tr>
<tr>
<td>Right atrial pressure (mm Hg)</td>
<td>2 (–4-10)</td>
<td>1 (–3-6)</td>
<td>1 (–3-12)</td>
</tr>
<tr>
<td>Pulmonary vascular resistance index (dyne·sec·cm⁻³·m²)</td>
<td>130 (47-278)</td>
<td>153 (48-379)</td>
<td>99 (29-181)*</td>
</tr>
<tr>
<td>Right ventricular stroke work index (J·beat⁻¹·m⁻²)</td>
<td>0.06 (0.01-0.20)</td>
<td>0.05 (0.01-0.10)</td>
<td>0.08 (0.03-0.22)*</td>
</tr>
</tbody>
</table>

Values given are median (range).
*p<0.05 vs. untreated nulliparous patients.
†p<0.05 vs. untreated parous patients.
TABLE 3. Hemodynamic Profile in Untreated and Treated Preeclamptic Patients and Normotensive Pregnant Women

<table>
<thead>
<tr>
<th>Systemic circulation</th>
<th>Preeclamptics, untreated (n=87)</th>
<th>ρ*</th>
<th>Normotensive controls (n=10)</th>
<th>ρ†</th>
<th>Preeclamptics, treated (n=47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats·min⁻¹)</td>
<td>74 (51–110)</td>
<td>&lt;0.05</td>
<td>82 (68–93)</td>
<td>NS</td>
<td>85 (62–135)‡</td>
</tr>
<tr>
<td>Mean intra-arterial pressure (mm Hg)</td>
<td>125 (92–156)</td>
<td>&lt;0.001</td>
<td>83 (81–29)</td>
<td>&lt;0.001</td>
<td>120 (80–154)‡</td>
</tr>
<tr>
<td>Cardiac index (l·min⁻¹·m⁻²)</td>
<td>3.3 (2.0–5.3)</td>
<td>&lt;0.001</td>
<td>4.2 (3.5–4.6)</td>
<td>NS</td>
<td>4.3 (2.4–7.6)‡</td>
</tr>
<tr>
<td>Stroke volume index (ml·beat⁻¹·m⁻²)</td>
<td>46 (25–75)</td>
<td>NS</td>
<td>51 (38–61)</td>
<td>NS</td>
<td>52 (32–82)‡</td>
</tr>
<tr>
<td>Systemic vascular resistance index (dyne·sec·cm⁻²·m⁻²)</td>
<td>3,003 (1,771–5,225)</td>
<td>&lt;0.001</td>
<td>1,560 (1,430–2,019)</td>
<td>&lt;0.005</td>
<td>2,212 (1,057–3,688)‡</td>
</tr>
<tr>
<td>Left ventricular stroke work index (J·beat⁻¹·m⁻²)</td>
<td>0.70 (0.40–1.16)</td>
<td>&lt;0.005</td>
<td>0.54 (0.43–0.64)</td>
<td>&lt;0.001</td>
<td>0.79 (0.48–1.27)</td>
</tr>
</tbody>
</table>

| Pulmonary circulation | Mean pulmonary arterial pressure (mm Hg) | 12 (3–26) | <0.05 | 9 (7–13) | <0.01 | 13 (0.5–30) |
| Pulmonary capillary wedge pressure (mm Hg) | 7 (–1–20) | NS | 5 (1–8) | <0.05 | 7 (0–25) |
| Right atrial pressure (mm Hg) | 2 (–4–10) | NS | 1 (0–2) | NS | 1 (–3–12) |
| Pulmonary vascular resistance index (dyne·sec·cm⁻⁵·m⁻²) | 131 (47–379) | <0.005 | 91 (63–128) | NS | 101 (8–317)‡ |
| Right ventricular stroke work index (J·beat⁻¹·m⁻²) | 0.06 (0.01–0.20) | NS | 0.05 (0.04–0.08) | <0.05 | 0.08 (0.01–0.22)‡ |

Values given are median (range)

*Differences between untreated preeclamptic patients and normotensive controls.
†Differences between pharmacologically treated preeclamptic patients and normotensive controls
‡p<0.05 vs untreated nulliparous patients.

Discussion

To the best of our knowledge this is the first study, after preliminary data published by our group, that assessed central hemodynamics measured with a Swan-Ganz catheter in completely untreated nulliparous and parous preeclamptic patients who developed what may be most likely defined as "pure preeclampsia." Chronic hypertension may have a marked influence on central hemodynamics, but we excluded such women in the selection of our patient population. Because it has been shown, particularly in parous women with preeclampsia, that there is often an unsuspected underlying hypertensive or renal disease, only patients who became normotensive and nonproteinuric after delivery were included in our study.

The absence of labor is a prerequisite for the assessment of the true pathophysiological hemodynamic state in preeclamptic patients. Uterine contractions are known to cause marked hemodynamic changes, most likely because of the autotransfusion effect of blood squeezed out of the contracting uterus. Indeed, hemodynamic studies in preeclamptic patients have shown a dramatic rise in cardiac output and in systemic and pulmonary blood pressures during labor and delivery. Therefore, patients who were in labor also were excluded.

Because the technique used for measuring central hemodynamics also could be an important variable, we will compare our results only with those obtained in other studies that used a Swan-Ganz catheter.

Parity and Position

Our results show that parity has no demonstrable effect on hemodynamic findings. It therefore is unlikely that heterogeneity with regard to parity is an important factor underlying the reported hemodynamic disparity in preeclampsia. We found no significant differences between cardiac output measured with patients in a supine or left lateral position. This...
Scatterplots showing left ventricular stroke work index (LVSWI) in 87 untreated (panel A) and 47 treated (panel B) preeclamptic patients plotted against pulmonary capillary wedge pressure (PCWP). Boundaries of normal nonpregnant left ventricular function are modified from Ross and Braunwald.

Figure 1.

Pharmacological Treatment

In contrast to the rather uniform pattern of a low cardiac index and a high systemic vascular resistance in untreated preeclamptic patients, we found a wide range of hemodynamic values in treated preeclamptic women, with even extremely high cardiac indexes and low systemic resistances in these patients. The different hemodynamic profile in treated and untreated patients also is clearly demonstrated in the left ventricular Starling plot. Because patients in both groups were similar with regard to clinical characteristics and severity of the preeclamptic state, the differences in hemodynamic profile most likely could be attributed to the administration of drugs and intravenous fluids in the treated group, whereas the untreated patients received no more than 20–30 ml
saline for insertion and flushing of the catheters. All preeclamptic women reported in previous hemodynamic studies, except one, had received and were receiving intravenous magnesium sulfate, a drug known to increase cardiac output to a marked but variable extent. In addition to the use of antihypertensive drugs, this may explain a large part of the reported hemodynamic variability and tendency to a high cardiac output in preeclamptic patients.

Some authors suggest that cardiac output may increase in the beginning of the development of preeclampsia and could fall with increasing severity of the disease. Our findings do not support that hypothesis. First, we found no correlation between the height of the diastolic blood pressure and the cardiac index. Second, diastolic blood pressures and the amount of proteinuria in our patients are similar to those reported in the literature in preeclamptic patients with high cardiac outputs.

Hemodynamic Pathophysiology in Preeclampsia

From our hemodynamic observations in untreated patients, we conclude that severe preeclampsia is hemodynamically characterized by a low cardiac output in the presence of an increased left ventricular afterload. Although untreated preeclamptic patients also show some variability in the hemodynamic expression of the disease, the reported extremes of the hemodynamic profile appear to reflect clinical management rather than the pathophysiological state.

There is general agreement that plasma volume is reduced in these patients, but we found no evidence of a significant reduction in cardiac preload. This may be explained in part by the relative insensitivity of our hemodynamic measurements. On the other hand, a reduced vascular capacitance due to venoconstriction with redistribution of intravascular volume from the splanchnic to the peripheral vascular bed cannot be excluded.

Acknowledgments

We thank Marieke W. de Jong, Jos Schot, Pict Struikj, and the nursing staff of the Intensive Care Departments, in particular 6-N, for excellent technical assistance.

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KEY WORDS - hemodynamics - preeclampsia - thermodilution • cardiac output • central venous pressure • pulmonary artery • pulmonary wedge pressure • vascular resistance
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_Hypertension_. 1991;17:1072-1077
doi: 10.1161/01.HYP.17.6.1072

_Hypertension_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1991 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

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