Anesthesiology
68:433–434, 1988

Effect of Preeclampsia on Carboxyhemoglobin Levels: A Mechanism for a Decrease in P_{50}

J. Reddy Kambam, M.D., Stephen Entman, M.D.,† Stephanie Mouton, M.D.,* Bradley E. Smith, M.D.‡*

COHb levels were measured in 15 preeclamptic pregnant women and 15 normal pregnant women to investigate the cause for the decrease in P_{50} associated with preeclampsia. The authors also included six normal and six preeclamptic pregnant patients from the above groups in the determination of P_{50}. Measurements of COHb levels were performed in a Radiometer OSM2 Hemoximeter®. Determination of P_{50} was done using an IL 237 Tonometer, a Radiometer, OSM2 Hemoximeter®, and a Corning® 168 pH/Blood Gas Analyzer. Preeclamptic pregnant patients had a mean COHb level of 2.8%, whereas normal pregnant women had a mean COHb level of 0.7% ($P < 0.001$). Preeclamptic patients also had a significantly lower (24.4 mmHg) P_{50} than normal pregnant women (P_{50} = 30.1 mmHg) ($P < 0.001$). The authors conclude that a significant elevation of COHb in preeclamptic pregnant women is partly responsible for a significant decrease in P_{50} seen in preeclampsia. (Key words: Hemoglobin, carboxy. Oxygen: oxyhemoglobin dissociation; P_{50}. Pregnancy: normal; preeclampsia; preeclamptic.)

WE HAVE PREVIOUSLY reported that preeclampsia (pregnancy-induced hypertension with proteinuria, edema, or both after 20 weeks gestation) is associated with a decrease in P_{50}.[1] It has also been shown that normal pregnancy is associated with an increase in P_{50}.[1–3] The mechanisms responsible for these changes in P_{50} in both normal and preeclamptic pregnancies have not been elucidated. However, recent studies suggest that there is increased red cell destruction, both intravascularly and extravascularly, in preeclampsia.[4,5] Evidence also suggests that endogenous production of carbon monoxide is elevated with increased heme catabolism,[6,7] and that an increase in carboxyhemoglobin levels causes a leftward shift in oxyhemoglobin dissociation curve.[8,9] Therefore, we undertook this study to examine the effect of preeclampsia on both COHb and P_{50}.

Materials and Methods

With prior approval from our Institutional Review Board for the Protection of Human Subjects, we measured COHb levels in 15 normal pregnant women (ages 18–40 yr) and 15 preeclamptic pregnant women (ages 18–38 yr) at or near term. We also determined P_{50} in the first six patients from each of the above groups of pregnant women. All the pregnant women included in this study were non-smokers. Five milliliters of venous blood was collected into a heparinized syringe from each of the informed volunteer patients. Of this blood, 100 μl was used in the measurement of COHb levels. We used a Radiometer, OSM2 Hemoximeter®, and deoxygenation capillary kit (Radiometer) in the measurement of COHb levels.

P_{50} Determination

After the COHb measurements, the remaining blood from six normal and six preeclamptic pregnant women was immediately subjected to closed tonometry in an IL 237 tonometer with gas mixtures containing 3.5% or 4.5% oxygen, 5.6% carbon dioxide, and balance nitrogen at 37° C for 15 min. Closed tonometry was performed to avoid the escape of carbon monoxide from the blood sample. There is evidence showing that open tonometry is associated with variable loss of carbon monoxide.[10] Results from our own laboratory also showed that, with open tonometry, there was more than 50% loss of carbon monoxide from the blood of preeclamptic patients. The mean (±SD) COHb levels before and after open tonometry were 2.5 ± 0.5% and 0.99 ± 0.1%, respectively; whereas, with closed tonometry, there was no decrease in COHb levels (before tonometry, 2.5 ± 0.5%; and after tonometry, 2.5 ± 0.4%). At the end of each tonometry, total hemoglobin, per cent COHb, and per cent oxygen saturation were measured in a Radiometer, OSM2 Hemoximeter. Simultaneously, blood gases were measured in a Corning 168 *p*H/blood gas analyzer. The measured P_{O_2} data were corrected to a *p*H of 7.40. A two-point saturation curve was plotted in the steep portion of the oxyhemoglobin dissociation curve, and P_{50} was obtained from the saturation curve. The Radiometer, OSM2 Hemoximeter, and the Corning 168 *p*H/blood gas analyzer were calibrated before each measurement.

The data were analyzed for statistical significance of difference by using a Student's *t* test (two-tailed *P*). A difference was considered significant if $P < 0.05$.

Results

There is a significant elevation of COHb levels in preeclamptic pregnant patients when compared to nor-

* Assistant Professor of Anesthesiology.
† Associate Professor of Obstetrics and Gynecology.
‡ Professor of Anesthesiology.

Received from the Departments of Anesthesiology and Obstetrics and Gynecology, Vanderbilt University School of Medicine, Nashville, Tennessee. Accepted for publication October 8, 1987. Supported by the Study Center for Anesthesia Toxicology of the Department of Anesthesiology of Vanderbilt University School of Medicine. Presented at the Annual Meeting, American Society of Anesthesiologists, Las Vegas, Nevada, October, 1986.

Address reprint requests to Dr. Kambam: Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee 37232.

TABLE 1. Effect of Normal and Preeclamptic Pregnancies on COHb and P_{50} Values

Subjects	COHb, %*		P_{50}, mmHg*	
	Mean ± SD	n	Mean ± SD	n
Normal Pregnant	0.7 ± 0.2	15	30.1 ± 0.14	6
Preeclamptic Pregnant	2.8 ± 0.7	15	24.4 ± 0.15	6

* Significance of difference between normal and preeclamptic pregnant women ($P < 0.001$), Student's *t* test, two-tailed *P*.

mal pregnant women (table 1) ($P < 0.001$). There is also a significant decrease in P_{50} in preeclamptic parturients when compared to normal parturients (fig. 1, table 1) ($P < 0.001$). There is no significant difference in paired COHb levels before and after closed tonometry. The mean COHb levels in the blood of six normal pregnant women before and after closed tonometry were 0.8 + 0.2% and 0.8 + 0.2%, respectively. Six preeclamptic pregnant patients had COHb levels of 2.5 + 0.6% and 2.5 + 0.5% before and after tonometry, respectively.

Discussion

Increased concentration of COHb has a direct effect on oxyhemoglobin causing a decrease in P_{50}.[8] COHb also has an inhibitory effect in the production of 2,3-DPG in red blood cells.[8] Catabolism of circulating red blood cells accounts for approximately 60% of the endogenous carbon monoxide.[11] The endogenous production of carbon monoxide occurs predominantly *via* the heme catabolic pathway, in which heme is broken down to equimolar amounts of bilirubin, iron, and carbon monoxide.

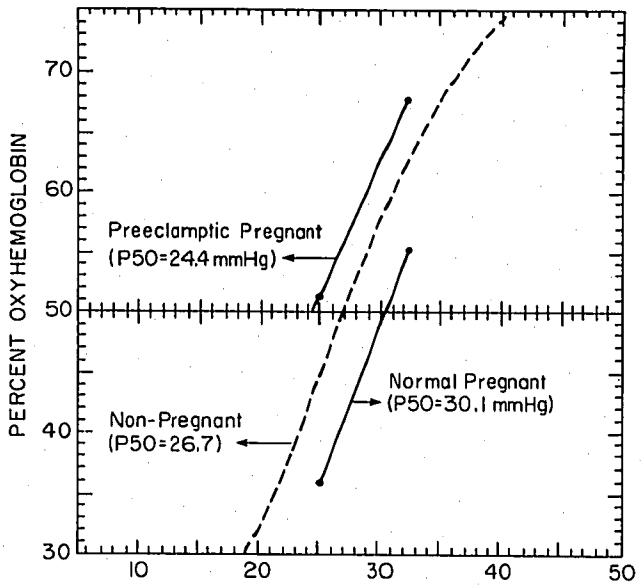

FIG. 1. Effect of normal and preeclamptic pregnancies on P_{50}. Only steep portions of oxyhemoglobin dissociation curves were shown for normal pregnant and preeclamptic pregnant women. The standard deviations were included in the text.

Our present data on COHb levels contradict the values we have reported previously.[1] The main reason for this discrepancy is due to the marked difference in the techniques we used in the measurement of COHb levels. In the previous report, we measured COHb levels after the blood sample was subjected to open tonometry with 400–500 ml flow of gas mixture. In this report, we measured the COHb levels before the blood samples were subjected to closed tonometry, and also at the end of closed tonometry.

Our results confirm that normal pregnancy is associated with an increase in P_{50}, and preeclamptic pregnancy is associated with a decrease in P_{50}. Our present data also demonstrate that there is a significant elevation of COHb levels in the blood of preeclamptic pregnant patients, and that the increased levels of COHb are partly responsible for the decrease in P_{50} in preeclamptic pregnant women.

References

1. Kambam JR, Handte RE, Brown WU, Smith BE: Effect of normal and preeclamptic pregnancies on oxyhemoglobin dissociation. ANESTHESIOLOGY 65:426–427, 1986
2. Bauer C, Ludwig M, Ludwig I, Bartels H: Factors governing the oxygen affinity of human adult and fetal blood. Respir Physiol 7:271–276, 1969
3. Darling RC, Smith CA, Asmussen E: Some properties of human fetal and maternal blood. J Clin Invest 20:739–747, 1941
4. Peck TM, Arias F: Hematological changes associated with pregnancy. Clin Obstet Gynecol 22:791–792, 1979
5. Entman S, Richardson LD, Killam AP: Altered ferrokinetics in toxemia of pregnancy. A possible indicator of decreased red cell survival. Clin Exper Hypertens[A] B2:171–178, 1983
6. Coburn RF, Williams WJ, Kahn SB: Endogenous carbon monoxide production in patients with hemolytic anemia. J Clin Invest 45:460–468, 1966
7. White P, Coburn RF, Williams WJ: Carbon monoxide production associated with ineffective erythropoiesis. J Clin Invest 46:1986–1988, 1966
8. Roughton FJW, Darling RC: The effect of carbon monoxide on the oxyhemoglobin dissociation curve. Am J Physiol 141:17–20, 1944
9. Kambam JR, Chen LH, Hyman SA: Effect of short-term smoking halt on carboxyhemoglobin levels and P_{50} values. Anesth Analg 65:1186–1188, 1986
10. Ledwith JW: Determining P_{50} in the presence of carboxyhemoglobin. J Appl Physiol 44:317–321, 1987
11. Logue GL, Rosse W, Smith WT: Endogenous carbon monoxide production. J Lab Clin Med 77:867–876, 1971