

Correlation between Bleeding Times and Platelet Counts in Women with Preeclampsia Undergoing Cesarean Section

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Platelet count and bleeding time and the correlation between these two variables in women with preeclampsia who received epidural or general anesthesia for cesarean section were evaluated. The study included 106 women with preeclampsia who were undergoing cesarean section and 94 healthy, term parturients receiving epidural anesthesia for labor analgesia or for cesarean section. Platelet counts were measured using an automated Coulter Counter, and bleeding times were measured using the modified Ivy bleeding time technique. Platelet count was significantly lower and bleeding time significantly prolonged in patients with preeclampsia compared with the control group ($P < 0.0001$). In the preeclampsia group, eight patients (7.5%) had thrombocytopenia (platelet count $< 100,000/\text{mm}^3$), whereas in the control group, all women had a normal platelet count ($> 150,000/\text{mm}^3$). All but one patient with thrombocytopenia had prolonged bleeding time. In addition, 34% of those women with severe preeclampsia and 13% with mild preeclampsia had prolonged bleeding time, although their platelet count was adequate. In the control group, 2% had abnormal bleeding time in the presence of a normal platelet count. There was good correlation between bleeding time and platelet count only when platelet count was lower than $100,000/\text{mm}^3$ ($r = -0.76$, $P < -0.02$). (Key words: Anesthesia: obstetrics; preeclampsia. Blood, coagulation: bleeding time; platelet dysfunction.)

WOMEN WITH PREECLAMPSIA frequently require cesarean section, and epidural anesthesia has emerged as an alternative to general anesthesia. However, epidural anesthesia is generally contraindicated in the presence of coagulopathy.¹ Thrombocytopenia occurs in approximately 18% of women with preeclampsia,² and this incidence may be as high as 50% in those with severe preeclampsia and eclampsia.³

In addition, a study by Kelton *et al.*⁴ indicated that although platelet count may be in the acceptable range, a functional abnormality of platelets in the form of prolonged bleeding time may exist in some women with preeclampsia. This platelet function abnormality, along with decreased platelet count, may be one of the end-organ manifestations of preeclampsia, and may constitute an additional risk to patients with preeclampsia receiving regional anesthesia. However, the relationship of the functional platelet abnormalities as evidenced by prolonged bleeding time to absolute platelet count has not been

clearly defined in women with preeclampsia who require anesthetic intervention for cesarean section.

We therefore studied bleeding time, platelet count, and the relationship between these two variables in a large group of patients with preeclampsia undergoing cesarean section under epidural or general anesthesia. For comparison, we also studied a group of normal, healthy, term parturients requesting epidural anesthesia for labor analgesia or for cesarean section.

Methods

The study included 106 women with preeclampsia undergoing cesarean section under epidural or general anesthesia. The study period extended from January, 1986, to July, 1988. A group of 94 healthy, term parturients receiving epidural anesthesia for labor analgesia or for cesarean section were included as a control group. In the preeclampsia group, 80 patients had mild preeclampsia with systolic pressure above 140 mmHg, diastolic pressure above 90 mmHg, proteinuria of > 0.3 g/l (1+ or 2+ by the urine dipstick measurement), and nondependent edema. Twenty-six patients had severe preeclampsia as evidenced by one or more of the following symptoms: systolic pressure above 160 mmHg, diastolic pressure above 110 mmHg, or proteinuria of 5 g/24h (3+ or 4+). The study was approved by the Institutional Review Board and informed consent was obtained from all patients. Patients with a history of bleeding disorders, significant hepatic or renal impairment, vascular disorders, or intake of aspirin or aspirin-containing drugs within the previous week, were excluded from the study.

In addition to routine laboratory tests upon admission, blood samples were obtained for platelet counts measured by the automatic Coulter Counter. Bleeding time was measured by modified Ivy bleeding time technique using a Surgicutt® device (International Technidyne Corporation), similar to a Simplate® device (General Diagnostic) but fully automatic. When the Surgicutt device is activated, a surgical steel blade housed in a plastic unit protrudes, makes a uniform incision 1 mm deep and 5 mm long. The main difference between the Simplate and Surgicutt is that after making the incision, the Surgicutt blade automatically retracts into the unit, thus eliminating variables of how long the device was applied to the skin and when it was removed. Prior to the incision, a sphygmomanometer cuff was applied to the arm and inflated to 40 mmHg, and the skin incision was made on the volar

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TABLE 1. Patient Characteristics (Mean ± SD)

	Preeclampsia (n = 106)	Control (n = 94)
Age (yr)	23.6 ± 6.5	23 ± 4.8
Height (cm)	160 ± 6.2	162 ± 4.2
Weight (kg)	79.6 ± 20.4	72.2 ± 14.6
Parity-primiparas	63	54
Multiparas	43	40
Gestational age (weeks)	36.4 ± 4.1	38 ± 3.4

aspect of the forearm. The blood drops were then wicked away every 30 s, and bleeding time was determined upon cessation of bleeding to the nearest 30 s. The test was discontinued after 15 min. The results were available to the anesthesiologist before administering the anesthetic. A bleeding time of more than 10 min and/or a platelet count of less than 100,000/mm³ were considered abnormal, and epidural anesthesia was not administered to these patients.

All women with preeclampsia received 6 g magnesium sulfate as a loading dose followed by 2–3 g/h. In addition, some patients with severe preeclampsia required other drugs such as hydralazine, nitroglycerine, or labetalol to control blood pressure. Invasive monitors such as pulmonary artery catheters or central venous catheters were inserted in some patients prior to administering anesthesia. In the preeclampsia group, bleeding times were measured before starting magnesium sulfate therapy in all patients. The indications for cesarean section were as follows: failed oxytocin induction, repeat cesarean section, twin gestation, breech presentation, failure of labor to progress, and severe preeclampsia. The data were analyzed by the *t* test, ANOVA, and Pearson correlation where appropriate, and *P* < 0.05 was considered significant. Values are expressed as mean ± SD.

Results

The patients in the two groups were of similar age, height, weight parity, and gestational age (table 1). Compared with the control group, patients with preeclampsia had significantly lower platelet count and longer bleeding time (*P* < 0.0001; table 2). In the preeclampsia group, 75 women received lumbar epidural anesthesia for cesarean section and 31 received general anesthesia. In the control group, 92 out of 94 women received epidural anesthesia. Two women in the control group with prolonged bleeding time (11 and 13 min, respectively) received intravenous opioids for labor analgesia.

Of the 106 women in the preeclampsia group, eight patients (7.5%) had a platelet count less than 100,000/mm³ and all except one had prolonged bleeding time (table 3, fig. 1). Thirteen patients (12%) had an adequate platelet count (100,000–150,000/mm³) and nine of the

TABLE 2. Preoperative Platelet Counts and Bleeding Times in Patients with Preeclampsia and Control Patients (Mean ± SD)

	Preeclampsia (n = 106)	Control (n = 94)
Platelet count (×10 ⁵ /mm ³)	226.6 ± 82.4*	266.5 ± 49.5
Bleeding time (min)	7.5 ± 3.5*	5.5 ± 2.0

* *P* < 0.0001.

13 had prolonged bleeding time. Of the remaining 85 women (80%) with a platelet count above 150,000/mm³, ten had abnormal bleeding time (table 3, fig. 1).

Overall, in patients with preeclampsia, eight (7.5%) had thrombocytopenia and 26 (24.5%) had prolonged bleeding time. In the control group, all women had a normal platelet count and two (2.1%) had prolonged bleeding time. All patients with prolonged bleeding time in the preeclampsia group received general anesthesia for cesarean section. In addition, those who refused regional anesthesia (five patients) received general anesthesia. There was good correlation between bleeding time and platelet count in those preeclamptic women with platelet count of less than 100,000/mm³ (*r* = -0.76, *P* < 0.02) and a fair correlation when the count was more than 100,000/mm³ (table 3).

Compared with patients in the control group, those with both mild and severe preeclampsia had significantly lower platelet count and longer bleeding time (*P* < 0.001; table 4). Nine women with severe preeclampsia (34%) and ten women with mild preeclampsia (13%) had prolonged bleeding time even though their platelet count was adequate (>100,000/mm³) (table 5). Compared with the control group, the number of women with adequate platelet count and abnormal bleeding time was significantly higher in the preeclampsia group (*P* < 0.01; table 5).

In the preeclampsia group, there was a significant decrease in the hematocrit from a preoperative value of 34.7 ± 4.0 to 30.5 ± 3.8 in the first postpartum day (*P* < 0.0001). Six of the eight patients with thrombocytopenia and prolonged bleeding time required packed cell and platelet transfusions during surgery or in the postpartum period. In the remaining patients, there was no significant correlation between preoperative platelet count and bleeding time and the decrease in hematocrit or the number of units of blood transfused.

TABLE 3. Number of Women with Abnormal Bleeding Times

Platelet count (× 10 ⁵ /mm ³)	Preeclampsia (n = 106)	Control (n = 94)	Correlation
Over 150 (range 151–435)	10/85	2/94	<i>r</i> = -0.36
101–150 (range 104–148)	9/13	0	<i>r</i> = -0.53
Less than 100 (range 44–96)	7/8	0	<i>r</i> = -0.76

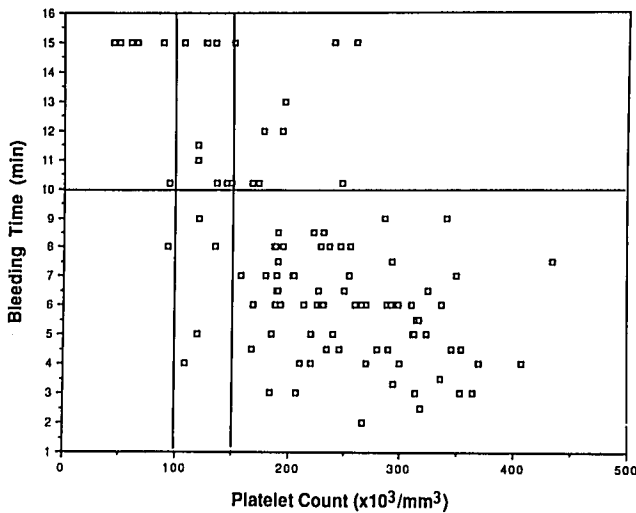


FIG. 1. Platelet counts and corresponding bleeding times in women with preeclampsia.

Discussion

Our findings indicate that platelet count is significantly lower and bleeding time is significantly prolonged in women with preeclampsia compared with healthy, term parturients. In addition, in many women with preeclampsia, bleeding time may remain prolonged, although they may have adequate platelet count. Furthermore, the incidence of abnormal bleeding time in the presence of normal platelet count increases with increasing severity of preeclampsia.

Bleeding time is still widely used to test the *in vivo* platelet function. Since the original description by Duke in 1910,⁵ the technique has undergone various modifications to increase sensitivity and reliability.⁶⁻⁸ Despite the simplicity of the technique, the reproducibility varies with the site of incision, length and depth of incision, skin temperature, capillary pressure, medications, and operator experience.⁶⁻⁸ In reports studying the bleeding time to measure *in vivo* platelet function, the modified Ivy template bleeding time technique has been both reproducible

TABLE 4. Preoperative Platelet Counts and Bleeding Times in Patients with Mild and Severe Preeclampsia and Control Patients (Mean \pm SD)

	Platelet Count ($\times 10^3/\text{mm}^3$)	Bleeding Time (min)	Correlation
Mild preeclampsia (n = 80)	233 \pm 77*	7.2 \pm 3.3*	r = -0.59
Severe preeclampsia (n = 26)	206 \pm 94*	8.5 \pm 3.9*	r = -0.68
Control group (n = 94)	266 \pm 49.0	5.5 \pm 2.0	r = -0.36

* $P < 0.001$.

TABLE 5. Number of Women with Adequate Platelet Count and Abnormal Bleeding Time in Preeclampsia and Control Groups

Mild preeclampsia (n = 80)	10/80 (12%)*
Severe preeclampsia (n = 26)	9/26 (34%)*
Control group (n = 94)	2/94 (2.1%)

* $P < 0.01$.

and accurate.^{9,10} However, strict attention to detail and meticulous technique are essential to obtain reproducible results.

The normal range for bleeding time is usually established by the individual laboratory. In the general population (males and nonpregnant females), it reportedly varies from 2.75 to 8 min with a mean of 4.75 ± 1.42 min.⁹ In many published reports and textbooks, the upper limit of normal bleeding time is less than 10 min.⁹⁻¹⁴ The data from our control group show that the bleeding time in healthy, term parturients is 5.5 ± 2.0 min. If we define abnormal bleeding time as two standard deviations above normal mean, the upper limit is still less than 10 min. However, this may be different from a value at which a patient is truly at risk for pathologic bleeding. We considered a bleeding time of less than 10 min (adequate for minor surgery¹⁵) and a platelet count of more than $100,000/\text{mm}^3$ (adequate for even major surgery¹⁵) as acceptable prior to epidural anesthesia in preeclampsia.

In our study, thrombocytopenia (platelet $< 100,000/\text{mm}^3$) occurred in eight preeclamptic women, and all except one patient had prolonged bleeding time. There was good correlation between bleeding time and platelet count ($r = -0.76$) in these patients. The inverse relationship between bleeding time and platelet count has been well documented, especially when platelet count is less than $100,000/\text{mm}^3$.¹¹ However, 19 patients with preeclampsia and adequate platelet count also had abnormal bleeding time. The reason for this is not entirely clear and may be related to the functional abnormality of platelets in these patients.⁴ The high incidence of platelet dysfunction in our study may be related to the severity of preeclampsia (many of our patients required vasodilators or labetalol for blood pressure control and invasive monitoring for perioperative management).

In our control group, all women had normal platelet count (greater than $150,000/\text{mm}^3$), and two had a prolonged bleeding time. Burrows and Kelton¹⁶ have shown that mild thrombocytopenia with platelet count of less than $150,000/\text{mm}^3$ frequently occurs even in healthy parturients, and epidural anesthesia was administered to some of these women without complication. In that study, however, a platelet count of less than $150,000/\text{mm}^3$ was considered abnormal, and the authors did not provide the actual range and mean values of platelet counts in women who received epidural anesthesia for labor anal-

gesia or for cesarean section. Bleeding times were not determined in this study. In another similar study,¹⁷ epidural anesthesia was administered to a number of normal pregnant women in whom the platelet count was subsequently found to be less than 150,000/mm.³ Three of these women who received epidural anesthesia had severe thrombocytopenia with platelet count well below 100,000/mm.³ The authors of that study, however, cautioned against administering regional blocks in obstetric patients with a platelet count of less than 100,000/mm,³ especially if they had associated platelet dysfunction.

Despite prolonged bleeding times, a normal, healthy individual (in the absence of drugs or diseases interfering with platelet function) will rarely develop significant bleeding in the epidural space, as attested by the large number of epidurals administered each year without serious sequelae. On the other hand, in patients with preeclampsia, studies have shown that, in addition to decreased platelet counts, there is increased platelet turnover,¹⁸ increased platelet activation and platelet consumption in the microvasculature,^{18,19} and decreased platelet lifespan.²⁰ Prolonged bleeding time may be a significant finding in these patients. However, the rationale for the abnormality in bleeding time with normal platelet count in preeclampsia needs further definition and will require additional *in vitro* and *in vivo* platelet function studies.

In summary, our study shows that in women with preeclampsia, platelet count is significantly lower and bleeding time prolonged compared with normal pregnant women. In addition, bleeding time may be abnormal in some patients with normal platelet counts. At present, the exact level of platelet count or bleeding time at which a patient is at risk for excessive bleeding into the epidural space is not known. Given the fact that each year many patients with preeclampsia receive epidural anesthesia without serious neurologic complications, the risk for such occurrence may be small. Nevertheless, it is important for anesthesiologists to be aware of the status of platelet function prior to administering epidural anesthesia to women with preeclampsia, especially those women with a severe form of the disease.

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