Effects of Platelet Transfusion on Post Cardiopulmonary Bypass Bleeding

Shyamal Premaratne,1 MD, Aziz M. Razzuk,2 MD, Deepthi R. Premaratne,3 MD, Mark M. Mugishi,4 MD, Nahidh W. Hasaniya,2 MD, and Amanda F. Behling,5 MD

SUMMARY

A common complication of cardiopulmonary bypass (CPB) surgery is post-operative bleeding that may result in re-exploration. Bleeding is often due to the coagulopathy that follows the procedure, rather than the surgical technique. Etiology of this coagulopathy has been attributed to platelet dysfunction. We reviewed the medical records of 592 patients who had undergone CPB surgery between 1992 and 1994. Bleeding times (both pre and post operative) in treated (those who received platelets) and untreated patients were recorded where available. Both groups showed a rise in bleeding time (295 sec versus 192 sec, respectively, \( p < 0.001 \)). However, the treated group had a greater increase in the bleeding time compared to the un-treated (\( p < 0.05 \)). The result was the same when we compared 2 subgroups with similar pre-operative bleeding times. When the treated group was subdivided into those who received >10 units of platelets and those who received <10 units, there was no significant difference in the increase in their bleeding times (\( p > 0.1 \)). Administration of platelets did not improve bleeding time abnormalities induced by CPB. Both treated and untreated groups had a significant rise in their bleeding times, irrespective of the amount of platelets administered. The mean rise in the bleeding time in patients who bled significantly to require surgical re-exploration (but did not receive platelets) was not significantly different from those who received platelets. These observations suggest that the administration of platelets has no clinical benefit in improving bleeding time following CPB. (Jpn Heart J 2001; 42: 425-433)

Key words: Platelets, Cardio Pulmonary Bypass, Transfusion, Bleeding Time

The coagulopathy that often follows cardiopulmonary bypass (CPB) surgery has been discussed at length in the literature. This has been attributed largely to an impairment of platelet function. Some have inferred low platelet ADP levels as a possible etiology, while others have postulated a selective depletion of alpha
granules in them. Whatever the mechanism may be, the clinical ramifications of this malfunction have been that many centers have been employing the use of prophylactic platelet concentrates to alleviate post-operative bleeding in CPB patients. Indeed, at one point, 14% of institutions were routinely giving platelets to all their post CPB patients, and another 28% were reserving platelets for such patients.

The economic and logistic demands that such a practice puts on an institution are staggering, not to mention the increased risk it presents to the patient from exposure to blood borne diseases. There have also been multiple reports condemning the use of routine platelet transfusions in CPB patients. The present study investigates the effectiveness of platelet transfusions at our medical center, not only as a prophylactic, but also as a therapeutic measure in patients who have undergone bypass surgery.

**PATIENTS AND METHODS**

The Institutional Review Board of the Queen's Medical Center in Honolulu, Hawaii, USA, approved this study. We reviewed the medical records of 592 patients who were subjected to a CPB between 1992 and 1994. Data from the charts were recorded documenting the operative procedure, bleeding times (both pre-and postoperative), postoperative bleeding rates for the first 12 hours in the intensive care unit, platelet counts, amounts and times of platelet administration, amounts of blood products administered, and other drugs given.

Analysis of the data was done in two parts. The first involved determining whether the administration of platelets affected postoperative bleeding times. To qualify for this section, the patient needed to have both a pre-and a postoperative bleeding time recorded. These patients were then divided into treated and control groups, based upon whether or not platelets had been administered between the two bleeding times. The treated group was subdivided into those patients who had received greater than 10 units of platelets, and those who had received less. The second part of the study involved a comparison of bleeding rates (milli liters per hour) postoperatively between those who had received platelets and those who had not. The bleeding rate of the first postoperative hour was compared to that of each of the subsequent eleven hours, and the mean percentage decrease in bleeding rate was calculated. A further subset of this included a comparison between the treated group and those in the control group who had required subsequent re-exploration.

**Statistical analysis:** The package used was the Statistical Analysis System (SAS) package for the Macintosh (version 3.0.1). Data were compared by mean
values and chi-square statistical tests. In the latter, a $P$ value of $<0.05$ was considered statistically significant.

**RESULTS**

**Patient profiles:** The 123 patients in the study were comprised of 89 men and 34 women. Their mean age was 61.2 years for the males and 64.9 for the females. The principal surgical procedures that the patients underwent were coronary artery bypass graft (CABG) surgery, valve repair/replacement, or a combination thereof. The operations were performed by seven different cardiac surgeons who used a Sarns 7400 MDX cardiopulmonary bypass machine and a Shiley S070/S bubble oxygenator. Bleeding times were done with a polystyrene template and an incision of standard length and depth in the arm.

**Platelet transfusion and bleeding times:** Of the 592 medical records reviewed, 138 patients had both pre and postoperative bleeding times recorded. Of these, 15 had received Aspirin, Persantine, or Amicar and were hence excluded. The remaining 123 patients were divided into control and treatment groups—80 had not received platelets while 43 had. These groups were otherwise comparable with respect to age, gender, medications, operating time, and surgical technique. The group who had received platelets had a mean preoperative bleeding time of $264 \pm 40$ seconds, and a mean postoperative bleeding time of $559 \pm 101$ seconds, a difference of 295 seconds representing a statistically significant increase ($p<0.001$). The control group had a mean preoperative bleeding time of $218 \pm 27$ seconds and a mean postoperative bleeding time of $410 \pm 53$ seconds-this too being a significant increase (192 seconds, $p<0.001$). The result was the same when we compared 2 subgroups with similar bleeding times. Those who had received platelets showed a greater increase in their postoperative rise in bleeding time compared to those who had received none (295 seconds versus 192 seconds), and this difference was statistically significant also ($p<0.05$).

The treated group of 43 patients was further divided into those who had received ten or more units of platelets ($n=21$), and those who had received less than ten ($n=22$). The increase in bleeding time for these groups did not differ significantly between them ($p>0.1$). Table I summarizes these findings. A comparison was also made between those patients in the un-treated group who were re-explored and those who had received platelets. The increase in bleeding time for the re-explored group was not significantly different from the increase seen in the platelet treated group (231 seconds versus 295 seconds respectively, $p>0.1$).

**Platelet transfusion and bleeding rates:** Four hundred and seventy-three patients qualified to be included in this part of the study. They were divided into treated ($n=184$) and control ($n=289$) groups, based on whether or not they had received
platelets at any time. Their bleeding rates were analyzed and standardized by expressing each hour of bleeding as a percentage increase or decrease from the first hour of bleeding (Figure 1). The absolute decrease in bleeding is also presented (Figure 2). In four of the first five time intervals, the control group showed a significantly greater decrease in bleeding rate compared to the treated group. In subsequent time periods, the differences between the groups was not significant. A comparison was made between those who had undergone re-exploration in the control group and the treated groups. These showed no differences in any of the time periods.

Table I. Comparison of Mean Pre and Postoperative Bleeding Times

<table>
<thead>
<tr>
<th>Compared groups</th>
<th>Mean preoperative time (Seconds)</th>
<th>Mean postoperative time (Seconds)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (No platelets)</td>
<td>218 ± 27</td>
<td>410±53</td>
</tr>
<tr>
<td>n=80, P&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated (With platelets)</td>
<td>264±40</td>
<td>559±101</td>
</tr>
<tr>
<td>n=43, P&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Of the 80 controls, 37 patients were allocated to a sub group where the mean preoperative bleeding time was 225±21 secs.

Of the 43 treated patients, 19 had a mean preoperative bleeding time of 227±29 secs. The mean postoperative bleeding times of these 2 sub groups whose preoperative bleeding times were similar (P>0.1) were compared and were 399±47 secs versus 541±70 secs respectively (P<0.001).

<10 Units of platelets   | 266±37                           | 654±174                          |
| n=22, P<0.001          |                                  |                                  |
>10 Units of platelets   | 263±75                           | 461±98                           |
| n=21, P<0.01           |                                  |                                  |

Mean difference between pre and postoperative bleeding times

<table>
<thead>
<tr>
<th>Compared groups</th>
<th>Mean difference (Seconds)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>192±55</td>
<td>0.05</td>
</tr>
<tr>
<td>n=80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet group</td>
<td>295±97</td>
<td>0.01</td>
</tr>
<tr>
<td>n=43</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
<10 Units of platelets    | 388±170                   | 0.1 |
| n=22                     |                           |    |
>10 Units of platelets    | 198±92                    | 0.1 |
| n=21                     |                           |    |
Figure 1. Mean percentage decrease in bleeding rate versus time (relative to postoperative hour 1).

Figure 2. Mean bleeding rates of control versus treated patients.
DISCUSSION

There is ample evidence to support the concept of platelet dysfunction as a cause of postoperative bleeding following CPB. However, the need to administer fresh platelets to patients following CPB is controversial. The clinical value of administering platelets to patients who do not have thrombocytopenia has come under increasing attack. Our study examines this problem in a retrospective fashion. It is possible to take two different approaches when analyzing the data in our study. The first is to assume that both groups, that is both the treated and untreated groups, are essentially identical (this is true for certain criteria as reported under 'RESULTS'). This being the case, the data comparing the two can be taken at face value, and direct comparisons can be made and conclusions drawn. The other is to assume that these groups are fundamentally different, because those patients who received platelets probably did so because they were either bleeding more or showed signs of a hemostatic disorder compared to those who did not receive platelets. Our data can be analyzed from both perspectives.

In the first phase of the study, we looked at the effects of platelet administration on bleeding time. It is a useful, inexpensive indicator of excessive post-operative transfusions, even though its accuracy has been questioned. All of these patients had a pre- and postoperative bleeding time done, and the treated group received platelets in the intervening period. If we assume that both groups are essentially identical, then it is obvious that the administration of platelets does not improve the bleeding time abnormalities induced by CPB. Both groups had a significant increase in their bleeding times following CPB. This was true regardless of the amount of platelets given, as the group that received greater than 10 units of platelets showed no advantage over the one that received less.

On the other hand, it can be argued that those patients who received platelets represent a group with a relatively greater coagulopathy, which is why they received platelets in the first place. Working under this assumption, the only conclusion that can be drawn from the data is that the administration of platelets alone is not sufficient to correct bleeding time abnormalities caused by CPB. This seems to be independent of the quantity of platelets given, as even those receiving greater than ten units of platelets were not able to compensate for their bleeding time abnormalities.

One interesting point, however, is that those patients who did not receive platelets but later required re-exploration did not differ significantly from the treated group, with regard to bleeding time. In other words, the mean rise in bleeding time in patients bleeding significantly enough to warrant eventual re-exploration was not different from those who received platelets. This is an important observation, because even if we maintain that the control and treated groups
are fundamentally different (the disorders in the treated group are inherently worse), there is no doubt that these differences can be minimized by comparing the treated group to the subset of controls who eventually require re-exploration. Ultimately, it suggests that the administration of platelets had no clinical effect on bleeding time following CPB, even when compared to patients in the control group with significant bleeding problems.

The next phase of the study compared the postoperative blood loss of those patients who had received platelets with those who had not. It was necessary to standardize the data (because initial baseline bleeding was so different between the two groups), and we therefore chose to express bleeding rates as a percentage of the initial (first hour) bleeding rate. Once again, if we assume that both the treated and the control groups are essentially identical, clearly the administration of platelets had no effect on the postoperative bleeding rate. In fact, in the first few hours, those patients who received platelets showed less of a decrease in their bleeding rates than those who did not.

It would seem, however, that since the initial bleeding rate of the treated group is so much higher than the initial rate of the untreated group, the two groups are in fact fundamentally different. If this is the assumption, then the only conclusion that can be drawn is that platelet transfusion seemed relatively ineffective in the first few hours following surgery, as there was no significant decrease in bleeding rate in the treated group until after the sixth hour. The other point that needs to be made is that, once again, those untreated patients who later required re-exploration did not have significantly different bleeding curves compared to treated patients. This adds strength to the contention that platelet administration is not effective in reducing postoperative blood loss, even when compared to those patients who did not receive platelets but were bleeding sufficiently to require re-exploration. Finally, when one examines the bleeding rate curves, it is apparent that the discrepancies between the treated and untreated curves essentially disappear by the eighth hour. We hypothesize that by this hour the patient's own platelets have regained effectiveness, causing intrinsic hemostasis, resulting in a merging of the two curves.

There is no evidence to support the contention that the administration of platelets in the postoperative CPB patient is effective prophylaxis or therapy for abnormal bleeding times or high bleeding rates. The evidence, in fact, suggests the contrary. Platelet administration may not be valuable at all. We think that in the absence of thrombocytopenia, whatever factors that led to the temporary endogenous thrombosthenia will have the same effect on the exogenous platelets transfused to these patients. Once these detrimental factors are eliminated, perhaps both endogenous and exogenous platelets will work normally. We recognize the limitations of a retrospective study, and realize that it is impossible to elimi-
nate the possibility that our control and treated groups are fundamentally different. We believe that a prospective study is indicated which would randomize patients for the receipt of platelets. It is our belief that platelet administration, in the absence of significant thrombocytopenia, will not prove to be effective in alleviating the platelet dysfunction caused by CPB. We feel that by the time the banked platelets develop any clinical function, the patient's own platelets will likewise have regenerated their clotting capacities (the eight hour period discussed earlier). If this is indeed the case, the expensive and sometimes hazardous practice of administering platelets to patients with bleeding diatheses will be reserved for those patients for whom it is truly indicated, especially after 8 hours postoperatively.

**REFERENCES**