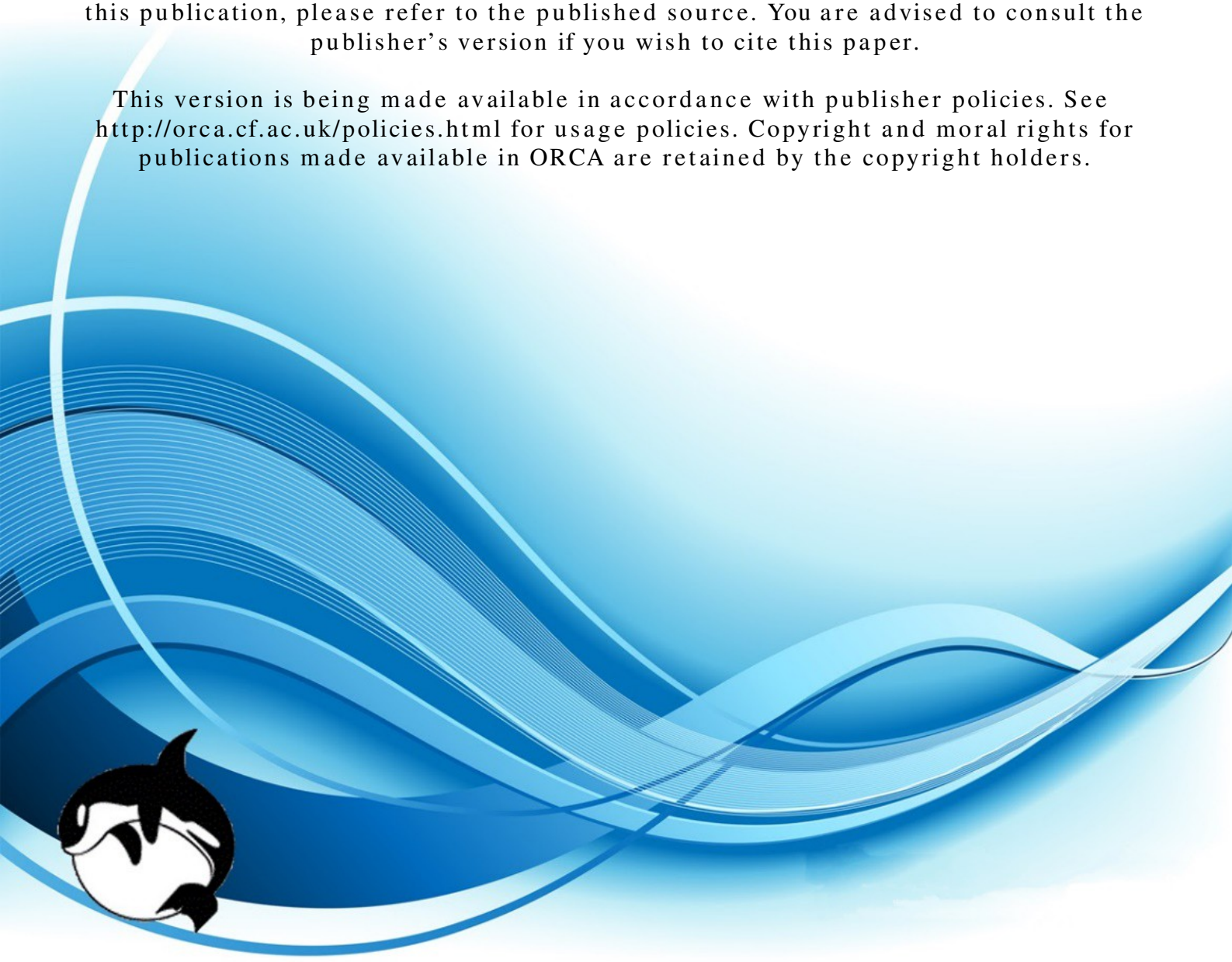

Platelet count and transfusion requirements during moderate or severe postpartum haemorrhage*

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Summary

Limited data exist on platelet transfusion during postpartum haemorrhage. We retrospectively analysed a single-centred consecutive cohort (n=347) with moderate-to-severe postpartum haemorrhage transfused according to national guidelines. 12/347 (3.4%) women required platelets. There were no differences between women who did and did not receive platelets with respect to age, initiation of labour or mode of delivery. Women receiving platelets had a lower platelet count than women who did not receive platelets pre-haemorrhage (median 135 vs 224 $X10^9.l^{-1}$) and at diagnosis of postpartum haemorrhage (median 114 vs 193 $X10^9.l^{-1}$) with 6 out of 12 women who received platelets being thrombocytopenic pre-delivery. Placental abruption was associated with the highest rate of platelet transfusion 3/14(21%). If antenatal thrombocytopenia or consumptive coagulopathy were not present, platelets were only required for bleeds exceeding 5000 ml. Early formulaic platelet transfusion would have resulted in many women receiving platelets unnecessarily. Using current guidelines the need for platelet transfusion is uncommon without antenatal thrombocytopenia, consumptive coagulopathy or bleeds >5000 ml. We found no evidence to support early fixed-ratio platelet transfusion.

Introduction

Postpartum haemorrhage is the leading cause of maternal mortality globally [1, 2]. In the UK, postpartum haemorrhage causes 75% of severe obstetric morbidity [3] and is an important cause of direct maternal mortality [4]. Postpartum haemorrhage may be associated with the depletion of coagulation factors and platelets due to dilutional and consumptive coagulopathies [5-7]. Studies have described the consequences of reduced coagulation factors and their replacement with fresh frozen plasma (FFP), cryoprecipitate and fibrinogen concentrate [8-12] but there are limited data on the need for platelet transfusion.

The optimal platelet transfusion trigger and target count is unknown, however, guidelines suggest that platelets should be transfused at 75 $x10^9.l^{-1}$ to maintain a count above 50 $x10^9.l^{-1}$ [13-16]. There is a trend to adopt fixed-ratio platelet transfusion in postpartum haemorrhage [12, 17-20], a practice directly extrapolated from major trauma [21] despite the coagulopathies of trauma and obstetric bleeding being markedly different [5-7, 22-24]. No studies have investigated whether this is an appropriate or safe strategy, and some groups describe good outcomes with low rates of platelet transfusion [25-27].

Changes in platelet count during postpartum haemorrhage are not well described. In this study we have analysed our previously-published dataset that was used to investigate the effect of fibrinogen and Fibtem levels on the progression of postpartum haemorrhage [28]. These data provides an opportunity to document changes in the platelet count and the requirement for platelet transfusion in a consecutive cohort of women during moderate or severe postpartum haemorrhage.

Methods

The study was approved by the South East Wales Research Ethics Committee. Data were collected prospectively on women experiencing moderate or severe postpartum haemorrhage between April 2012 - March 2013 in a single hospital [28]. Women were included if, in the opinion of the recruiting clinician, they had bled more than approximately 1500 ml, or if they bled approximately 1000-1500 ml and had an additional risk factor (caesarean section, uterine atony, placental abruption, placenta praevia, microvascular oozing or cardiovascular instability).

At study entry a full blood count (FBC) was taken. Subsequent FBCs and decisions to transfuse platelets were taken at the discretion of the treating clinicians and were based on national and local guidelines [14, 15]. The last platelet count before the haemorrhage was identified, taken on admission to the delivery suite or in the late antenatal period. Additional variables included patient characteristics, precipitants of haemorrhage, gravimetrically-measured total blood loss [29], transfusion of red blood cells (RBC), FFP and

platelets. The main precipitant of the postpartum haemorrhage was recorded as surgical/genital tract trauma including uterine rupture, placental abruption, adherent or retained placenta, placenta praevia or uterine atony. If no precipitant was recorded, the case was retrospectively allocated to one of the above groups.

The largest fall in platelet count was calculated by subtracting the lowest platelet count measured during the bleed from either the last platelet count before haemorrhage or that at study entry, whichever was higher (if the platelet count increased the 'fall' was defined as zero). Data were analysed using SPSS version 20 (IBM, Amrock, NY, USA).

Receiver operator characteristic (ROC) curves were used to investigate whether platelet count before the bleed had started or at study entry were predictive of progression to bleeds > 2500 ml or the need for platelet transfusion.

Results

There were 6187 deliveries during the study period. Three hundred and fifty-six (six percent) women had a moderate or severe postpartum haemorrhage. Full data were available for 347 women and are reported here. Characteristics of the women are shown in Table 1. In 29 cases the retrospective assessment of blood loss was less than the recruitment criteria.

Twelve women received platelets, comprising 3.4% of those who had a postpartum haemorrhage. Women who received a platelet transfusion were of similar age, body mass index, and labour and delivery characteristics to women who did not. The women who received platelets had similar blood loss at study entry to those that did not, but had larger total blood losses; a higher proportion of women who received platelets had blood loss > 2500 ml compared with those who did not. Women who received platelets were more likely to have had a placental abruption (Table 1). The haemoglobin concentration measured on the last FBC before haemorrhage and the FBC at study entry was similar between women who did and did not receive platelets. Women who received platelets had lower platelet counts both before haemorrhage and at study entry, and lower Clauss fibrinogen and Fibtem A5 at study entry, suggestive of consumptive coagulopathy (Table 1).

Neither platelet count before haemorrhage nor at study entry were predictive of haemorrhage > 2500 ml (ROC area under the curve (95% CI) 0.50 (0.40-0.60) and 0.45 (0.35-0.55) respectively) or the need for RBC transfusion (ROC 0.50 (0.43-0.57) and 0.47 (0.41-0.54 respectively). The platelet count before haemorrhage and at study entry were predictive of the need for a platelet transfusion (ROC 0.85 (0.73-0.97) and 0.84 (0.96-0.72) respectively).

The platelet count before haemorrhage, at study entry and the lowest platelet count recorded according to the cause of haemorrhage are shown in Table 2. In 14 cases the cause of bleeding was not recorded in the study data, but was retrospectively identified based on the clinical records. Platelet counts before haemorrhage and at study entry were similar for all causes of haemorrhage. The median (IQR [range]) largest fall in platelet count for the whole cohort was 48 (25-71 [0-257]) $x10^9.l^{-1}$. After study entry there was a small fall in platelet count 5 (0-32 [0-168]) $x10^9.l^{-1}$.

The two most common causes of postpartum haemorrhage, surgical/trauma-induced and uterine atony, were associated with median falls after study entry of 1 $x10^9.l^{-1}$ and 7 $x10^9.l^{-1}$ respectively. A platelet count < 75 $x10^9.l^{-1}$ was seen in eight (2%) women with postpartum haemorrhage. The proportion of women with a lowest platelet count < 75 $x10^9.l^{-1}$ was highest for placental abruption (1/14, 7%) and for uterine atony it was (2/148, 1%).

If the platelet count is adjusted to take account of platelet transfusion by subtracting 30 $x10^9.l^{-1}$ per unit of platelets transfused from the measured count [30], 11 (3%) women would have had a platelet count < 75 $x10^9.l^{-1}$.

Women who received platelets fell into three categories: thrombocytopenia before the bleed; placental abruption and massive haemorrhage > 5000 ml (Table 3). The causes of thrombocytopenia before the bleed were pre-clampsia, gestational, hereditary and immune mediated. One woman was diagnosed with gestational thrombocytopenia at the time of the bleed but subsequently continued to have a platelet count of about 100 x 10^9/L post delivery and may have had a mild immune thrombocytopenia. Women with postpartum haemorrhage due to abruption were the most likely to receive platelets (3/14, 21%). Platelets were given to 5/141 (4%) women with trauma-induced bleeding, although all 5 were thrombocytopenic before the bleed onset. Of the 6 women with normal platelet counts prior to the onset of bleeding, 2 had abruptions and one an amniotic fluid embolism. The remaining 3 women had very large bleeds between 5000-5500 ml and all received ≥ 8 units RBCs and ≥ 12 units FFP. In the study 5 women had a postpartum haemorrhage ≥5000 mL, 4 were transfused platelets and in the single case that was not transfused the lowest measured count was 79 $x10^9.l^{-1}$.

If a strategy of fixed-ratio platelet transfusion without monitoring had been used, then 4: 4: 1 (RBC: FFP: platelet pool) replacement would have resulted in 32 women receiving platelets. Of these 32 women, seven were transfused platelets and 25 were not; conversely five women who received platelets would not have been transfused. A strategy of 6: 4: 1 replacement would have resulted in nine women receiving platelets. Of these nine women, four were transfused platelets and five were not, whilst eight women who received platelets would not have been transfused.

Discussion

This study shows that platelet transfusion is rarely required to treat moderate or severe postpartum haemorrhage if current guidelines are followed [13, 14, 16, 31]. The incidence of platelet transfusion was 3.4% of cases of moderate or severe postpartum haemorrhage. Platelets were most commonly given to women who were thrombocytopenic before the onset of haemorrhage, or for consumptive coagulopathies caused by placental abruption and amniotic fluid embolism. Platelet transfusion was also required for massive haemorrhage ≥ 5000 ml in the absence of antenatal thrombocytopenia or a consumptive coagulopathy. There was no difference between the women who did or did not receive platelets with respect to age, body mass index, induction of labour or mode of delivery. The only precipitant of haemorrhage associated with an increased need for platelet transfusion was placental abruption.

This cohort is typical of UK tertiary practice, with a 5.8% incidence of moderate or severe postpartum haemorrhage and 0.6% incidence of haemorrhage > 2500 ml [3]. Our management at the time of the study was based on national and local guidelines [14, 15], which recommended transfusing platelets if the count was < 75 $x10^9.l^{-1}$ to prevent a fall to < 50 $x10^9.l^{-1}$. These guidelines appear to have been followed because only two women who had a platelet count < 75 $x10^9.l^{-1}$ (counts of 72 $x10^9.l^{-1}$ and 74 $x10^9.l^{-1}$, measured after the postpartum haemorrhage had resolved) did not receive platelets and both women with a platelet count < 50 $x10^9.l^{-1}$ received platelets. Retrospective review may suggest a tendency to over-transfuse platelets because, in some cases, platelets were transfused to maintain a count > 75 $x10^9.l^{-1}$ rather than > 50 $x10^9.l^{-1}$. Platelets were given to some women after the postpartum haemorrhage had resolved to reduce the risk of recurrence. We were not able to assess whether there was variability in practice between clinicians. There does not appear to have been a tendency to under-transfuse platelets in this cohort, supporting the conclusion that the need for platelet transfusion is uncommon in postpartum haemorrhage.

Women who were transfused platelets had lower platelet counts before haemorrhage and at study entry than those who were not transfused platelets. In contrast, haemoglobin concentration was similar for women who were or were not transfused platelets, suggesting that thrombocytopenia at these measurement points was not a consequence of the amount of haemorrhage. Half of the women who were given a platelet transfusion had thrombocytopenia before haemorrhage. This was either inherited, gestational/immune mediated, or due to abruption or pre-eclampsia. In one case the aetiology was unclear and may have been due to gestational or immune thrombocytopenia. All bleeds in these cases were precipitated by surgical intervention. Some platelet transfusions could, therefore, be anticipated before delivery.

Placental abruption was the cause of bleeding associated with the highest proportion of women requiring platelet transfusion, secondary to consumptive coagulopathy [6, 7, 23, 32]. The importance of consumption in placental abruption was

confirmed because all cases that required platelets also had severe hypofibrinogenamia < 2g.l^{-1} at study entry. Furthermore, women who received platelets for any reason had lower fibrinogen and Fibtem A5 at study entry than those who did not.

Amniotic fluid embolism also causes consumption [23]. The single case reported here had a fibrinogen < 0.5 g.l^{-1} at diagnosis and a lowest platelet count of 85 x10^9.l^{-1} despite 4 platelet pools suggesting that the nadir would have been well below 75 x10^9.l^{-1} if platelets had not be given. Thrombocytopenia due to consumption is, therefore, an important cause of low platelets during postpartum haemorrhage. A low Fibtem A5 early in the bleed may be a useful indicator that consumption is likely and the likelihood of requiring platelet transfusion is increased [32].

Women who received platelets had larger total blood loss than those that did not, however, haemorrhage < 5000 ml secondary to atony or surgery/trauma was not associated with platelet counts < 75 x10^9.l^{-1}. Postpartum haemorrhage, in the absence of consumption or antenatal thrombocytopenia, is therefore an uncommon indication for platelets unless very large haemorrhage occur suggesting that early unmonitored platelet transfusion during postpartum haemorrhage would result in many unnecessary transfusions. All women who received platelets secondary to massive haemorrhage in our study required ≥ 8 units RBCs. In a recent study of women receiving ≥ 8 units RBCs with median blood loss 6000 ml, platelets < 75 x10^9.l^{-1} were seen in over 50% of cases confirming that very large haemorrhages are an important reason for platelet transfusion [33]. Recent guidelines suggest transfusing platelets if 8 units of RBC have been transfused and a platelet count is not available [16].

A case control study reported that a platelet count < 80 x10^9.l^{-1} at the time of delivery was associated with an increased risk of postpartum haemorrhage [34]. A further study has reported that platelets < 100 x10^9.l^{-1} and fibrinogen < 3g.l^{-1} was associated with a 19-fold increased risk of postpartum haemorrhage [35]. Our data showed that the platelet count prior to bleeding and at study entry were not associated with progression to haemorrhage ≥ 2500 ml or the need for RBC transfusion, although most women in the study had moderate or severe postpartum haemorrhage at inclusion. Low fibrinogen has previously been shown to be associated with progression to severe postpartum haemorrhage in our cohort [28] and this may suggest that hypofibrinogenaemia is a more significant risk factor for progression to severe postpartum haemorrhage than thrombocytopenia.

The average fall in platelets during postpartum haemorrhage was small, particularly for atony and trauma-related bleeds. A previous report measured serial platelet counts during severe postpartum haemorrhage and also found minimal changes in platelet count [36]. This suggests that, in the absence of consumption, platelet counts remain relatively stable until very large bleeds have occurred.

Some authors suggest that fixed-ratio platelet transfusion is an appropriate strategy during severe postpartum haemorrhage [17, 18, 20]. In our cohort we estimate that, if fixed-ratio transfusion had been used, multiple platelets would have been given to women with platelets counts well above those recommended in guidelines and women with clinically significant thrombocytopenia would not have received platelets. This finding is supported by others who have moved away from formulaic shock packs and shown a substantial decrease in platelet transfusion associated with improved outcomes [26, 27].

Weaknesses of the study are that it is a retrospective analysis of a cohort recruited to analyse the impact of fibrinogen on subsequent progression of postpartum haemorrhage. Although the platelet count at study entry was taken at a standardised time, all other counts were at the clinicians' discretion and so varied widely. Platelet counts were not always performed immediately prior to transfusion and so the lowest platelet count may not have been recorded. It is not known whether the platelet transfusions given during this study affected clinical outcomes.

This study shows that platelet transfusion is rarely required in postpartum haemorrhage and identifies pre-delivery thrombocytopenia, consumptive coagulopathies and massive postpartum haemorrhage (> 5000 ml) as risk factors. We found no evidence to support fixed-ratio platelet transfusion for postpartum haemorrhage. Recent guidelines [13] also recommended against fixed-ratio platelet transfusion during postpartum haemorrhage but suggest that if 8 units of RBCs have been transfused and no platelet count is available then a pool of platelets may be given [16].

Key tools for the physician to identify patients most at risk of requiring platelet transfusion in postpartum haemorrhage are knowledge of the pre-delivery platelet count to identify pre-existing thrombocytopenia, early identification of consumptive coagulopathies during bleeds (potentially through point of care testing), and meticulous contemporaneous measurement of blood loss. In the absence of pre-existing thrombocytopenia, a consumptive bleed or blood loss greater than 5000 ml it appears that the risk of a critically low platelet count requiring platelet transfusion in postpartum haemorrhage is very low and that including platelets in massive haemorrhage packs for postpartum haemorrhage is unnecessary until 8 units of RBC have been reached.

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