

# Online Research @ Cardiff

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: <http://orca.cf.ac.uk/101949/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Jones, R. M., de Lloyd, L., Kealaher, E. J., Lilley, G. J., Precious, Elizabeth, Burckett st Laurent, D., Hamlyn, V., Collis, R. E. and Collins, Peter 2016. Platelet count and transfusion requirements during moderate or severe postpartum haemorrhage. *Anaesthesia* 71 (6) , pp. 648-656.  
10.1111/anae.13448 file

Publishers page: <http://dx.doi.org/10.1111/anae.13448> <<http://dx.doi.org/10.1111/anae.13448>>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See <http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



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

R. M. Jones,<sup>1</sup> L. de Lloyd,<sup>2</sup> E. J. Kealaher,<sup>3</sup> G.J. Lilley,<sup>2</sup> E. Precious,<sup>4</sup> D. Burckett st Laurent,<sup>1</sup> V. Hamlyn,<sup>1</sup> R. E. Collis<sup>2</sup> and P. W. Collins<sup>5</sup>

*1 Research Registrar, 2 Consultant, 3 Foundation Programme Doctor, Department of Anaesthetics and Pain Control, Cardiff and Vale University Health Board, Cardiff, UK,*

*4 Welsh Core Academic Trainee, 5 Professor of Haematology, Institute of Infection and Immunity, School of Medicine, Cardiff University, Cardiff, UK*

### Contributors

D. Bruynseels,<sup>1</sup> J. E. Hall<sup>2</sup> and J. Sanders<sup>3</sup>

*1 Research Registrar, 2 Professor, Department of Anaesthetics and Pain Control, 3 Reader, Department of Obstetrics, Cardiff and Vale University Health Board, Cardiff, UK*

*Correspondence to: P. W. Collins*

*Email: [peter.collins@wales.nhs.uk](mailto:peter.collins@wales.nhs.uk)*

*\* Presented at the Obstetric Anaesthetists' Association conference, Torquay, UK, May 2015.*

Short title: Platelets and postpartum haemorrhage

## 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  $\times 10^9 \cdot l^{-1}$ ) and at diagnosis of postpartum haemorrhage (median 114 vs 193  $\times 10^9 \cdot l^{-1}$ ) 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  $75 \times 10^9 \cdot l^{-1}$  to maintain a count above  $50 \times 10^9 \cdot l^{-1}$  [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 Fibtet 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 Fibtex 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])  $\times 10^9.l^{-1}$ . After study entry there was a small fall in platelet count 5 (0-32 [0-168])  $\times 10^9.l^{-1}$ .

The two most common causes of postpartum haemorrhage, surgical/trauma-induced and uterine atony, were associated with median falls after study entry of 1  $\times 10^9.l^{-1}$  and 7  $\times 10^9.l^{-1}$  respectively. A platelet count  $< 75 \times 10^9.l^{-1}$  was seen in eight (2%) women with postpartum haemorrhage. The proportion of women with a lowest platelet count  $< 75 \times 10^9.l^{-1}$  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  $\times 10^9.l^{-1}$  per unit of platelets transfused from the measured count [30], 11 (3%) women would have had a platelet count  $< 75 \times 10^9.l^{-1}$ .

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-clampsis, 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  $100 \times 10^9/L$  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  $\geq 8$  units RBCs and  $\geq 12$  units FFP. In the study 5 women had a postpartum haemorrhage  $\geq 5000$  mL, 4 were transfused platelets and in the single case that was not transfused the lowest measured count was  $79 \times 10^9.l^{-1}$ .

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  $\geq 5000$  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  $< 75 \times 10^9 \cdot l^{-1}$  to prevent a fall to  $< 50 \times 10^9 \cdot l^{-1}$ . These guidelines appear to have been followed because only two women who had a platelet count  $< 75 \times 10^9 \cdot l^{-1}$  (counts of  $72 \times 10^9 \cdot l^{-1}$  and  $74 \times 10^9 \cdot l^{-1}$ , measured after the postpartum haemorrhage had resolved) did not receive platelets and both women with a platelet count  $< 50 \times 10^9 \cdot l^{-1}$  received platelets. Retrospective review may suggest a tendency to over-transfuse platelets because, in some cases, platelets were transfused to maintain a count  $> 75 \times 10^9 \cdot l^{-1}$  rather than  $> 50 \times 10^9 \cdot l^{-1}$ . 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 hypofibrinogenemia  $< 2\text{g.l}^{-1}$  at study entry. Furthermore, women who received platelets for any reason had lower fibrinogen and Fibtex A5 at study entry than those who did not.

Amniotic fluid embolism also causes consumption [23]. The single case reported here had a fibrinogen  $< 0.5\text{g.l}^{-1}$  at diagnosis and a lowest platelet count of  $85 \times 10^9.\text{l}^{-1}$  despite 4 platelet pools suggesting that the nadir would have been well below  $75 \times 10^9.\text{l}^{-1}$  if platelets had not be given. Thrombocytopenia due to consumption is, therefore, an important cause of low platelets during postpartum haemorrhage. A low Fibtex 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  $< 5000\text{ml}$  secondary to atony or surgery/trauma was not associated with platelet counts  $< 75 \times 10^9.\text{l}^{-1}$ . 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  $\geq 8$  units RBCs. In a recent study of women receiving  $\geq 8$  units RBCs with median blood loss  $6000\text{ml}$ , platelets  $< 75 \times 10^9.\text{l}^{-1}$  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  $< 80 \times 10^9.\text{l}^{-1}$  at the time of delivery was associated with an increased risk of postpartum haemorrhage [34]. A further study has reported that platelets  $< 100 \times 10^9.\text{l}^{-1}$  and fibrinogen  $< 3\text{g.l}^{-1}$  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  $\geq 2500\text{ml}$  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.

### **Acknowledgements**

The authors thank the staff of the delivery suite at University Hospital of Wales for their many contributions to the study.

The Rotem machine and reagents used in the study were loaned without charge by TEM International. No competing interests declared.

## References

1. Say L, Chou D, Gemmill A, et al. Global causes of maternal death: A WHO systematic analysis. *The Lancet Global Health* 2014; **2**: e323-33.
2. World Health Organisation. Maternal mortality. Fact sheet N°348. Updated November 2015, 2015. [www.who.int/mediacentre/factsheets/fs348/en/](http://www.who.int/mediacentre/factsheets/fs348/en/) (accessed 12/01/2016).
3. Health Improvement Scotland. Scottish Confidential Audit of Severe Maternal Morbidity: reducing avoidable harm. 9<sup>th</sup> Annual Report, 2013. <http://healthcareimprovementscotland.org/his/idoc.ashx?docid=5fb640e2-d079-48cc-ad49-a58f6929b685&version=-1> (accessed 12/01/2016).
4. Knight M, Kenyon S, Brocklehurst P, Neilson J, Shakespeare J, Kurinczuk JJ, eds, on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care – Lessons Learned to Inform Future Maternity Care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009-12. Oxford: National Perinatal Epidemiology Unit, University of Oxford, 2014. <https://www.npeu.ox.ac.uk/mbrance-uk/reports> (accessed 12/01/2016).
5. Allard S, Green L, Hunt BJ. How we manage the haematological aspects of major obstetric haemorrhage. *British Journal of Haematology* 2014; **164**: 177-88.
6. Collis RE, Collins PW. Haemostatic management of obstetric haemorrhage. *Anaesthesia* 2015; **70 s1**: 78-86.
7. Thachil J, Toh C-H. Disseminated intravascular coagulation in obstetric disorders and its acute haematological management. *Blood Reviews* 2009; **23**: 167-76.
8. Ahmed S, Harrity C, Johnson S, et al. The efficacy of fibrinogen concentrate compared with cryoprecipitate in major obstetric haemorrhage - an observational study. *Transfusion Medicine* 2012; **22**: 344-9.
9. Bonnet M-P, Deneux-Tharoux C, Dupont C, Rudigoz R-C, Bouvier-Colle M-H. Transfusion practices in postpartum hemorrhage: a population-based study. *Acta Obstetrica et Gynecologica Scandinavica* 2013; **92**: 404-13.
10. de Lloyd L, Bovington R, Kaye A, et al. Standard haemostatic tests following major obstetric haemorrhage. *International Journal of Obstetric Anesthesia* 2011; **20**: 135-41.
11. Pasquier P, Gayat E, Rackelboom T, et al. An observational study of the fresh frozen plasma: red blood cell ratio in postpartum hemorrhage. *Anesthesia and Analgesia* 2013; **116**: 155-61.
12. Shields LE, Wiesner S, Fulton J, Pelletreau B. Comprehensive maternal hemorrhage protocols reduce the use of blood products and improve patient safety. *American Journal of Obstetrics and Gynecology* 2015; **212**: 272-80.
13. Hunt BJ, Allard S, Keeling D, Norfolk D, Stanworth SJ, Pendry K. A practical guideline for the haematological management of major haemorrhage. *British Journal of Haematology* 2015; **170**: 788-803.
14. Royal College of Obstetricians and Gynaecologists. Postpartum haemorrhage, prevention and management (Green-top guideline No. 52), 2009. <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg52/> (accessed 12/01/2016).

15. Thomas D, Wee M, Clyburn P, et al. Blood transfusion and the anaesthetist: management of massive haemorrhage. *Anaesthesia* 2010; **65**: 1153-61.
16. Collins PW, Abdul-Kadir R, Thachil J. Management of coagulopathy associated with postpartum haemorrhage: guidance from the SSC of the ISTH. *Journal of Thrombosis and Haemostasis* 2016; **14**: 205-10.
17. Onwuemene O, Green D, Keith L. Postpartum hemorrhage management in 2012: predicting the future. *International Journal of Gynecology and Obstetrics* 2012; **119**: 3-5.
18. Pacheco LD, Saade GR, Costantine MM, Clark SL, Hankins GD. The role of massive transfusion protocols in obstetrics. *American Journal of Perinatology* 2013; **30**: 1-4.
19. Pavord S, Maybury H. How I treat postpartum hemorrhage. *Blood* 2015; **125**: 2759-70.
20. Saule I, Hawkins N. Transfusion practice in major obstetric haemorrhage: lessons from trauma. *International Journal of Obstetric Anesthesia* 2012; **21**: 79-83.
21. Holcomb JB, Tilley BC, Baraniuk S, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma. The PROPPR randomized clinical trial. *Journal of the American Medical Association* 2015; **313**: 471-82.
22. Frith D, Brohi K. The pathophysiology of trauma-induced coagulopathy. *Current Opinion in Critical Care* 2012; **18**: 631-6.
23. Levi M. Pathogenesis and management of peripartum coagulopathic calamities (disseminated intravascular coagulation and amniotic fluid embolism). *Thrombosis Research* 2013; **131**: S32-4.
24. Solomon C, Collis RE, Collins PW. Haemostatic monitoring during postpartum haemorrhage and implications for management. *British Journal of Anaesthesia* 2012; **109**: 851-63.
25. James AH, Paglia MJ, Gernsheimer T, Grotegut C, Thames B. Blood component therapy in postpartum hemorrhage. *Transfusion* 2009; **49**: 2430-3.
26. Mallaiah S, Barclay P, Harrod I, Chevannes C, Bhalla A. Introduction of an algorithm for ROTEM-guided fibrinogen concentrate administration in major obstetric haemorrhage. *Anaesthesia* 2015; **70**: 166-75.
27. Mallaiah S, Chevannes C, McNamara H, Barclay P. Use of ROTEM® in major obstetric haemorrhage. *Anaesthesia* 2015; **70**: 760-1.
28. Collins PW, Lilley G, Bruynseels D, et al. Fibrin-based clot formation as an early and rapid biomarker for progression of postpartum hemorrhage: a prospective study. *Blood* 2014; **124**: 1727-36.
29. Lilley GJ, Collis RE. Gravimetric measurement of blood loss versus visual estimation in simulated postpartum haemorrhage. *International Journal of Obstetric Anesthesia* 2013; **22**: S10.
30. Slichter SJ. Evidence-based platelet transfusion guidelines. *ASH Education Program Book* 2007; 172-8.
31. Kozek-Langenecker SA, Afshari A, Albaladejo P, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. *European Journal of Anaesthesiology* 2013; **30**: 270-382.
32. McNamara H, Mallaiah S, Barclay P, Chevannes C, Bhalla A. Coagulopathy and placental abruption: Changing management with ROTEM-guided fibrinogen concentrate therapy. *International Journal of Obstetric Anesthesia* 2015; **24**: 174-9.

33. Green L, Knight M, Seeney F, et al. The haematological management and transfusion requirements of women who required massive transfusion for major obstetric haemorrhage in the UK: a population based study. *British Journal of Haematology* 2015; DOI: 10.1111/bjh.13864
34. Dikman D, Elstein D, Levi GS, et al. Effect of thrombocytopenia on mode of analgesia/anesthesia and maternal and neonatal outcomes. *Journal of Maternal-Fetal and Neonatal Medicine* 2014; **27**: 597-602.
35. Simon L, Santi TM, Sacquin P, Hamza J. Pre-anaesthetic assessment of coagulation abnormalities in obstetric patients: usefulness, timing and clinical implications. *British Journal of Anaesthesia* 1997; **78**: 678-83.
36. Charbit B, Mandelbrot L, Samain E, et al. The decrease of fibrinogen is an early predictor of the severity of postpartum hemorrhage. *Journal of Thrombosis and Haemostasis* 2007; **5**: 266-73.