Adherence to guidelines on red blood cell transfusions in women having post-partum haemorrhage

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ABSTRACT

INTRODUCTION: Transfusion of blood products occurs frequently as part of the treatment of post-partum haemorrhage, but since it is both expensive and has potentially severe complications, prescription of blood products should be restricted. The aim of this study was to examine if restrictive red blood cell transfusion (RBC-T) practice for obstetric patients was in line with national Danish guidelines.

METHODS: A retrospective quality assurance study was conducted at Rigshospitalet, Denmark. The study counted the participation of the Department of Anaesthesiology and Surgery, the Juliane Marie Centre, the Danish Blood Bank and the Department of Obstetrics. Patients were identified via the patient database of the Danish Blood Bank in 2015-2017, and patient files were read.

RESULTS: Out of 16,698 delivering women, 196 (1.2%) received one or more RBC-T from 2015 to 2017. A total of 133 women (67.9%) received more than one RBC-T and the median was two. The most common reason for RBC-T was a "low haemoglobin level (Hb) + anaemic symptoms" (37.0%). A total of 20.3% of all RBC-Ts were prescribed based simply on a low Hb. The most common symptom of anaemia was dizziness.

CONCLUSIONS: The majority of RBC-Ts for obstetric patients were conducted in line with the guidelines. However, 6.0% of RBC-Ts were registered to be in discrepancy with the guidelines and 20.3% of RBC-Ts were prescribed on the "low Hb" criterium solely. It is possible, though, that the 20.3% is overestimated due to insufficient descriptions of indications for RBC-T in patient files.

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TRIAL REGISTRATION: The study was approved by the management at Rigshospitalet.

Post-partum haemorrhage (PPH) occurs in 5-15% of all deliveries and is a main cause of maternal morbidity and mortality worldwide, especially in developing countries, although an increasing number has been described in the developed countries [1]. PPH is often defined as a blood loss ≥ 500 ml within the first 24 hours following vaginal delivery and ≥ 1,000 ml following caesarean delivery, but several alternative definitions exist in the literature. In clinical practice, the amount of blood lost during childbirth is typically estimated visually and determining the exact post-partum blood loss is an evident challenge. Suctioning underlay, obstetric drapes and visual estimation are the most frequently used methods [2].

The main course of PPH is *uterine atony*, followed by *retained uterine contents* and *laceration,* whereas *coagulation disorder* is described to be the fourth-most common aetiology [3]. Obviously, the primary treatment of PPH is to stop the bleeding. Given that oxytocin stimulates contraction of the myometrium and reduces blood flow to the uterus, injection of 10 IU to all women after giving birth is recommended as prophylaxis against PPH in Denmark [3].

Haemodynamic stabilisation with fluid treatment and blood component therapy may be the next step in the treatment of PPH. According to the Danish National Board of Health and The Danish Blood Bank, blood component therapy should be considered when the haemoglobin level (Hb) falls < 4.3 mmol/l and/or if the patient has symptoms of anaemia at the same time. These recommendations are considered restrictive as long as the bleeding is controllable [4]. In addition, the 2015 guideline states that post-partum Hb should be measured only if the patient has symptoms of anaemia. In comparison, Dutch guidelines recommend blood component therapy when the Hb falls < 3.7 mmol/l [5], whereas in England the corresponding figures are an Hb < 4.3 mmol/l in combination with anaemic symptoms [6]. Germany, Austria and Switzerland have prepared a common guideline which recommends transfusion when the Hb is 4.3 mmol/l, until haemostasis is assured [7].

We performed a quality assurance study of the transfusion practice among women in labour, at Rigshospitalet, 2015-2017. *We hypothesised that transfusion practice was gentler than recommended, and that maternal complaints of dizziness, tiredness or malaise, and being pale would often lead to transfusion, regardless of the Hb. With an increasing focus on a short hospital stay even for the new families, we assumed that an Hb of 4.3 mmol/l might be considered "the transfusion level"*

ORIGINAL ARTICLE

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even without complaints and/or symptoms. Previously, interdisciplinary simulation training regarding PPH patients has been imparted at Rigshospitalet, but it was unknown if this practice had affected the everyday transfusion practice [8].

METHODS

This was a retrospective quality assurance study conducted at Rigshospitalet, Department of Anesthesiology and Surgery, Juliane Marie Centre, in collaboration with the Danish Blood Bank and the Department of Obstetrics. The hospital's blood bank identified women who received blood coded and issued to the Department of Obstetrics between January 2015 and December 2017 inclusive. The inclusion criteria were women with PPH who received red blood cell transfusion (RBC-T) within the first 24 hours after delivery. The exclusion criteria were bleeding < 500 ml, bleeding > 24 hours after birth, RBC-T during pregnancy, blood ordered for the new-born, including intrauterine RBC-T.

A pre-defined data collection form was used to save information on type of birth (vaginal delivery or caesarean section); reason for RBC-T; blood volume lost before, during and after surgery; symptoms of anaemia; blood pressure and pulse; number and type of blood product; Hb; complications after RBC-T; ordering department; and oral or intravenous (IV) iron supplements. Pre-specified reasons for RBC-T were recorded, i.e., large blood loss, symptoms of anaemia and low Hb or low Hb in combination with symptoms of anaemia. The main indication for RBC-T was extracted from the journal notes and only one indication was cited for each blood product prescription.

Each prescription of RBC-T was included and analysed, and some patients had more than one prescription.

Trial registration: This study was approved by the management at Rigshospitalet.

TABLE 1 / Indications for red blood cell transfusions in 196 women receiving 281 transfusions at the Department of Obstetrics, Rigshospitalet, 2015-2017.

	Transfusions, n (%)			
Indication	operating theatre	postnatal ward	not registered	total
Acute blood loss	51 (18.1)	5 (1.9)	1 (0.4)	57 (20.4)
Symptoms	13 (4.6)	41 (14.6)	0	54 (19.2)
Hb	5 (1.8)	52 (18.5)	1 (0.4)	58 (20.7)
Hb combined with symptoms	0	104 (37.0)	0	104 (37.0)
Other indications	0	2 (0.7)	0	2 (0.7)
No indications	2 (0.7)	3 (1.1)	1 (0.4)	6 (2.2)
Total	71 (24.1)	207 (73.7)	3 (1.2)	281 (100.0)

Hb = haemoglobin level.

RESULTS

The Department of Obstetrics, Rigshospitalet, conducted 16,698 deliveries in the three-year period from January 2015 through December 2017. During the period, 4,068 (24.4%) were diagnosed with PPH. In total, 196 (1.2%) of all women giving birth had an RBC-T. In addition, 25 women (12.8%) received plasma and 18 women (9.2%) also received platelets. A total of 133 (67.8%) women received more than one RBC-T and the median was two.

In all, 54 women (27.6%) were transfused after a caesarean section and 142 (72.4%) after vaginal birth. Among the 281 RBC-Ts, 224 (79.7%) were given within 48 hours after the bleeding and the remaining 57 (20.3%) were transfused after more than 48 hours. The indications for RBC-T are presented in **Table 1**.

In the patient files, 162 transfusions were prescribed due to either a low Hb or a low Hb in combination with anaemic symptoms. The distribution of these prescriptions of blood products in relation to the Danish National Guideline [4] (Hb < 4.3 mmol/l in combination with anaemic symptoms) is presented in **Table 2**.

The average blood loss in the 196 women having RBC-T was 2,261 ml and the median was 2,200 ml. **Figure 1** shows a possible correlation between the number of RBC-Ts and the estimated blood loss.

The most common symptom of anaemia was dizziness. This was seen prior to 110 (39.1%) of the 281 transfusions; followed by: tiredness (26.7%), hypotension (9.3%) and dyspnoea (7.8%). A total of 54 (19.2%) of the transfusions were prescribed based on symptoms of anaemia alone. In this group, the most common symptom was also dizziness (50.9%), followed by tiredness (27.3%), dyspnoea (27.3%) and hypotension (25.5%).

In all, 141 (71.9%) of the transfused women received an oral iron supplement when discharged from hospital. Nine (4.6%) had their iron supplement paused due to obstipation and 40 (20.4%) did not receive iron supplements. Thirty-one (15.8%) patients received intravenous iron. The most common reasons for the prescription of intravenous iron rather than oral iron were obstipation and a low Hb.

Five women (1.8%) experienced mild complications after RBC-T in the form of a febrile non-haemolytic transfusion reaction. No severe reactions were seen.

A few patients suffered from rare diseases that could influence the treatment strategy after PPH, i.e., hypofibrinogenemia and Von Willebrand disease that can lead to an increased bleeding tendency [9, 10].

DISCUSSION

The findings from this survey have raised a number of important issues. The transfusion rate was found to be 1.2%, which is consistent with other similar studies [11-14]. "Low Hb in combination with anaemic symptoms"

TABLE 2 / Pretransfusion haemoglobin levels (Hb), 2015-2017.

Hb, mmol/l	Transfusions, n (%)
< 4,3[a]	106 (65.4)
≥ 4,3	56 (34.6)

a) Cf. [4].

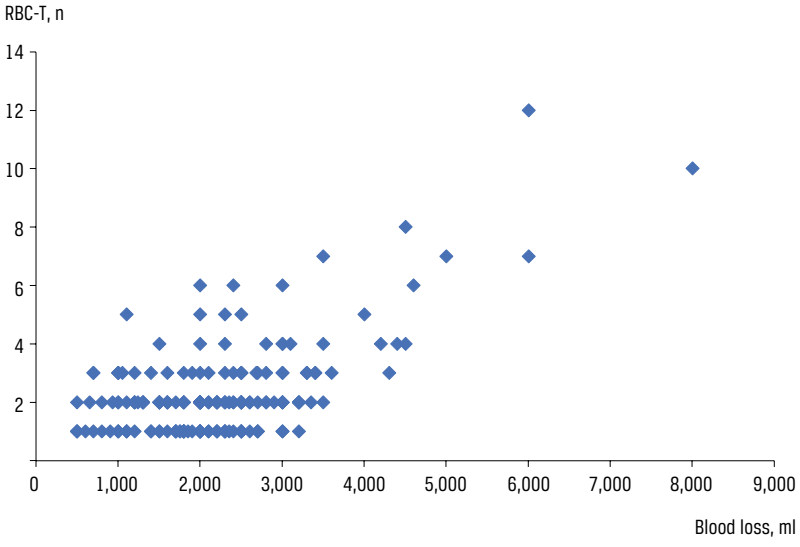
was the most common indication for transfusion of a blood product, leading to 37.0% of the transfusions. The second-most common indications were "low Hb" and "blood loss" (18.0%). 32.1% received one RBC-T and 67.9% received two or more RBC-Ts. In a study from 2009, Parker et al found that 94% received two RBC-Ts or more [6], similar to what Markova et al found in a Danish study, concluding that 89% received two or more RBC-Ts [11]. Analogous studies from the US and Holland have also reported a median of two RBC-Ts [13, 15]. This median of two RBC-Ts is not surprising since it is a well-known practice to prescribe RBC-T in pairs [11]. However, evidence of this clinical practice does not exist, but it might be understood as a commission bias, i.e., a non-rational cognitive factor that influences our decision making: ("If one is good, then two are twice as good") [16]. This heuristic has been recognised at Rigshospitalet and was previously articulated in order to reduce waste and avoid over-transfusion by focusing on changing the transfusion policy [17]. This would primarily be relevant when blood products are prescribed solely on the Hb criteria. It is worth noticing that a larger number of women received two or more RBC-T in the study by Markova et al [11] than in our study. It is therefore possible that the increased focus has already had an effect.

The present study examined the RBC-T practice at the Department of Obstetrics, Rigshospitalet, from 2015 to 2017. The Danish Health Authority recommends an haemoglobin transfusion limit of 4.3 mmol/l, in combination with anaemic symptoms. We examined the adherence to the Danish guidelines and found that 65.4% of transfusions were in accordance with the recommended Hb limit of 4.3 mmol/l. According to the patient files, 18.5% of the transfusions at the obstetric ward were ordinated on the Hb criteria solely, and perioperatively this occurred in 1.8% of the cases. This means that every fifth transfusion (20.3%) is prescribed without registration of any symptoms indicating transfusion. Among the 58 transfusions prescribed on the Hb criteria, 17 (6%) were in discrepancy with guidelines, due to an Hb ≥ 4.3 mmol/l. Apart from these 6%, all transfusions based solely on the Hb criteria are in discrepancy with guidelines. It is possible, though, that the patients had experienced symptoms and that these were registered in the record and are therefore potentially in accordance with guidelines. In comparison, Parker et al found that 32% of transfusions in 2006-2007 were made in discrepancy with guidelines [6] and Silverman et al found this number to be 32% in 1994-2002 [12]. Although clinicians should not be restricted to treat only according to guidelines, it is desirable that the majority of prescriptions are in line with guidelines. Compared with our European neighbours, our results seem less problematic. But overall, a reduction has been observed in the number of RBC-T in Denmark and in most European countries [17].

Fifty-four patients (19.2%) were transfused because of symptoms, i.e., 27% mainly due to tiredness. Prick et al examined the effect of RBC-T on "quality of life" (using tiredness as primary outcome) and found only a very limited and non-significant effect [5]. Because the effect was only minor, the authors argue for a restrictive approach for RBC-T. With this study in mind, it is worth considering if the symptom "tiredness" should be an indication for RBC-T.

Although severe complications are seen very rarely, with mild complications seen regularly, blood is still considered an expensive and potentially risky treatment of PPH. Non-acute anaemia can be treated both pre- and post-partum with iron supplements. In Denmark, it has been standard to treat anaemia with oral iron supplements when there is no indication for RBC-T [18]. As an alternative, Holm et al showed that IV iron reduces tiredness within 12 weeks after PPH and that IV supplements had an effect earlier than oral [18]. IV iron supplement prescription to the women in our study was not the primary objective, and the number of cases found was too limited to draw any conclusions. IV iron treatment may be an obvious focus area in the future, when working towards reducing the number of RBC-T.

FIGURE 1 / Number of red blood cell transfusions (RBC-T) by estimated blood loss.



There are obvious limitations to this study. This was a retrospective medical record review, and the indication for transfusion may not have been registered correctly and the timing of the laboratory results and clinical decisions are difficult to ascertain. Specifically, decisions to transfuse may be taken during a clinically stressful situation with a large and ongoing blood loss, and therefore the level of correct registrations might have been inadequate.

In Denmark, the Danish Health and Medicines Authority published "National Clinical guideline about transfusion of blood products" in October 2018. Here, it is emphasised that the indication for RBC-T should be "Hb < 4.3 mmol/l and/or clinical symptoms of anaemia in hospitalised patients with a stable circulation and without heart disease….". The recommendation continues: "Use a dose of one1 portion of red blood cells and re-evaluate". "The purpose of transfusion is to relieve clinical symptoms and organ ischaemia, not to normalise the Hb … Clinical symptoms of anaemia include chest pain, orthostatic hypotension or tachycardia not responding to fluid treatment". Exactly the same wording can be found in the 2015 guidelines from the Danish Patient Safety Authority. However, in contrast, these latter guidelines include a chapter on post-partum women: "Due to the special haemodynamic conditions after birth with, i.e., gradual normalisation of the large plasma volume of the grave, it may be difficult to assess a possible transfusion requirement from the Hb shortly after birth. The Hb in women who have given birth should therefore only be measured when the physician considers blood transfusion based on clinical symptoms such as fainting, extreme paleness and constant headache, etc. Blood transfusion may, in these cases, be considered at Hb < 4.3 mmol/l".

CONCLUSIONS

Although there seems to be a minor discrepancy between these two guidelines, and complete alignment of the two would be preferable, we conclude that the obstetricians at Rigshospitalet manage to manoeuvre competently between clinic and recommendations.

Approximately 20% were transfused without any ongoing symptoms being registered in the patient files. This is either in concordance with the most recent guidelines or it might be explained, in part, by the busy and challenging clinical work life. It is also possible that the percentage is higher due to the method chosen in this study, which cannot account for relevant clinical considerations not registered in the patient files. However, a registration of both the Hb and clinical symptoms seems to be advisable.

In summary, there appeared to be acceptable compliance with the national guidelines and the prescription policy at Rigshospitalet. 6% were transfused despite an Hb ≥ 4.3 mmol/l, but since guidelines can never give absolute guidance, this must be considered an acceptable level. Our main recommendation is to implement a single set of guidelines with a clear statement of the relevance of the post-partum Hb.

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