Case Report

Patient blood management when blood is not an option: a report of two cases

Jaewoong Jung^, Misoon Lee^, Youjin Kang^, Sung-Hwan Cho^

Department of Anesthesiology and Pain Medicine, Soonchunhyang University Bucheon Hospital, Soonchunhyang University College of Medicine, Bucheon, Gyeonggi-do, Republic of Korea

Correspondence to: Sung-Hwan Cho, MD, PhD. Department of Anesthesiology and Pain Medicine, Soonchunhynag University Bucheon Hospital, Soonchunhyang University College of Medicine, 170, Jomaru-ro, Bucheon, 14584, Gyeonggi-do, Republic of Korea. Email: singaring@schmc.ac.kr.

Abstract: There are many patients who refuse to receive blood transfusions for religious or other reasons. Bloodless medicine and surgery are no longer new concept, but patients who refuse blood transfusion are still transferred to the bloodless center, regardless of patients' intention, for treatment. Here, we discuss the need for patient blood management when blood is not an option to treat them. Two patients of advanced age were transferred to our bloodless center due to refusal of transfusion. They are Jehovah's Witnesses and refused to receive blood transfusion despite life-threatening anemia and severe underlying diseases. Patient blood management protocols including iron supplementation, subcutaneous erythropoietin, folic acid and vitamin B were implemented to improve hematopoiesis, and supportive care was also performed to treat underlying diseases. Levels of Hemoglobin/Hematocrit and their symptom gradually improved about a week after treatment, and their condition had gradually stabilized. They were discharged safely. We treated patients of advanced age with severe underlying diseases and life-threatening anemia using patient blood management due to refusal of a blood transfusion. The patient blood management may be a useful alternative strategy, which meet the needs of patients who refuse blood transfusions as well as the need to reduce the use of blood products due to limited supply.

Keywords: Bloodless medical and surgical procedures; blood conservation strategy; hematopoiesis; case report

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Introduction

Blood transfusion is an essential treatment, which is difficult to replace. However, there are many patients who refuse to receive transfusion for religious, such as Jehovah's Witnesses (JWs), or other reasons. According to their website (www.jw.org), there are more than 8.6 million JW in 240 countries. Some clinicians may still consider the transfusion absolutely necessary for the treatment of anemia. And refusing blood transfusion is perceived as also rejecting other treatment, forcing the patients to either receive blood transfusion or be discharged from the hospital. It is almost impossible to obtain consent for a blood transfusion from JW patients and their caregivers even in life-threatening situations. Many patients are referred to our bloodless center due to their refusal of blood transfusion. Their treatment requires consideration not only from medical perspective but also from an ethical standpoint.

"Bloodless medicine and surgery" are no longer new concepts, and there have been many reports over the past several decades. Particularly, developments in research, education, and protocols have been made through the effort of academic societies, such as the Society for the Advanced of Blood Management (SABM), Association

^ ORCID: Jaewoong Jung, 0000-0003-0624-1713; Misoon Lee, 0000-0001-7470-0921; Youjin Kang, 0000-0002-4480-0136; Sung-Hwan Cho, 0000-0003-1669-7773.

Table 1 Bloodless management drug protocol of anemia in Jehovah's Witnesses patients at our hospital

Hb level	Drug	Dosage	Procedures
Hb 5–7 g/dL	rHuEpo	300 IU/kg/day	S.C. every other day for 1 week
	I.V. iron	200 mg/day	I.V. once daily for up to 10 days
	Folate	1.0 mg/day	Oral once daily for 2 weeks
	Vitamin B_{12}	1.0 mg/day	I.M. once daily for 2 weeks
Hb <5 g/dL	rHuEpo	600 IU/kg/day	S.C. every other day for 2 weeks (or I.V. once daily for 5 days)
	I.V. iron	200 mg/day	I.V. once daily for up to 2 weeks
	Folate	1.0 mg/day	Oral once daily for 2 weeks
	Vitamin B_{12}	1.0 mg/day	I.M. once daily for 2 weeks

Hb, hemoglobin; I.M., intramuscular; I.V., intravenous; rHuEpo, recombinant human erythropoietin; S.C., subcutaneous.

for the Advancement for Blood and Biotherapies (AABB), and the Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis (NATA) (1-4). These efforts in developing bloodless treatment options have resulted in patient blood management (PBM). Fortunately, many countries, including the USA, European nations, Australia, Japan and Korea, have reported significant results with bloodless treatments (5-12). Here, we report the treatment of two JW patients without blood transfusion, and discuss strategies for reducing blood transfusions and how to manage JW patients. We present the following case in accordance with the CARE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-21-3013/rc).

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institution and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). This study was approved by the Soonchunhyang Institutional Review Board (IRB No. 2021-06-033) and the requirement for informed consent was waived because all data were obtained by retrospective chart review. We have our bloodless management drug protocol of anemia (*Table 1*), but the protocol was performed at the discretion of the attending physicians.

Case 1

A JW woman in her eighties (height, 151 cm; weight 62 kg) with congestive heart failure (CHF), atrial fibrillation, hypertension, and a history of old cerebrovascular accident was diagnosed with stage 5 chronic kidney disease (CKD) at another hospital and underwent hemodialysis three times a week. Her main symptom was dizziness, and she was transferred to our bloodless center due to refusal of a blood transfusion. Initial laboratory findings were hemoglobin (Hb), 4.5 g/dL; hematocrit (Hct), 13.4%; platelet count, 257×10^9/L; blood urea nitrogen (BUN), 51.8 mg/dL; and creatinine (Cr), 1.5 mg/dL.

We set up a meeting with the Jehovah's Witness Hospital Liaison Committee and discussed with a nephrologist, cardiologist and pulmonologist for multidisciplinary planning. After the meeting, we explained the need for blood transfusion to treat the patient's life-threatening condition, but the patient and her caregivers refused to receive the transfusion. PBM with conservative treatment was initiated after obtaining written informed consent for refusal of blood transfusion. First, subcutaneous recombinant human erythropoietin (rHuEpo) (20,000 IU, Epokine®; CJ HealthCare, Seoul, Korea) and intravenous iron (200 mg, Venoferrum®; JW Pharmaceutical, Seoul, Korea) with folic acid and vitamin B_{12} were administered every 2 days to increase the patient's red cell mass, considering her age and condition to avoid abrupt elevation of Hb. Whenever necessary, 20–40 mg of furosemide was injected according to changes in the patient's urine volume.

On hospitalization day (HD) 14, despite low Hb, hemodialysis was begun three times a week due to continuing increase in BUN and Cr. Fortunately, there were no complications and relatively stable vital signs were maintained. After dialysis, the levels of BUN and Cr gradually decreased, while Hb begun to increase (*Table 2*). The patient's condition

Table 2 Laboratory findings in Case 1

Hospital day	1	2	3	4	5	6	7	8	9	11	14†	15	17	19	21	23	26	28
Hb (g/dL)	4.5	4.0	4.1	4.3	4.2	4.0	4.2	4.5	4.8	5.6	6.1	6.4	6.7	7.4	7.3	8.0	8.2	9.1
Hct (%)	13.4	12.0	12.5	13.1	13.0	12.7	13.8	14.8	15.6	18.8	20.4	22.0	23.6	26.0	25.7	28.1	27.7	31.1
BUN (mg/dL)	51.8	56.1	64.2	65.7	71.5	76.9	74.6	77.3	78.9	83.3	82.0	57.2	35.5	24.1	18.9	20.2	31.4	21.4
Cr (mg/dL)	6.1	7.2	7.6	8.6	9.1	9.6	9.5	9.8	10.3	10.7	10.9	8.7	6.0	5.1	4.9	5.3	7.8	6.3

†, until HD 14, supportive care with PBM was performed, but BUN and Cr continuously increased. Despite low Hb levels, hemodialysis was started three times a week. At the same time, Hb levels also gradually increase. BUN, blood urea nitrogen; Cr, creatinine; Hb, hemoglobin; Hct, hematocrit; HD, hospital day; PBM, patient blood management.

Table 3 Laboratory findings in Case 2

	HD 1	HD 5	HD 9 (POD 0)	POD 1	POD 2†	POD 3	POD 5	POD 6	POD 8	POD 9‡	POD 12	POD 16	POD 19	POD 23	POD 26	POD 30
Hb (g/dL)	11.1	10.7	10.4	8.3	6.6	5.1	4.1	4.2	3.5	3.4	4.3	7.5	8.3	9.0	10.0	10.8
Hct (%)	34.7	32.4	31.3	24.9	20.0	15.7	13.1	13.3	11.5	12.0	15.4	27.0	29.8	32.4	36.0	37.4
Platelet count ($\times 10^9$/L)	90	120	151	98	44	40	33	41	46	39	67	117	110	83	105	160

†, from POD 2, Hb and Hct levels markedly decreased, and supportive treatment with PBM was started on POD 3. ‡, the lowest Hb level was detected on POD 9 and Hb and Hct levels subsequently recovered. Hb, hemoglobin; Hct, hematocrit; HD, hospital day; PBM, patient blood management; POD, postoperative day.

also gradually stabilized, and she was transferred to the local clinic on HD 28. The patient complied well with the treatment without any complaints, and she and her caregiver were very satisfied with the treatment.

Case 2

A JW woman in her nineties (height, 140cm; weight 36kg) with CHF, CKD and hypertension was diagnosed left femur neck fracture due to a fall, and was transferred to our bloodless center for surgery. Initial laboratory findings were Hb, 11.1 g/dL; Hct, 34.7%; platelet count, 90×10^9/L; BUN, 47 g/dL; and Cr, 22 mg/dL. After a meeting with the Jehovah's Witness Hospital Liaison Committee, including a cardiologist, nephrologist, and orthopedic surgeon, the need for blood transfusion was explained considering the patient's poor condition and the risk for perioperative bleeding. However, the patient and her caregivers refused the transfusion and also refused cardiopulmonary resuscitation and prolongation treatment. After receiving written informed consent for these wishes, perioperative treatment was initiated to treat the underlying diseases and restore general condition. The surgeon decided to administer 500 mg intravenous iron (Ferinject®; JW Pharmaceutical) without rHuEpo.

Bipolar hemiarthroplasty was performed under spinal anesthesia and stable vital signs were maintained during the operation. The operation took about 65 min. Estimated blood loss was 100 mL and urine output was 200 mL, and a total of 300 mL crystalloid (Plasma Solution A®; CJ HealthCare) was administered.

However, levels of Hb, Hct and platelets gradually decreased to life-threatening levels from postoperative day (POD) 3 (*Table 3*), with an Hb level of <6 g/dL and complaints of breathing difficulty, dizziness, generalized weakness and leg edema. Pulmonary congestion and acute renal failure were diagnosed. Conservative treatment was started consisting of maintaining input/output balance with fluid restriction and diuretics, supplying oxygen, and administering total parenteral nutrition under absolute bed rest. At the same time, 120 μg subcutaneous darbepoetin-α (Nesp Prefilled Syringe®, Kyowa Kirin Korea Co., Seoul, Korea) was administered per week. And 200 mg intravenous iron with folic acid and vitamin B_{12} were administered daily, with an additional 10,000 IU of subcutaneous rHuEpo (Epokine®, CJ HealthCare) administered every other day. For effective erythropoiesis, darbepoetin-α was administered with rHuEpo because darbepoetin-α has greater

potency (13). Eltrombopag (Revolate tab®, Novartis Korea, Seoul, Korea) was also administered orally to prevent platelet reduction.

Hb, Hct and platelet counts decreased to their lowest level on POD 9, but increased gradually thereafter in response to treatment. Her symptoms also gradually improved with the improvement in laboratory findings. The most serious problem was pulmonary congestion. This was managed intensively by the pulmonologist for 2 weeks, and the patient recovered well without any complications. The patient was discharged on POD 30 with an Hb level of 10.8 g/dL and Hct of 37.4%. During the treatment, the patient was somewhat anxious, but she endured well to avoid blood transfusion. She and her caregiver were satisfied that she was treated without blood transfusion.

Discussion

In our cases, the patients were of advanced age and had severe underlying diseases with severe anemia. As treating these patients without transfusion is a challenge for the medical team, both patients were transferred to our bloodless center. The main key to treatment without transfusion was to provide extensive supportive care with hematopoietic stimulation to produce new blood cells.

The strategies of PBM involve optimization of Hb/Hct with improving hematopoiesis and minimizing blood loss (2,14). Oral iron supplementation is generally recommended, but our patients did not tolerated oral iron therapy due to their advanced age and severe underlying diseases. Therefore, intravenous iron and subcutaneous erythropoietin were administered while treating the underlying cardiac and renal diseases. At the same time, nutritional supplementation with folate and vitamin B_{12} were also performed to enhance red blood cell production. Minimizing blood loss is critical, but there was no evidence of active or occult bleeding in either of our cases. Therefore, we focused only on treating the patients' underlying disease and increasing Hb/Hct. Some bloodless centers attempt to increase Hb by no more than 1 g/dL per week to avoid thrombotic complications (2). However, in our cases, aggressive treatment was needed because their advanced age and serious underlying diseases made it impossible for them to withstand very low level of Hb (lowest levels of 4.0 and 3.4 g/dL, respectively).

Beauchamp and Childress (15) described four principles in relation to medical ethics: respect for autonomy, beneficence, non-maleficence, justice. Applying these principles to JW patients, their autonomous choice of refusing transfusion should be respected, and the medical team should make efforts to develop and acquire new treatments that can benefit these patients without forcing them to choose between transfusion or discharge from hospital. Along with the low birth rate, disasters such as the current COVID-19 pandemic are resulting in reducing levels of blood donation and supply, and the issue of blood distribution must be considered. PBM has been developed to treat patients with evidence-based and multidimensional approaches. Many experiences of treatment without transfusion, including cardiac surgery (16,17), liver transplantation (7,11) and lung transplantation (18), have accumulated through treatment of JW patients, and concept such as PBM and "bloodless medicine and surgery" have been spreading around the world. Blood transfusion is still one of the best treatments if used appropriately, but is no longer the only treatment option for some patients. Considering the ethical/legal issues, acceptance and respect of the patients' decision to refuse blood transfusion, and treating with advances in bloodless medicine are the main factors for reducing the burden on the medical team.

In conclusion, we reported JW patients with life-threatening anemia using PBM without transfusion. PBM may be a useful alternative strategy for these problems, although the PBM should be further standardized and spread globally through education. PBM may meet the needs of patients who refuse blood transfusion.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-21-3013/rc

Peer Review File: Available at https://apm.amegroups.com/article/view/10.21037/apm-21-3013/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-21-3013/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institution and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). This study was approved by the Soonchunhyang Institutional Review Board (IRB No. 2021-06-033) and the requirement for informed consent was waived because all data were obtained by retrospective chart review.

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