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PERIOPERATIVE MANAGEMENT OF JEHOVAH'S WITNESSES

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ABSTRACT

There are approximately 8.5 million Jehovah's Witnesses (JWs) worldwide, with 101,246 currently live in Korea. JWs have refused allogenic blood transfusion on religious grounds since 1945. This has presented challenges and ethical dilemmas for anesthesiologists and related healthcare staff in providing care to this group. Due to the rapid increase in the membership of JWs in Korea, physicians, especially anesthesiologists, should be prepared to manage JW patients, because they are usually the ones who are responsible for transfusion during the perioperative period. An informed consent to recommended treatment is at the heart of this guideline. JWs' refusal of blood transfusion is a legally protected right. Administration of blood products against their will is a potentially criminal act subject to prosecution. This review examines the perioperative issues and management of JWs. The history and beliefs of JWs, their impact on ethics and the law, and various management options throughout the perioperative period are discussed here.

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Introduction

JWs are well known to the medical community for their refusal of allogeneic blood transfusion. The care of JW patients can pose an ethical dilemma for the anesthesia care team, because we are usually the ones who are responsible for transfusion during the perioperative period. On the one hand, we would like to respect the patient's autonomy but on the other hand as medical doctors we have taken the Hippocratic Oath to do no harm. Their membership is estimated to be more than 8.5 million people in 240 countries, including approximately 101,246 in Korea. The principal aim of this article is to present an overview of the history of the JW movement to provide better understanding of their point of view, the ethical and medicolegal issues of their beliefs, and the perioperative management which they may be amenable to accept.

History

JW originated as a branch of the Bible Student Movement, which developed in Pennsylvania, in the 1870s by Charles Taze Russell, who also co-founded Zion's Watch Tower Tract Society in 1881. Since 1931 its members are called JWs based on biblical passages (Isaiah 43:10 to 12 and Hebrews 12:1, 2). JWs have a close tied community and usually meet three times a week in the Kingdom Hall for religious discussion based upon topics from its official publications, The Watchtower and Awake! The main principles are that the Bible is infallible and that errors were introduced into all denominations through its misinterpretation. JWs believe in the literal interpretation of the bible and salvation is dependent on being faithful to the word of Jehovah. The JW beliefs (The Watchtower, 2009) are as follows: (i) Christ's second coming and Armageddon are imminent and involve God restoring humans and the Earth to the perfection of Eden; (ii) a righteous 144 000 will be resurrected to a royal priesthood in Heaven, the rest of humanity being resurrected to a lower plane; (iii) the soul is a living thing and may die; and (iv) death is a state of non-conscious, non-existence. Russell died in 1916, succeeded by Joseph Rutherford, who was followed by Nathan Knorr in 1942, after which control moved to a leading council. The Watchtower, the official journal of the JWs, published the following medical related doctrines: (i) blood transfusions were deemed unacceptable in 1945; (ii) vaccinations were deemed acceptable in 1952;9 and (iii) organ transplants were equated to cannibalism in 1967 (deemed a matter of conscience or choice in 1980).

Belief about blood

A basic teaching of the faith of JWsis that life is sacred. They believe that life is given by God and belongs to God and that

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He is the only one with the right to determine how to use it. This basic premise is the basis for the following action policies. They are politically neutral, do not recognize secular authority and salute flags, pledge allegiance, join service organizations, enlist in the military, take any interest in civil government, must satisfy a minimum monthly time requirement to their ministry and they refuse blood transfusions. JWs believe that the Bible is the true word of God. Their beliefs and teachings are based on various Biblical passages(Watch Tower Bible and Tract Society, 2008).In 1945, The Watchtower prohibited the practice of blood transfusions, based on the strict literal interpretation of 3 biblical passages: (i) Genesis 9:4, 'But flesh with the life thereof, which is the blood thereof, shall you not eat.' (ii) Leviticus 17:10,'And whatever man there be of the house of Israel, or of the strangers that sojourn among you, that eats any manner of blood; I will even set my face against that soul that eats blood, and will cut him off from among his people.'(iii) Acts 15:29, 'that you abstain from meats offered to idols, and from blood, and from things strangled, and from fornication, from which if you keep yourselves, you shall do well. Fare you well.' JWs believe that human blood is sacred and a potential vector for sin, whereas Christ's blood is Holy and is the only blood that can redeem them. Therefore, they take the view that putting the blood of another creature into their bodies [intravenous (IV) or oral routes] violates biblical law. The prohibition of blood transfusion is the golden rule and is a sign of respect for the sanctity of life. JWs believe that anyone who willingly transfuses blood breaks divine law and loses any hope of achieving eternality. Furthermore, those who are unrepentant for their action may undergo ostracism and excommunication from the organization. They also state there is no denial to people transfused against their will, or by mistake, or against children whose behavior was taken by physicians to maintain health and life. They also emphasize the support and assistance for those who wish to continue to be followers of the faith. JWs have 13 Hospital Liaison Committees working in Korea and 1700 throughout the world. These committees are available at any time to assist with the management of patients in preparing for elective or emergency surgical procedures. Where the patient has consented, they also assist clinicians in finding suitable treatment options for individual JW patients. These maintain lists of clinicians with considerable experience and these can be shared on request on a case-by-case basis. The development of transfusion therapy has brought about a change of the position of JW on what may be considered acceptable. The Watchtower Society states that blood fractions may be used by a personal conscientious decision and blood fractions (plasma proteins and bilirubin) 'naturally' move between mother and fetus, and therefore, other minor fractions may be considered acceptable in 1990.Table1summarizes the acceptability of blood products and transfusion related procedures in JWs (Lawson *et al.,* 2015), (Mason *et al.,* 2015).

Ethical and Legal Issues

An adult with capacity has the right to receive sufficient information to make an informed consent about the recommended treatment and may choose to accept or refuse the physician's recommendation. JWs' refusal of blood transfusion is a constitutionally protected right in many countries. Administration of blood products against the wishes of a competent patient is a potentially criminal act subject to prosecution. The refusal of blood transfusions causes an ethical dilemma between the patient's autonomy and the physician's obligation. The case of Schloendorff v. New York Hospital [105 N.E. 92 (NY 1914)] is often cited as the landmark case for patient's autonomy or the right of a competent adult to accept or refuse care and need of consent for medical procedures. Judge Benjamin Cardozo wrote in the court's opinion that "every human being of adult years and sound mind has a right to determine what shall be done with his own body, and a surgeon who performs an operation without his patient's consent commits an assault for which he is liable in damages. This is true except in cases of emergency where the patient is unconscious and where it is necessary to operate before consent can be obtained."Many precedents have since supported this right, including the Roe v. Wade decision [410 U.S. 113 (1973)] and Harrell v. St. Mary's Hospital Fetus decision (Fla. Dist. Ct. App. 1996).In legal cases from 1960s, however, the courts often challenged the JW patient's autonomy to refuse blood on grounds that they were "irrational" in balancing risks and benefits. By the 1980s, the courts began deciding in favor of the JW patients based on the rights of a capacitated adult to accept or decline medical intervention. The landmark legal case is Malette v. Shulman in 1990 in Canada (72 O.R. 2d 417). As a result, citing physicians for battery when transfusing patients against their will became possible in the court of law. Recently, the Supreme Court of Korea (2009DO14407) have also ruled for the first time that the woman with capacity undergoing total hip replacement arthroplasty must be allowed to refuse blood transfusion. In this case, the Supreme Court think that the main issue should be which value is more superior between "the self-determination right by a patient" and "protecting life duty by a doctor" when a Jehovah's Witness patient reveals his intention of refusal of blood transfusion. When these two conflicting values are compared, the former is not always superior to the latter. The former is equal to the latter only when special conditions are met. Only in this special exceptional case, the doctor can be exempted from the duty of protecting life and he can choose any proper treatment by using his professional discretion (Kim, 2014).

JWs carry an advance medical directive cardprohibiting any blood transfusions. These are legally binding documents outlining treatments an individual would not consent to in the future, if they lost capacity. These advance directives are helpful to both patients and physicians because they allow JWs to clearly delineate their individual decisions regarding which derivatives of plasma or cellular components and/or blood conservation strategies are acceptable. Physicians must respect the wishes of patients expressed in an advance directive card that is correctly signed unless physicians have good reason to believe that the patient has changed their wishes since signing the document. This form releases the healthcare providers and the institution from liability. Physicians should always keep in mind about principles of bioethics and act in the patient's best interest. While honoring the patient autonomy and freedom of religious practice, physicians must adhere to the "Hippocratic Oath" that instructs them to "apply, for the benefits of the sick, all measures which are required."The physician's desire for nonmaleficence and beneficence may conflict with patient's autonomy. Physicians must disclose any risks associated with refusal of a potentially life-saving blood transfusion and advise on acceptable alternative treatment strategies and the capability of the healthcare facility to provide them. The physician must understand the JWs' beliefs and views regarding blood transfusion and take time to engage in unbiased dialogue with the patient. The physician should discuss and document specific acceptances and objections, the limitation, and the changes to the plan for intraoperative management. The JW patient should be informed that currently there are no well-accepted oxygen-carrying blood substitutes, which is the typical objective of a red blood cell (RBC) transfusion. In particular, anesthesiologists must be certain they are capable of fulfilling the patient's needs; otherwise, they should not agree to provide anesthesia. Anesthesiologists have the right to refuse to anesthetize an individual in an elective situation, and both anesthesiologist and surgeon should provide nonemergency care to the patient only if all parties can agree on the approach to blood management. If a medical professional should feel they cannot work under the proposed constraints associated with refusal to use blood products, a referral to another appropriately skilled clinical or team should be made and recorded in the notes and an appropriate explanation be given to the family. Physicians must respect the patient's decision on the plan of care even in critical circumstances. If the patient has lost capacity but has an advance directive with documented decisions, no one, including family members, can change the documented treatment plan. If the lost capacity patient has no advance directive, then the family member or person with the Power of Attorney must make healthcare decisions in harmony with the patient's known wishes, which includes not merely the patient's clinical interests, but their belief, values. Physicians cannot be considered as violation of their legal or professional responsibilities when they honor the right of a competent adult patient to decline medical treatment. Conversely, physicians may be held liable and lay themselves open to legal action by the patient if they fail to respect the competent patient's choice to refuse blood transfusion. Particularly complex management issues and legal requirements arise when children of JWs are involved. JW children may not certainly appreciate potential risk of death with refusal of blood. Patients who identified as religious faith may influence medical recovery by asking for prayers from one's faith community, having prayers answered, and God providing care providers with knowledge and guidance (Woods and Ironson, 1999) (Hoffman, 2016). JW parents, therefore, may perceive their religious faith in their child's care as critical to holistic care and recovery.

In pediatrics, parents have the authority to give consent by proxy, based on the assumption that their interests lie in protecting the child's welfare. However, the physician's legal and ethical obligation finally rests with the child patient and not the wishes of the parents (Kohrman *et al.,* 1995).Woolley provided an overview of legal decisions among Western countries regarding forced transfusion of JW children and adolescents. In the case of children, courts in the United States, Canada, United Kingdom, and Australia recognize parental rights to raise children as they see fit under the condition that parents do not make decisions that may permanently harm their child (Dwyer, 1996) (Hoffman, 2016).As such, courts in the western world consistently rule in favor of overriding parental objections when the child's physical safety is at risk (Woolley, 2005) (Hoffman, 2016). In the review of several court publications of Korea concerning parent-physician disagreements over the care of children, the court also gave a hand to physicians, especially when parental objections were based on religion (Kim, 2015). For emergency situations Where in the status of JW is not known, there is no advance medical directive card, and there is no time to secure an informed consent, the physician caring for the patient is expected to perform to the best of their ability, which may include the administration of blood. Relatives or associates who suggest that a patient would not accept a blood transfusion must be invited to produce evidence of the patient's JW status in the form of an applicable advance directive card and without which blood should be administered in life threatening circumstances. And if the patient is JW, it is the duty of the physician to respect the competently expressed views of the patient even if this amounts to death for lack of blood transfusion (Milligan *et al.,* 2004). In urgent situations in which the patient is unconscious or mentally incompetent and the position regarding alternative treatment to blood is unclear or there is no consensus among family members, best practice favors that physicians seek guidance from the hospital's ethics committee and legal advisors regarding appropriate action to be taken.

Preoperative Management

Bleeding has been shown to increase morbidity and mortality, especially with blood loss of >500 mL in adults, irrespective of preoperative Hemoglobin (Hb) levels (Spence *et al.,* 1990). Major surgery (defined as blood loss > 500 ml) should be performed only if the medical center has the facility for all elements of patient management. JWs need a whole approach throughout the perioperative period. A preoperative multidisciplinary discussion is obligatory for planning surgery. This discussion should include, to a minimum, a senior anesthesiologist, a senior surgeon, a senior hematologist, a senior nurse and the Hospital Liaison Committee, with the patient's consent. Basically, the preoperative evaluation should include a medical chart review and personal or family history of unexpected bleeding or clotting issues following medical or dental procedures and current medications or herbal supplements that may cause coagulopathy and laboratory testing that includes a complete blood count, iron studies (iron level, total iron binding capacity, and ferritin), a reticulocyte count, vitamin B_{12}, folate, and coagulation profile. In addition, physicians establish and record which, if any, fractions of blood components are acceptable to the JW patient and the extent of any refusal, particularly in situations where the withholding of blood is likely to lead to loss of life.

Preoperative anemia: The 3 main causes of anemia are acute blood loss, red cell destruction, and decreased erythropoiesis. Generally, a transfusion trigger of an Hb level of 6-8 g/dL or less (restrictive strategy) can be tolerated by relatively healthy, younger patients. Those who are older, critically ill, or have severe cardio respiratory disease may require a transfusion trigger of 9-10 g/dL (liberal strategy) (Consensus conference, 1988). A multicenter, randomized, controlled clinical trial demonstrated that a restrictive strategy had a lower 30-day mortality compared to a liberal strategy (Hébert *et al.,* 1999). Anemia tolerance to adapt to low hemoglobin levels is a key principle in JW, and studies have shown that healthy individuals tolerate an acute isovolemic drop in hemoglobin as low as 4-5 g/dL with no signs of tissue hypoxia (Weiskopf *et al.,* 1998). Several reviews also suggest that mortality as a result of lack of blood is a relatively uncommon event in JWs, as is anemia-related death. However, Hb concentrations <5 g/dL are associated with an increased morbidity and mortality, with an odds ratio of 1.82–2.04 for every 1 g/dL decrease in Hb (Shander *et al.,* 2014), and Spence and colleagues (1990) demonstrated that Hb < 5 g/dL concentration becomes an independent predictor of mortality. For elective surgeries,

preoperative correction of anemia (if Hb is < 7-8 g/dl) can be achieved by administering recombinant erythropoietin (rEPO), which is the most frequently used erythropoiesis-stimulating agent (ESA) such as epoetin alfa. The response appears to be dose dependent with an increase in reticulocyte count being seen within 10 days and new erythropoiesis within 1–6 weeks. Preoperative regimens of epoetin alfa are summarized in Table 2 (McCartney *et al.,* 2014). A systematic review for the International Study of Perioperative Transfusion (ISPOT) group and other studies have shown an increase in Hb concentration and reduction in allogeneic transfusion with both the pre- and postoperative use of rEPO. While the benefits of ESAs often outweigh the risks for patients who cannot be transfused, nonpharmacologic and pharmacologic methods should be considered for deep venous thrombosis prophylaxis.
In addition, either oral or I.V. iron should be supplemented to correct any iron deficiency. Nutritional anemia, in particular iron deficiency anemia, is common in the surgical population. If surgery is performed within 6 weeks or emergency case, the patient does not respond to oral iron and their Hb is still < 13 g/dl, IV iron should be considered. Due to poor oral absorption secondary to inflammatory processes caused by the postoperative surgical stress, poor patient compliance due to gastrointestinal side effects, and the delayed efficacy of oral iron supplementation, IV replacement is preferred over oral therapy. Additional administration may be needed because the effect of the IV iron on erythropoiesis may only last up to 10 days. Ferric gluconate (ferrlecit) and iron sucrose (venoferrum) are preferred to LMW iron dextran due to faster administration and fewer side effects. Vitamin B_{12} and folate should also be replaced if a preoperative deficiency is identified.

Correction of coagulopathy: Although a review of the reference recommends against routine preoperative anticoagulation screening for patients with negative bleeding history, coagulation profiles should be checked for JWs. Any subsequent management depends on the detection of a preoperative abnormality. The first step of the management is to discontinue any drugs (NSAIDs, antiplatelet agents, warfarin) or herbal remedies (garlic or ginger) for a certain period of time to correct coagulopathies. The American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines can provide guidance on the appropriate timeframe for holding these medications based on half-life and bleeding risk for intermediate to high risk procedures (Table 3) (Narouze *et al.,* 2015). These guidelines are for near-complete resolution of drug effects, and in cases where there may be more thrombotic concerns, some would recommend a shorter interval (2–3 half-lives) (Levy *et al.,* 2013). Common preoperative situation is antagonism of anticoagulant drugs, such as warfarin. Vitamin K is essential for the production of clotting factors II, VII, IX, and X and proteins C, S, and Z. The IV Vitamin K is associated with faster correction of international normalized ratio (4–8 h) vs oral (up to 24 h), which should be given slowly 10 mg over 30-60 min. (repeated after 12 h if required) because of severe anaphylactoid reactions. Prothrombin complex concentrates (Beriplex, Octaplex) provide a source of the four vitamin K dependent coagulation factors, which is a well known antagonist of warfarin excess. The initial dose varies depending on the international normalized ratio and is given with vitamin K. There are several case reports discussing its successful use in JWs (Bhardwaj *et al.,* 2007) with a single bolus of 20 IU/kg over 15 min. Octaplex does not contain human albumin and may be more acceptable to JWs. Recombinant factor VIII and IX concentrates may have a role in patients who refuse cryoprecipitate or fresh frozen plasma. Bolliger and colleagues (2009) described their use, with other agents, in JWs, with successful prevention of major blood loss and coagulopathy. Recombinant factor VIIa (rFVIIa, off-label use) is a more acceptable agent to JWs, which is produced without human blood or plasma. It improves thrombin generation after vascular injury and may also inhibit fibrinolysis by activating thrombin-activatable fibrinolysis inhibitor. A common optimal dose is 40-65 g/kg, repeated after 15-30 min. if no response. Although successful results have been achieved in hemorrhagic situations (cardiac surgery, postpartum hemorrhage), current evidence does not show that rFVIIa reduces mortality or improves other direct outcomes. Thromboembolic events are increased by use of rFVIIa to treat spontaneous intracranial hemorrhage and in adult cardiac surgery (Lipworth *et al.,* 2012). Desmopressin is a synthetic analogue of antidiuretic hormone vasopressin without its vasoconstrictive effects. It stimulates hepatic release of clotting factor VIII and endothelial release of tissue plasminogen activator and von Willebrand factor (vWF). Possibly, the release of vWF leads to an increase of platelet adhesiveness, resulting in a significant shortening of the bleeding time. A preoperative test dose is 0.3 ug/kg IV over 30 min. to ascertain patient response. Its use for hemophilia and von Willebrand disease is well known. Several studies have also reported a beneficial effect in JW patients, however, Cochrane review states that while desmopressin reduces perioperative blood loss, the benefit is clinically meaningless (Carless *et al.,* 2004).

Intraoperative Management

One of the most important plans to reduce the risk of transfusion in JW patients is to minimize blood loss. Routine monitoring of blood loss and coagulopathy through visual evaluation, laboratory tests, and perioperative monitoring [heart rate, blood pressure (BP), oxygen saturation, and urine output] is essential. For the evaluation of ongoing coagulopathy, surgeons and anesthesiologists need to inspect the surgical field of excessive microvascular bleeding and to conduct the laboratory testing of coagulation profile [thromboelastography (TEG) or rotational thromboelastometry (ROTEM)], Coagulopathy can be corrected intraoperatively as discussed earlier.

Surgical measures: The main principles of 'bloodless surgery' are meticulous hemostasis. A very experienced surgeon with expertise in bloodless surgery have to operate on patients with high risk of bleeding. Use minimally invasive technique (endoscopic or laparoscopic), hemostatic devices (diathermy, ultrasonic scalpels, local vasoconstrictor injection), and topical hemostatics (fibrin glue, sealant, bone wax). If surgery is complex and lengthy, a staged surgery should be considered. Also, positioning by elevation of operation site, arterial tourniquets of peripheral limb or joint, and anti-shock garments in trauma or obstetric patients by compression of the abdomen and lower limbs can have profound effects on the rate of bleeding.

Blood transfusion methods: *Autologous blood transfusion.* Autologous blood transfusion is the collection of blood from a single patient and reinfusion back to the same patient when required. This is in contrast to allogenic blood transfusion where blood from anonymous donors is transfused to the recipient.

Table 1. Acceptability of different blood products and transfusion related procedures in JWs

Generally not acceptable	May be acceptable	Generally acceptable
Red cells	Red cell fractions: Hb (human, animal, synthetic, e.g. Hemopure®)	Crystalloids and colloids Rep Orecombinant factor VII a artificial blood substitutes
White cells	White cell fractions: Interferons or Interleukins	
Plasma (fresh frozen plasma)	Plasma fractions: Albumin, Globulins including immunoglobulins, Cryoprecipitate, Clotting factors	
Platelets	Platelet fractions: Platelet factor 4	
PAD	Acute hypervolemic hemodilution* Acute normovolemic Hemodilution* Intraoperative/postoperative cell salvage* Cardiopulmonary bypass* Extracorporeal membraneoxygenation* Renal dialysis* Plasmapheresisepidural blood patch* Transplants	

Abbreviations: Hb, hemoglobin; rEPO, recombinant erythropoietin; PAD, preoperative autologous donation
*a continuous contact with their own circulation and the circuit with no priming with allogenic blood

Table 2. Suggested dosing of EPO, IV iron for preoperative anemia

Etiology of anemia	Elective surgery of>3 wk beforesurgery	Elective surgery of <3 wk before surgery
Anemia of Ch disease with normal iron stores (ferritin >100 ng/mL, iron saturation >20%)	EPO 600 Units/kg SC weekly starting 21 d before surgery, oral iron	EPO 300 Units/kg SC daily, starting 10 d Before surgery and up to 4 d Postoperatively, oral iron
Anemia of Ch disease with low iron stores (ferritin <100 ng/mL, iron saturation <20%)	EPO 600 Units/kg SC with 125 mg ferric Gluconate IV weekly starting 21 d Before surgery	EPO 300 Units/kg SC with 125 mg ferric Gluconate IV daily, starting 10 d before Surgery and up to 4 d postoperatively
Iron deficiency anemia (ferritin <20 ng/mL)	LMW iron dextran 1000 mg IV	LMW iron dextran 1000 mg IV

Abbreviations: Ch, chronic; EPO, epoetin alfa; IV, intravenously; LMW, low molecular weight; SC, subcutaneously

Table 3. Half-life and recommendations for holding medications before intermediate to high risk bleeding procedures based on 2015 ASRA guidelines

Drug	Half-Life	Stop Before Surgery
Aspirin	15–20 min, irreversible	Continue if secondary prevention, hold for minimum of 6 d If primary prevention
Clopidogrel	7–8 h, irreversible	7 d
Prasugrel	2–15 h, irreversible	7-10 d
Ticagrelor	6–9 h	5 d
Dipyridamole	40 min alpha/10 h beta	2 d
Dabigatran	12–17 h (28 h renal disease)	4–5 d (6 d renal disease)
Rivaroxaban	9–13 h	3 d
Apixaban	15–24 h	3-5 d
Warfarin	Variable	5 d and INR normalized

Abbreviations: ASRA, American Society of Regional Anesthesia and Pain Medicine; INR, international normalized ratio

The main purpose of autologous blood transfusion is to reduce the risk of transmission of infection and to protect an increasingly scarce resource. There are 3 main methods of autologous transfusion: Preoperative autologous donation (PAD), Acute normovolemic hemodilution (ANH), and Intraoperative and postoperative blood salvage (Cell saver). In PAD, typically 4 units of whole blood are collected weeks in advance of an elective procedure, stored in the blood bank and transfused back to the patient when required. PAD is unacceptable to JWs because of the separation of blood from the body. With the ANH technique, whole blood is collected at the induction of anesthesia and blood volume restored by crystalloid or colloid. Consequently, surgical blood loss will have fewer red cells and reduced factors per milliliter of blood, and whole blood is then reinfused when the majority of anticipated blood loss is complete. The reduced blood viscosity of hemodilution enhances microcirculation flow and improves tissue perfusion and enhances cardiac output with reduced myocardial O_2 consumption while reinfusion of platelets and coagulation factors corrects any coagulopathy that arises out of perioperative blood loss. This is particularly useful in cardiac surgery, where the harvested blood is not heparinized, cooled, or run through a CPB circuit, providing improved coagulation after separation from CPB. This may be acceptable to JWs only if a closed circuit is used (Shander *et al.,* 2004), (Marsh *et al.,* 2002). An alternative and more acceptable approach is acute hypervolemic hemodilution, which does not involve withdrawal of blood. This technique has been studied in JW undergoing major surgery and found to be well tolerated. However, acute hypervolemic hemodilution cannot replace ANH to reduce homologous transfusions, but for blood losses <40% of blood volume acute hypervolemic hemodilution appears to be superior. This technique may be inappropriate in patients with cardiac compromise (Singbartl *et al.,* 1999).

Intraoperative and postoperative cell salvage (CS) is the collection and reinfusion of blood lost during and after surgery. Shed blood is collected from suction or/and surgical drains and centrifuged, washed, mixed with heparinized saline and reinfused back to the patient via a leukocyte depletion filter (LDF). The RBCs are suspended in normal saline with a hematocrit level of 50%-80%. The process removes free Hb, plasma, coagulation factors, platelets, heparin, cytokines, and activated leukocytes. It may be acceptable to some JW if the blood is not stored and must be kept in a continuous contact with the patient's own circulation. It is used when the anticipated blood loss is 20% or more of the patient's estimated blood volume and has the advantage that the returned blood is warm and has normal concentrations of 2,3-DPG (Sikorski *et al.,* 2017). and normal biconcave disc shape to fresh blood (Hovav *et al.,* 1999).

It is contraindicated in situations, where the blood is likely to be contaminated (infection, amniotic fluid, bowel contents, bone chips, malignancy) and sickle cell anemia. There are many potential complications associated with CS, such as dilutional coagulopathy (when > 3,000 mL infused), non-immune hemolysis, air or fat embolism, febrile non-hemolytic transfusion reactions, infection, microaggregates causing microembolism, and incomplete washing leading to contamination with activated leucocytes, cytokines. However, the 6-year study period of the Cleveland Clinic suggested that CS is safer than allogenic blood transfusion as well as PAD, the incidence of adverse events of CS was 0.027% compared to 0.14% with allogenic transfusion and 0.16% with PAD (Domen, 1998). CS is a standard tool used for blood conservation (Carless *et al.,* 2010), and considered safe and efficacious for orthopedic, especially cardiac surgeries (Al-Mandhari *et al.,* 2015), (Goel *et al.,* 2007), and (Wang *et al.,* 2009). The evidence for their use in obstetrics or malignancy is less strong, but LDFs help to remove or lessen tumor cells (Kumar *et al.,* 2014), (Elias *et al.,* 2001), WBCs, and amniotic fluid, besides bacterial infection.

Red cell substitutes: Due to the increased demand for blood transfusion and concerns about blood-borne infections, development of artificial blood substitutes, especially Hb-based oxygen carriers, is under intensive focus. However, although many important steps have been taken to date, no oxygen-carrying blood substitutes are approved for use by the U.S. Food and Drug Administration (FDA). Side effects and short half-life are the two main reasons that they did not met criteria for being approved. RBC substitutes are of mainly two types: perfluorocarbon (PFCs) and Hb-based oxygen carriers (HBOCs). HBOCs deliver oxygen by facilitated diffusion using human or bovine Hb or recombinant Hb. Bovine Hb has some advantages over human Hb, including unlimited access, higher resistance to degradation of heme, the use of chloride ion instead of 2,3-DPG as an allosteric effector present in plasma, and possibly acceptable to JWs. Currently, a polymerized bovine Hemopure has been used for management of anemia in JW patients under compassionate-use FDA guidelines with varying success but is rejected by the U.S. FDA due to its adverse effects including hypertension, safety and toxicity issues attributed to vasoactivity, and oxidative stress. Another polymerized Bovine Oxyglobin is the first product approved by the U.S. FDA and the European commission for veterinary use. Human derived Hemospan and MP4 is now under clinical trial as an oxygen carrier. PFCs are liquid perfluorocarbons, emulsified with a phospholipid surfactant suspended in saline, that dissolve large amounts of oxygen. They are chemically inert and totally artificial. One main advantage of PFCs is for people refusing blood or proteins derived from humans or animals. The 1st generation product Fluosol-DA approved by the FDA for use in percutaneous transluminal coronary angioplasty has been withdrawn from the market due to marginal efficacy, a short effective half-life, temperature instability, low oxygen-carrying capacity, and adverse effects such as acute complement activation and disruption of pulmonary surfactant. The 2nd generation product are rejected by clinical trials due to some side effects such as complications in determining the effective dose for administration (OxyFlour) and increased risk of stroke (Oxygent) (Tao *et al.,* 2014).

Deliberate hypotensive anesthesia: Deliberate hypotensive anesthesia is a widely used technique for decreasing intraoperative bleeding and improving the visibility of the operating field. Deliberate hypotension (DH) is described as controlled reduction and maintenance of BP in range of mean arterial pressure (MAP) of 50-65 mmHg or intraoperative reduction of baseline MAP to 30%. The MAP range is based on the lower limits of autoregulation of cerebral blood flow. It has been indicated in oromaxillofacial surgery, endoscopic sinus or middle ear microsurgery, spinal surgery and other neurosurgery (aneurysm), major orthopedic surgery (hip or knee replacement, spinal), prostatectomy, cardiovascular surgery, liver transplant surgery and surgeries on JWs. Various pharmacological agents and general interventions can induce deliberate hypotension. Pharmacological agents can be classified by how to use. Primary agents (used only alone) include inhalation agents (desflurane, isoflurane, sevoflurane), vasodilators (nitroglycerin, sodium nitroprusside, trimethaphan, adenosine, and alprostadil), remifentanil, and agents used in epidural or spinal anesthesia. Secondary agents (used only as adjuncts with primary agents) include angiotensin-converting enzyme inhibitors and clonidine. Also, some agents can be used alone or adjunctively: calcium channel blockers, -adrenoceptor antagonists, and fenoldopam. General interventions for DH are positioning and the mode of ventilation. Placing the operation site higher than the heart reduces the hydrostatic BP, thus decreasing the driving pressure for blood extravasation. In addition, the anesthesiologist can cause hyperventilation to produce hypocapnia induced cerebral vasoconstriction in order to reduce blood loss during neurosurgical procedures and also to decrease venous return by increased intrathoracic pressure, which may reduce cardiac output. Degoute (2007) recommended either the use of an epidural anesthesia or the combination of remifentanil with either propofol or an inhalation agent (isoflurane, desflurane, sevoflurane) for the greatest efficacy and ease of use to toxicity ratio. The use of epidural anesthesia, however, is limited to abdominal or lower extremity surgery.

Deliberate hypothermia: Deliberate hypothermia has been used successfully in JW patients in conjunction with other therapies by decreasing metabolic O_2 requirements (about 7% for each degree below the basal level) and increasing the dissolved portion of oxygen without impairing oxygen extraction. The core temperature monitoring can be done using tympanic membrane, pulmonary artery, distal portion of the esophagus and nasopharynx probes because These sites constitute anatomical areas of highly perfused tissues whose temperature is uniform and high in comparison to the rest of the body (Sessler, 2014). Mild hypothermia is defined as ranging from 1.5C to 2C below body core temperature (Sessler, 2014) while moderate hypothermia constitutes a body core temperature of 35C. The three most common complications associated with mild hypothermia are a three-fold increase in morbid myocardial events (Frank *et al.,* 1997), a three-fold increase in the risk of surgical wounds infection and prolonged hospitalization (Kurz *et al.,* 1996), and finally, increased blood loss and transfusion requirements (Smied *et al.,* 1996). Intraoperative hypothermia to target core temperature near 35C can usually be achieved passively simply by uncovering patients in a typically cool operating room. Passive cooling, however, requires administration of sufficient anesthesia to prevent thermoregulatory vasoconstriction. If rapid cooling is required, infusion of refrigerated IV fluids is effective (reducing mean body temperature 0.5C/L) (Sessler *et al.,* 1990).

A cooling blanket is relatively not efficient because little skin surface contacts the mattress. Deliberate hypothermia is usually accompanied by hemodilution to counteract a potential detrimental effect of increased blood viscosity and systemic vascular resistance. Though hypothermia causes an increased affinity between oxygen and hemoglobin, it does not impair tissue oxygen extraction. Deliberate hypotension and hypothermia should be used judiciously in patients with significant cardiovascular, cerebrovascular, hepatic, and renal compromise while particularly effective in reducing transfusion requirements in JW patients.

Pharmaceutical Agents: Although ANH, CS, DH, and deliberate hypothermia are the major intraoperative techniques utilized in the JW who refuses blood transfusion, various pharmaceutical agents may be of benefit as well. As previously discussed, erythropoiesis can be enhanced preoperatively and postoperatively using erythropoietic agents: rEPO and iron, vitamin B_{12}, and folic acid supplementation.

Antifibrinolytics. Fibrinolysis is a physiological process where the activated plasminogen removes excess fibrin and promotes better fibrin clot formation and wound healing. Tissue plasminogen activator (t-PA) and other activators of plasminogen are first line agents in lysis therapy. Inhibitors of this process act at the step where plasminogen is converted to plasmin, by reversely blocking the lysine binding sites of plasmin or by active inhibition of plasmin via serine protease inhibition. The drugs used for inhibition of fibrinolysis are the lysine analogues, tranexamic acid and ε-aminocaproic acid, and the serine protease inhibitor, aprotinin.

Aprotinin. Aprotinin is a broad-spectrum protease inhibitor isolated from bovine lung that reversibly complexes with the active serine residue in various proteases in plasma, reversibly inhibits trypsin, kallikrein, plasmin, elastase, and is the most potent antifibrinolytic agent. Aprotinin clearly decreases bleeding and transfusion requirements. However, The Blood Conservation Using Antifibrinolytics in a Randomized Trial (BART) study demonstrated an increased risk of death with aprotinin, secondary to adverse effects on renal and cardiac function. Despite multiple studies reporting its efficacy, several reports questioned its safety, leading to its temporary removal from the U.S. market. After a reanalysis of the data, the European Medicines Agency recommended in 2012 that its suspension in the European Union be lifted, and it is currently being reintroduced in Europe for prophylactic use in adult patients who are at high risk of major blood loss undergoing isolated coronary artery bypass graft surgery. The European Society of Anesthesiology task force reported on aprotinin use in a perioperative setting and has current suggestions for its use (European Society of Anesthesiology Task Force, 2015).

Tranexamic acid. Tranexamic acid is a lysine analog that reversibly binds to the lysine-binding sites on plasminogen to inhibit its affinity to bind to multiple proteins including fibrin. It is 7 to 10 times more potent than ε-aminocaproic acid on a molar base and has more sustained antifibrinolytic activity in tissues (Nilsson, 1980), (Andersson *et al.,* 1968).

ε-Aminocaproic acid. ε-Aminocaproic acid is a synthetic inhibitor of plasminogen activation. Compared to most countries using Tranexamic acid, it is most extensively used in the U.S. for costs. Side effects include hypotension, cardiac arrhythmias, rhabdomyolysis, and renal dysfunction. The efficacy of tranexamic acid and aprotinin to reduce blood loss and transfusion is established in patients undergoing cardiac surgery and liver transplantation with no indication of an increased risk of thrombotic complications (Molenaar *et al.,* 2007). However, there are far less safety and efficacy data regarding ε-aminocaproic acid, and further large safety trials are warranted.

Postoperative Management

The aims of postoperative management are to minimize continuing blood loss, promote hemostasis, correct any coagulation defects and optimize oxygen delivery and consumption. Optimizing oxygen delivery is dependent on Hb concentration, cardiac output, and Hb saturation which may be manipulated using fluids, inotropes and increasing the FiO_2. Oxygen consumption is minimized by continuation of hypothermia, sedation, and paralysis. Postoperative CS can be employed in managing blood loss and subsequent anemia. Care was taken to limit the blood of volume taken for analysis by using of pediatric sampling tubes and microanalyzers. Point-of-care tests arterial or venous blood gas sampling and TEG/ROTEM should be employed. Pharmacological methods include the administration of hemostatic agents to stop bleeding, erythropoietic agents to promote RBC production, antihypertensives to reduce rebleeding associated with hypertension, and the conservative use of anticoagulants and antiplatelet agents. Additionally, maintaining normovolemia with crystalloid or colloid solutions in the face of anemia is crucial to maintaining adequate tissue perfusion.

Conclusion

The number of JW is increasing worldwide and management of the JW patients who refuses blood transfusion involves specific medical, ethical, and legal considerations. The physician must be knowledgeable about the JWs' beliefs on blood transfusion and the available resources at his or her institution. Successful care requires a holistic approach focusing on preoperative optimization, referral to an appropriate environment for surgery, and perioperative blood-conservation techniques

REFERENCES

Al-Mandhari S, Maddali MM, Al-Bahrani MJ. 2015. Cell salvage during coronary artery bypass surgery and allogenic blood exposure. *Asian Cardiovasc Thorac Ann.,* 23:913-6.

Andersson L, Nilsoon IM, Colleen S, Granstrand B, Melander B. 1968. Role of urokinase and tissue activator in sustaining bleeding and the management thereof with EACA and AMCA. *Ann NY Acad Sci.,* 146:642–58.

Bhardwaj M, Bunsell R. 2007. Beriplex P/N: an alternative to fresh frozen plasma in severe haemorrhage. Anaesthesia., 62: 832–4.

Bolliger D, Sreeram G, Duncan A, Molinaro RJ, Szlam F, Chen EP, *et al.* 2009. Prophylactic use of factor IX concentrate in a Jehovah's Witness patient. *Ann Thorac Surg.,* 88:1666–8.

Carless PA, Henry DA, Moxey AJ, O'Connell D, Brown T, Fergusson DA. 2010. Cell salvage for minimising perioperative allogeneic blood transfusion. *Cochrane Database Syst Rev.,* 3:CD001888.

Carless PA, Stokes BJ, Moxey AJ, Henry DA. 2004. Desmopressin use for minimising perioperative allogenic blood transfusion. *Cochrane Database Sys Rev.,* 1:CD001884.

Consensus conference, 1988. Perioperative red blood cell transfusion. *JAMA*, 260(18):2700-3.

Degoute CS. 2007. Controlled hypotension: a guide to drug choice. *Drugs*, 67:1053-1076.

Domen RE. 1998. Adverse reactions associated with autologous blood transfusion: evaluation and incidence at a large academic hospital. *Transfusion*, 38:296-300.

Élias D, Billard V, Lapierre V. 2001. Use of the cell saver in oncologic surgery. *TATM*, 3:25- 8.

European Society of Anaesthesiology Task Force Reports on Place of Aprotinin in Clinical Anaesthesia. Aprotinin: is it time to reconsider? *Eur J Anaesthesiol.,* 2015;32:591–5.

Frank SM, Fleisher LA, Breslow MJ, Higgins MS, Olson KF, Kelly S. *et al.* 1997. Perioperative maintenance of normothermia reduces the incidence. of morbid cardiac events: a randomized clinical trial. *JAMA*, 277:1127-34.

Goel P, Pannu H, Mohan D, Arora R. 2007. Efficacy of cell saver in reducing homologous blood transfusions during OPCAB surgery: a prospective. randomized trial. *Transfus Med.,* 17:285-9.

Hébert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, *et al.* 1999. A multicenter, randomized, controlled clinical trial of. transfusion requirements in critical care. Transfusion requirements in critical care investigators, canadian critical care trials group. *N Engl J Med.,* 340:409-17

Hoffman A. 2016. Jehovah's Witness parents' refusal of blood transfusions: ethical considerations for psychologists. *Journal of Health Psychology.,* 21: 1556–65.

Hovav T, Yedgar S, Manny N, Barshtein G. 1999. Alteration of red cell aggregability and shape during blood storage. *Transfusion*, 39:277-81.

Kim MG. 2015. Autonomy rights on refusal of blood transfusion of Jehovah's Witness and it's limits. *Korean Journal of Family Law,* 29: 295-334.

Kim YT. 2014. A Study of the medical practice and the right of patients to self-determination- focusing on supreme court decision 2009 DO14407. Delivered on June 24, *The Korea Society of Law and Medicine,* 15:3-29.

Kohrman A, Clayton EW, Frader JE, Grodin MA, Moseley KL, Porter IH, *et al.* 1995. Informed consent, parental permission, and assent in pediatric. practice. *American Academy of Pediatrics,* 95:314-317.

Kumar N, Chen Y, Zaw AS, Nayak D, Ahmed Q, Soong R, *et al.* 2014. Use of intraoperative cell- salvage for autologous blood transfusions in. metastatic spine tumour surgery: a systematic review. *Lancet Oncol.,* 15:e33-41.

Kurz A, Sessler DI, Lenhardt RA. 1996. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of wound infections and temperature group. *N Engl Med.,* 344:1209-15.

Lawson T, Ralph C. 2015. Perioperative Jehovah's Witnesses: a review. *Br J Anaethe.,* 115:676-87.

Levy JH, Faraoni D, Spring JL, Douketis JD, Samama CM. 2013. Managing new oral anticoagulants in the perioperative and intensive care unit. setting. *Anesthesiology,* 118:1466–74.

Lipworth W, Kerridge I, Little M, Day R. 2012. Evidence and description in off-label prescribing: recombinant factor VIIa. *Br Med J.,* 344:d7926.

Marsh JC, Bevan DH. 2002. Haematological care of the Jehovah's Witness patient. *Br J Haematol.,* 119:25–37.

Mason CL, Tran CK. 2015. Caring for the Jehovah's Witness Parturient. *Anesth Analg.,* 121:1564–9

McCartney S, Guinn N, Roberson R, Broomer B, White W, Hill S. 2014. Jehovah's Witnesses and cardiac surgery: a single institution's experience. *Transfusion*, 54:2745–52.

Milligan LJ, Bellamy MC. 2004. Anaesthesia and critical care of Jehovah's Witnesses. *Contin Educ Anaesth Crit Care Pain.,* 4:35-9.

Molenaar IQ, Warnaar N, Groen H, Tenvergert EM, Slooff MJ, Porte RJ. 2007. Efficacy and safety of antifibrinolytic drugs in liver transplantation: a systematic review and meta- analysis. *Am J Transplant.,* 7:185–94.

Narouze S, Benzon HT, Provenzano DA, Buvanendran A, De Andres J, Deer TR, et al. 2015. Interventional spine and pain procedures in patients on antiplatelet and anti- coagulant medications: guidelines from the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain. *Reg Anesth Pain Med.,* 40:182–212.

Nilsson IM. 1980. Clinical pharmacology of aminocaproic and tranexamic acids. *J Clin Pathol Suppl (R Coll Pathol).,* 14:41–7.

Sessler DI, Moayeri A, Støen R, Glosten B, Hynson J, McGuire J. 1990. Thermoregulatory vasoconstriction decreases cutaneous heat loss. *Anesthesiology*, 73(4):656-60.

Sessler DI. 2014. Temperature regulation and monitoring. In: Miller RD, editors. Miller's Anesthesia. 8th ed. Elsevier, p1622-46.

Shander A, Javidroozi M, Naqvi S, Aregbeyen O, Caylan M, Demir S, *et al.* 2014. An update on mortality and morbidity in patients with very low postoperative hemoglobin levels who decline blood transfusion (CME). *Transfusion*, 54:2688–95.

Shander A, Rijhwani TS. 2004. Acute normovolemic hemodilution. *Transfusion*, 44(12Suppl):26S–34S.

Sikorski RA, Rizkalla NA, Yang WW, Frank SM. 2017. Autologous blood salvage in the era of patient blood management. *Vox Sang,* 112:499-510.

Singbartl K, Schleinzer W, Singbartl G. 1999. Hypervolemic hemodilution: an alternative to acute normovolemic hemodilution? a mathematical analysis. *J Surg Res.,* 86;206-12

Smied H, Kurz A, Sessler DI, Kozek S, Reiter A. 1996. Mild Intraoperative hypothermia increases blood loss and allogeneic transfusion requirements during total hip arthroplasty. *Lancet*., 347:289-92

Spence RK, Carson JA, Poses R, Pello M, Alexander J, Popovich J, *et al.* 1990. Elective surgery without transfusion: Influence of preoperative hemoglobin level and blood loss on mortality, *The American Journal of Surgery,* 159:320-4.

Tao Z, Ghoroghchian PP. 2014. Microparticle, nanoparticle, and stem cell-based oxygen carriers as advanced blood substitutes. *Trends Biotechnol.,* 32:466-73.

The Watchtower. Are all religions good? 2009(Aug).

Wang G, Bainbridge D, Martin J, Cheng D. 2009. The efficacy of an intraoperative cell saver during cardiac surgery: a meta-analysis of randomized trials. *Anesth Analg.,* 109:320-30.

Watch Tower Bible and Tract Society. Keep yourself in God's love. 2008.

Weiskopf RB, Viele MK, Feiner J, Kelley S, Lieberman J, Noorani M, *et al.* 1998. Human cardiovascular and metabolic response to acute, severe isovolemic anemia. *JAMA*., 279:217-21.

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