

# Management of patients who refuse blood transfusion

## Address for correspondence:

Dr. N Kiran Chand,  
Assistant Professor,  
Department of Anaesthesiology  
and Critical Care,  
Vijayanagar Institute of Medical  
Sciences Bellary,  
Karnataka - 583 101, India.  
E-mail: nkiranchand  
@yahoo.com

**N Kiran Chand, H Bala Subramanya, G Venkateswara Rao**

Department of Anaesthesiology and Critical Care, Vijayanagar Institute of Medical Sciences, Bellary, Karnataka, India

## ABSTRACT

A small group of people belonging to a certain religion, called Jehovah's witness do not accept blood transfusion or blood products, based on biblical readings. When such group of people are in need of health care, their faith and belief is an obstacle for their proper treatment, and poses legal, ethical and medical challenges for attending health care provider. Due to the rapid growth in the membership of this group worldwide, physicians attending hospitals should be prepared to manage such patients. Appropriate management of such patients entails understanding of ethical and legal issues involved, providing meticulous medical management, use of prohaemostatic agents, essential interventions and techniques to reduce blood loss and hence, reduce the risk of subsequent need for blood transfusion. An extensive literature search was performed using search engines such as Google scholar, PubMed, MEDLINE, science journals and textbooks using keywords like 'Jehovah's witness', 'blood haemodilution', 'blood salvage' and 'blood substitutes'.

**Key words:** Blood haemodilution, blood salvage, blood substitutes, Jehovah's witness

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## INTRODUCTION

A small group of patients refuse blood transfusion, usually based on religious beliefs and faith (e.g., Jehovah's witnesses [JW]). The JW religion, founded in 1872, by Charles Taze Russell during the Adventist movement in Pittsburgh is an international organization, the followers of which believe that the Bible is the true word of God. In 1931, the organization officially became known as the 'Jehovah's witnesses'.<sup>[1]</sup> They are politically neutral, do not salute flags, enlist in the military nor vote in public elections. They celebrate neither Christmas nor birthdays, and must satisfy a minimum monthly time requirement to their ministry.

In 1945, the governing body of the JW 'The Watchtower', introduced the blood ban, based on the strict literal interpretation of several scriptural passages of New world Translation of Bible such as:<sup>[2,3]</sup>

Everything that lives and moves will be food for you. Just as I gave you the green plants, I now give you everything.

However you must not eat meat that has its lifeblood still in it. New International Bible, Genesis 9:34.

Because the life of every creature is its blood. That is why, I have said to the Israelites, 'You must not eat the blood of any creature, because the life of every creature is its blood; anyone who eats it must be cut-off'. New International Bible, Leviticus 17:14.

It seemed good to the Holy Spirit and to us not to burden you with anything beyond the following requirements: You are to abstain from food sacrificed to idols, from blood, from the meat of strangled animals and from sexual immorality. You will do well to avoid these things. New International Bible, Acts 15:28-29.

Currently, there are more than 7.5 million JW globally and around 37,913 in India, and their number is rapidly increasing.<sup>[4,5]</sup>

When confronted with such set of patients, blood free major surgery will be a great challenge to both

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**Table 1: Position of the Jehovah's witness on medical treatment****Position**

Accept all forms of medical treatment except blood transfusions  
 Are not exercising a right to die  
 Are keen to cooperate with medical professionals

**Table 2: Acceptability of blood products and transfusion related procedures in Jehovah's witnesses**

Acceptability	Blood/products/related procedures
Unacceptable	Whole blood
	Packed red cells
	Plasma
	Autologous predonation
	Cardiopulmonary bypass
Acceptable	Renal dialysis
	Acute hypovolaemic haemodilution
	Recombinant erythropoietin
	Recombinant factor VIIa
	Platelets
May be acceptable ('matters of conscience')	Clotting factors
	Albumin
	Immunoglobulins
	Epidural blood patch
	Cell saver

the anaesthetic and surgical teams. It is important to explain all the available options to patients who refuse blood and blood products.<sup>[6,7]</sup>

It is also important to know the position of the JW on the medical treatment, [Table 1] and which blood or blood products are acceptable to them [Table 2].<sup>[3,8]</sup>

The problems associated with their management highlights a growing healthcare issue-the supply, safety, appropriate use of blood products and the techniques learnt from treating such patient may prove beneficial to all undergoing major surgery.

Relevant literature search was performed using search engines like Google scholar, PubMed, MEDLINE, professional websites, textbooks, and science journals to identify such studies using such keywords as 'Jehovah's witness', 'blood haemodilution' 'blood salvage' and 'blood substitutes' for the period 2005-2013. During the search, the authors have concentrated on randomized clinical trials, case reports, review articles, and editorials.

In this article, we will discuss the ethical and legal issues in addition to scientific and technical challenges for the anaesthesiologist and the surgeon.

**Ethical and legal issues**

Respect for patient's autonomy and human rights

require obtaining informed consent before any medical intervention. This is fundamental to good medical practice. The rejection of blood transfusions cause an ethical dilemma between the patient's freedom to accept or to reject a medical treatment even unto death (i.e., autonomy), and the physician's duty to provide optimal treatment.<sup>[9]</sup>

It is better to discuss with patients the specifics of blood transfusion refusal, if possible.<sup>[10,11]</sup> A mentally competent individual has an absolute moral and legal right to refuse or reject the consent for medical treatment or transfusion except when he has diminished decision-making capacity or a legal intervention mandates treatment.<sup>[12,13]</sup>

**Advance directives**

Many JW carry an 'advance directive' prohibiting blood transfusion and often have executed a detailed Health Care Advance Directive (Living Will). Copies are usually lodged with their General Practitioner, family and friends. Case law is now very clear that such an advance directive is legally binding.

**Emergency situations**

When the status of JW is not known, and there is neither blood card nor time for contemplation or no advance directive, the doctor caring for the patient is expected to perform to the best of their ability, which may include the administration of blood. Relatives or friends who suggest that a patient would not accept a blood transfusion must be asked to provide documentary evidence and without which blood should not be withheld in life-threatening circumstances. And if the patient is JW, it is the duty of the healthcare provider to respect the competently expressed views of the patient even if this amounts to death for lack of blood transfusion.<sup>[8]</sup>

**Children**

Based on the belief that any decision taken by parents or guardians, lie in safeguarding the interest of child welfare, they have the right to give consent by proxy. However, the physician's legal and ethical obligation finally rests with the child patient and not the wishes of the parents. The American Academy of Paediatrics recommends health care providers to recognise and respect the importance of religion in personal, spiritual and social lives of patients and 'to avoid unnecessary polarisation when conflict over religious practices arises'.<sup>[14]</sup>

For elective procedures, a full and candid discussion among the anaesthetists, surgeon, parents, and child (if

old enough to understand) is essential. It is important to convince that every attempt will be made to avoid blood, but also convey that a doctor would not allow a child to let die for lack of blood transfusion. In UK, children under 16 years of age can legally give consent if they can understand the issues involved (Gillick Competence). If consent for transfusion is refused and it is thought unreasonable to go ahead with surgery without the freedom to transfuse, a request to the appropriate courts for 'specific issue order' can be made, which allows transfusion without removing all parental authority. Where time does not permit application to the courts, blood should be given. Failure to give life-saving treatment to a child could render the doctor vulnerable to criminal prosecution.<sup>[8]</sup>

Various techniques and interventions for the pre-operative, intra-operative and post-operative strategies have been developed and used over time.

## PRE-OPERATIVE OPTIMISATION

Health care givers should take steps pre-operatively to minimise or plan for the risk factors that are associated with transfusions, such as stopping anticoagulation therapy, starting antifibrinolytic therapy or correcting pre-operative anaemia.<sup>[15,16]</sup> In the trauma and critical care, a higher index of suspicion for blood loss and a more aggressive approach including early surgical intervention should be instituted.<sup>[6,17]</sup>

Essentially, the pre-operative evaluation should include a medical chart review and questions regarding bleeding history (previous surgical complications, bleeding complications after trauma, dental procedures and family history of bleeding disorders) and current medications or herbal supplements that may cause coagulopathy (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], fish oil); and laboratory testing that includes haemoglobin (Hb), haematocrit, platelet count, and coagulation profile.<sup>[15,18]</sup>

In addition, providers should question the JW patient on specific blood product interventions that the physician may or may not use.

### Approach to pre-operative anaemia

The three main reasons for anaemia are blood loss, haemolysis and decreased erythropoiesis. In an acute setting, transfusion is usually recommended when Hb levels falls below 10 g/dL and is almost always required for Hb below 6 g/dL, with the understanding

that a certain low level of Hb puts the patient at an unacceptable risk.<sup>[15,19]</sup> But, a multicentre, randomised, controlled clinical trial demonstrated that a restrictive transfusion strategy (maintenance of Hb concentration at 7-9 g/dL) had a lower 30 days mortality compared to a liberal strategy (maintenance of Hb at 10-12 g/dL).<sup>[20]</sup>

Furthermore, there is physiological ability to adapt to low Hb levels and studies have shown that isovolemic drop in Hb in a healthy individual to as low of 4-5 g/dl is well tolerated without signs of hypoxia.<sup>[21,22]</sup> Isovolemic status can be achieved by infusion of isotonic crystalloids or colloids to maintain systolic blood pressure and tissue perfusion.<sup>[23]</sup>

Assessment of adequate oxygen (O<sub>2</sub>) delivery can be measured with mixed venous O<sub>2</sub> levels and O<sub>2</sub> extraction ratios; and is important in patients with cardiac or vascular disease. Also, the anticipated degree and rate of blood loss and O<sub>2</sub> consumption should be considered.<sup>[24]</sup>

For elective surgeries, pre-operative correction of anaemia (if Hb is < 7-8 g/dl) can be achieved by administering recombinant erythropoietin 3-4 weeks prior, high dose iron therapy for Iron deficiency and Vitamin B<sub>12</sub> and Folate as supplements for erythropoiesis.<sup>[25]</sup> For IV iron therapy, iron sucrose is preferred to iron dextrose because of fewer complication rates.<sup>[26]</sup>

### Correction of coagulopathy

Any anticoagulants, including but not limited to aspirin, NSAIDs, antiplatelet agents, and warfarin, should be discontinued for an appropriate period for coagulopathies to correct. The American Society of Anaesthesiologists (ASA) Task Force on Perioperative Blood Transfusion and Adjuvant Therapies recommends administration of Vitamin K or other warfarin antagonists if clinically acceptable.<sup>[15]</sup> Oral Vitamin K is preferred over intravenous route.<sup>[27,28]</sup>

As platelet concentrates, fresh frozen plasma and cryoprecipitate are not acceptable to JW prothrombin complex concentrate, which contains only factor II, VII, IX and X can be administered if JW accepts blood fractionates.<sup>[27]</sup> A more acceptable option is recombinant activated factor VII (rFVIIa) that is produced without using any human blood or plasma. Several trials have shown that rFVIIa helps control bleeding from surgery

or severe trauma, reducing the need for red blood cell (RBC) transfusions and improving haemostasis.<sup>[15,17]</sup> Case reports have shown successful use of rFVIIa during gastrointestinal bleeding, cardiac surgery, postpartum haemorrhage, and head trauma in JW patients.<sup>[17,29]</sup>

## INTRAOPERATIVE MANAGEMENT

One of the most important strategies to reduce the risk of transfusion in patients who refuse blood transfusion is to minimise blood loss. These can be grouped as surgical and anaesthetic measures.

### Surgical measures

Adopt principles of 'bloodless surgery', so as to reduce the need for blood transfusion in the perioperative period. Senior surgical staff with expertise in bloodless surgery have to operate on patients with high risk of bleeding. Use minimally invasive procedures, where possible (e.g., laparoscopic or endoscopic) or staged procedures.<sup>[30]</sup>

Surgeons can reduce blood loss by direct control of bleeding points, use of haemostatic devices such as diathermy and harmonic scalpel, infiltration of the surgical wound with local vasoconstrictors, and application of topical haemostatics such as fibrin glue or thrombin gel or bone wax. Also, patient positioning, such as elevation of the surgical site, and tourniquets can have a profound effect on the rate of bleeding.<sup>[17,25]</sup>

### Anaesthetic measures

Senior personnel should be involved. Venous congestion and venous ooze may be minimised by careful positioning and avoidance of high intra-thoracic pressures and hypercapnia. Regional techniques, where possible, will minimise blood loss. Serial measurement and correction of coagulation profile and ionised calcium should be considered in long cases.

Invasive monitoring should be considered to optimise tissue oxygen delivery, which is dependent upon Hb concentration, cardiac output and Hb saturation. These factors may be manipulated using fluids, inotropes and increasing the FiO<sub>2</sub>.

$$O_2 \text{ delivery (DO}_2\text{)} = \text{Cardiac Output} \times (1.39 \times \text{Hb} \times \text{SaO}_2) + 0.02 \times \text{PaO}_2$$

### Blood transfusion methods

#### Autologous blood transfusion

Jehovah's witness acceptance of autologous donation

and reinfusion remains at the discretion of the individual and often hinges on ensuring that the diverted blood is maintained in continuity with the circulatory system at all times. Of the three main techniques for autologous transfusion - pre-operative autologous blood donation (PAD), acute normovolemic haemodilution (ANH) and intra-operative and post-operative cell salvage, PAD is unacceptable to JW. ANH is a blood conservation technique and is done by collecting the patient's whole blood at the induction of anaesthesia with simultaneous infusion of a crystalloid or colloid solution to maintain a normovolemic status.<sup>[6,31]</sup>

Acute normovolemic haemodilution reduces blood viscosity, systemic vascular resistance and enhances cardiac output with reduced myocardial O<sub>2</sub> consumption while reinfusion of platelets and coagulation factors corrects any coagulopathy that arises out of perioperative blood loss. ANH is acceptable to JW only if it is done in a continuous circuit.

#### Acute hypervolemic haemodilution

An alternative and more acceptable approach is acute hypervolemic haemodilution, which does not involve withdrawal of blood. This technique has been studied in JW undergoing major surgery and found to be well tolerated.<sup>[32]</sup> This technique may be inappropriate in patients with cardiac compromise.

#### Intra and post-operative cell salvage: (Cell saver)

With the cell-saver technique, shed blood is suctioned from the wound, centrifuged, washed, mixed with an additive/anticoagulant solution and then re-infused via a filter (leucocyte depleted) as required. It may be acceptable to some JW if the blood is not stored and the circuitry is in continuity with the patient's own circulation. It is used when the expected blood loss is more than 20% of total body volume and has the advantage that the returned blood is warm and has normal concentrations of 2,3-diphosphoglycerate. It is contraindicated in situations, where the blood is likely to be contaminated (e.g., sepsis, contamination with intestinal contents, and malignant disease) and sickle-cell anaemia.

#### Red blood cell substitutes

The problems associated with the supply, storage and safety of blood has led to the research for RBC alternatives. Two major groups of Red cell substitutes are perfluorocarbons and Hb solution. Hb based oxygen carriers (HBOCs) are chemically modified

Hb solutions containing polymerised, conjugated, or liposome-encapsulated Hb.<sup>[33]</sup>

Currently, HBOCs are not approved by the U.S. Food and Drug Administration (FDA) and remain in phase III clinical trials. While reports showed that HBOCs may improve chances of survival from anaemia secondary to acute bleeding or haemolysis, studies also found an increased chance of adverse events, including myocardial infarction and pulmonary hypertension.<sup>[34]</sup> Numerous case reports have described the use of HBOC on compassionate grounds as a bridge in severely anaemic JWs before erythropoiesis recovers.<sup>[35-37]</sup>

## HYPOTENSIVE ANAESTHESIA

Deliberate or controlled hypotension during the intra-operative period is a method to reduce blood loss. Usually, it is achieved by a reduction in systemic vascular resistance and/or cardiac output. Most studies define the criteria for this technique as a reduction of systolic blood pressure to 80-90 mmHg, a mean arterial pressure (MAP) of 50-65 mmHg, or a 30% reduction in baseline MAP.<sup>[38]</sup> The MAP range is based on the lower limits of autoregulation of cerebral blood flow.<sup>[39]</sup>

Various pharmacological and nonpharmacological means can induce hypotension. Pharmacological agents can be primary (used alone only) and include inhalational agents (e.g., halothane, isoflurane, sevoflurane), vasodilators (e.g., nitroglycerin, sodium nitroprusside, trimethaphan, adenosine, alprostadil), remifentanyl, propofol and spinal anaesthesia or secondary agents (used as adjuncts to primary) that include angiotension converting enzyme inhibitors, clonidine, dexmedetomidine, calcium channel blockers,  $\beta$ -adrenoreceptor antagonists and fenoldopam.

Positioning the operative field above the heart reduces the hydrostatic blood pressure thereby decreasing extravasation of blood. Induced hyperventilation can cause hypocapnia leading to cerebral vasoconstriction and decreased blood loss in neurosurgical patients.<sup>[38]</sup>

## DELIBERATE HYPOTHERMIA

Controlled lowering of the body temperature can decrease metabolic O<sub>2</sub> consumption and used in patients who refuse blood transfusion. Lowering the body temperature to 30-32°C can decrease total body O<sub>2</sub> consumption by approximately 48% (approximately 7% for each degree drop) below basal levels and increase

dissolved O<sub>2</sub> in blood. A fall in temperature below this can cause hypothermia induced arrhythmias, hence, temperature monitoring is a must.

Controlled cooling is attained by decreasing ambient room temperature, decreasing temperature of intravenous fluids, or using a cooling blanket. It should always be used in conjunction with ANH to counteract hypothermia-induced increases in blood viscosity and systemic vascular resistance. Although hypothermia causes an increased affinity between oxygen and Hb, 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.

## PHARMACOLOGICAL AGENTS

Apart from the ones mentioned earlier, blood loss can be minimised by using haemostatic agents such as:

### Antifibrinolytics

Widely studied and used agents are synthetic lysine analogues ( $\epsilon$  - aminocaproic acid and tranexamic acid) and aprotinin. While 2006 ASA practice guidelines advocates the use of antifibrinolytics in cases where significant blood loss is anticipated, a 2008 blood conservation using Antifibrinolytics in a Randomised Trial (BART) questioned the ASA recommendations.

### $\epsilon$ - Aminocaproic acid and tranexamic acid

$\epsilon$  - Aminocaproic acid and tranexamic acid act by inhibiting plasmin mediated fibrinolysis. These agents attach to the lysine binding site serine protease plasminogen, preventing plasminogen's activation into plasmin when co-localised to fibrin.<sup>[40]</sup>

Though reliable data is available in reducing pre-operative blood loss and transfusion requirements in cardiac surgeries, the data with respect to safety and dosing are not consistent and need further large safety trials.<sup>[41]</sup>

### Aprotinin

Aprotinin is a non-specific serine protease inhibitor and earlier was recommended for decreasing blood loss and transfusion during coronary artery bypass surgeries.<sup>[42]</sup> As the 'BART' study demonstrated that the aprotinin increased mortality secondary to its adverse effects on renal and cardiac function, its use has been limited to investigational purposes only.

## Desmopressin

Desmopressin (1-deamino-8-d-arginine vasopressin) is a synthetic analogue of the vasopressin. It has poor vasopressor activity and enhanced antidiuretic activity, but it notably serves as a haemostatic agent. It stimulates the endothelial release of factor VIII and von Willebrand factor, enhancing platelet aggregation.<sup>[25]</sup> Its use for haemophilia and von Willebrand disease is well established. However, evidence does not support its use in patients without bleeding disorders.<sup>[25,40]</sup>

## POST-OPERATIVE MANAGEMENT

During the immediate post-operative period, many of the previously discussed methods remain applicable. Requirement for monitoring the patient in intensive care unit whenever major blood loss is anticipated should be kept in mind. The non-invasive techniques include close surveillance for bleeding, adequate oxygenation, and restricted phlebotomy. Post-operative cell salvage is effective in managing blood loss and subsequent anaemia. Pharmacological methods include the administration of haemostatic agents to stop bleeding, erythropoietic agents to promote erythropoiesis, antihypertensives to reduce rebleeding, and the conservative use of anticoagulants and antiplatelet agents. Maintaining normovolemia with crystalloid or colloid solutions in the face of anaemia is crucial to maintaining adequate tissue perfusion.

## SUMMARY

The number of JW is on the rise worldwide, and management of patients who refuse blood transfusion is replete with innumerable challenges. Treating JW involves ethical and legal issues as well as the need for planning and execution of strategies to maintain normovolemia as well as O<sub>2</sub> delivery. The bedrock of management include counselling patients about blood salvage techniques, optimisation of pre-operative haematological abnormalities and adopting techniques to minimise blood loss, and blood conservation throughout the perioperative period.

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