



## Perioperative Management of Patients Refusing Blood Products

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### Abstract

The Jehovah's Witnesses are best known to outsiders for their refusal of blood products, even such a refusal may result in death. In years, a "bloodless surgery" was developed with the aim of avoid blood transfusions and improve patient outcome, shifting from a product-centred to a patient-centred approach. An accurate teamwork is needed to define a perioperative transfusion-alternative program, individualized for patients' characteristics and surgical procedure. The objective of this article is to review how to properly manage, in the perioperative period, patients who refuse blood transfusions.

### Keywords

Blood transfusion refusal, Jehovah's Witnesses, Transfusion alternative program, Perioperative management

### Manuscript Body Text

Two surveys, performed in 1981 and 1995, reported that about 80% of physicians have treated at least one JW in emergency surgery and more than 50% of physicians have transfused patients when needed, despite signed refusal statement [6,7]. In case of massive bleeding, more than 50% of physicians stated they did not regret their decision, while 26% of them would not tell the patient about transfusion [8]. To better provide medical assistance to these patients, it's important to know the precise position of the JW on medical treatment and which blood products are acceptable to them: whole blood, packed red cells, platelets, plasma and preoperative autologous donation (PAD) are totally unacceptable. Matter of personal choice are the use of albumin, immunoglobulins and clotting factors [9,10]. JW who accept blood products forbidden, would be subjected to permanent disfellowship and excommunication from the church, followed by enforced shunning and social isolation by their own family members, relatives and friends [11]. Patient's will must have been accurately communicated and documented in medical record, because the refusal of medical treatment from an adult patient must be respected by the clinicians, whatever the reasons for such refusal. While in USA autonomy is generally interpreted by referring to respect for a person's privacy and the right to be left in peace, the European approach tends to place a limit on the right to autonomy in the form of the duty to assist and save persons exposed to serious danger, particularly life-threatening events. In regard to the degree to which pre-treatment declarations are held to be binding, Article 9 of the Convention on Human Rights and Biomedicine states that "The previously expressed wishes relating to a medical intervention by a patient who is not, at the time of intervention, in a state to express his or her wishes shall be taken into account" [1,12]. The only exception to patient wish to reject blood transfusion in case of life treat, is for children not came of age. In such cases the social authorities are called in and the children are taken care of [13]. Not only JW refuse blood transfusion, there is a recent increase in popularity of transfusion avoidance strategies along with a generally greater awareness among physicians of transfusion risks (ABO incompatibility, infections, immune suppression) and escalating costs. This approach is called "bloodless surgery", shifting from a product-centred approach to

### Introduction

Jehovah's Witnesses (JW) originated near Pittsburg (Pensylvania) in the 1870s, when Charles T. Russel formed a movement based on a literal millennialist interpretation of the Bible. However, it was until 1945 that the Watch Tower Bible and Tract Society (the legal organization of leaders of the Congregation of JW, usually known simply as the Watch Tower Society) concluded that blood transfusions are contrary to divine law. JW refuse transfusions of whole blood, of red and white corpuscles, platelets and plasma. They also refuse both natural and recombinant haemoglobin, although positions differ among them regarding blood-derived products such as albumin, immunoglobulin and coagulation factors [1,2]. The ethical and legal issues raised by the refusal of a potentially life-saving transfusion are dramatic and they are a matter of debate even among JW; for these reasons perioperative caring of these patients can be a challenge for clinicians [3,4]. Furthermore, there is a recent increase in popularity of transfusion avoidance strategies along with a generally greater awareness among physicians of transfusion risks and escalating costs. This approach is called "bloodless surgery", aimed to improve patient outcome [5]. This article reviews how to properly manage, in the perioperative period, patients who refuse blood transfusions.

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patient-centred approach, defined as “the timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize haemostasis and minimize blood loss in an effort to improve patient outcome” [5]. The bloodless medicine was initially developed to provide necessary treatment to patients of this faith, but administering bloodless care to JW, valuable lessons can be learned about the transfusion avoidance strategies.

A team approach is needed to define a perioperative transfusion-alternative program that has to be based on three basic principles: anemia tolerance, optimize red blood cell mass and minimize blood loss. The perioperative transfusion-alternative protocol must be individualized for patients' characteristics and surgical procedure, choosing the combination of different strategies. Preoperative planning involves estimating the patient's blood volume, the expected blood loss and defining a tolerable transfusion threshold. If blood losses are provided to be higher than the transfusion threshold, an increase in preoperative hematocrit, increasing the red blood cell mass, and a reduction in threshold for allogenic blood transfusion have to be considered.

The first pillar of the transfusion-alternative protocol is the appropriate tolerance of anemia, in particular acute normovolemic anemia. This involves reconsidering the standard policy on anemia treatment. Some still use a transfusion trigger of a hematocrit of 30% or a hemoglobin level of 10 g/dl for all patients, thresholds that date back to an article by Adams and Lundy published in 1942. Literature shows the importance to maintain a normovolemia via simple volume replacement. With adequate volume, oxygen consumption is maintained over a wide range of hemoglobin levels. The two main mechanisms responsible for the maintenance of adequate tissue oxygenation are an increase in cardiac output and an increase in tissue oxygen extraction. The first mechanism results from the decreased blood viscosity and sympathetic stimulation. The second mechanism results from a redistribution of blood flow to areas of high metabolic demand and from improved microcirculation. Preoperative planning requires a careful clinical assessment of the bleeding risks and a thorough laboratory screening, including standard hematological parameters [14]. It's easy to understand the importance of extensively question patient for previous suspect bleeding episodes and medications affecting coagulation (e.g. NSAIDs, steroids). Standard coagulation tests screen are of main concern, but in some hospitals preoperative coagulation advanced assessment involve the use of viscoelastic tests, thromboelastography (TEG) or rotational-thromboelastometry (ROTEM), to study and correct any abnormalities in platelet function, clot strength, and fibrinolysis. Viscoelastic tests can be used also during the intraoperative period to reduce blood loss, red cell transfusion requirement and critical care duration [15,16].

The second basic principle of the transfusion-alternative protocol is to optimize red blood cell mass with iron, folate or vitamin B12. To improve the hemoglobin values, even without anemia, it's possible to require haematology expertise to augment red cell mass using human recombinant erythropoietin, approved by the United States Food and Drug Administration for the treatment of anemia secondary to chronic renal failure, secondary to zidovudine therapy in patients with HIV infection, and secondary to cancer chemotherapy. Many JW accept erythropoietin off-label indications to maintain and enhance erythropoiesis [17].

Another way to prepare JW patient to surgery, is to optimize hemodynamic to get the highest O<sub>2</sub> tissue delivery (DO<sub>2</sub>); one of the main determinant of DO<sub>2</sub> is the cardiac output (CO) and hemoglobin concentration has, indeed, a minor role. A meta-analysis of eighteen studies [18] assessed the impact of blood transfusion on DO<sub>2</sub>: four studies did not reveal any change in DO<sub>2</sub>; the other studies reported an increased in DO<sub>2</sub>, with no effect on O<sub>2</sub> peripheral extraction (VO<sub>2</sub>) in nine of them. These results suggest the importance of adaptive mechanisms to maintain VO<sub>2</sub> independently of DO<sub>2</sub> by increasing cardiac output and tissue oxygen extraction. The hemoglobin cut-off may therefore be ineffective to assess the need for red blood cell

transfusion [19]. In critically ill patients, anemia should be managed to avoid oxygen supply dependency (oxygen delivery less than twice consumption) and to maintain moderate oxygen delivery reserve (DO<sub>2</sub>/VO<sub>2</sub> > 3) [20].

The third pillar of the transfusion-alternative protocol is to minimize blood loss, either by minimizing the bleeding or by recovering shed blood. Patient positioning and the maintenance of normothermia are simple cost-effective techniques to reduce bleeding. Surgical haemostasis is of main relevance and must be matter of priority. Diathermy dissection, harmonic scalpel and LigaSure device are safe and effective surgical tool, which can reduce blood loss. Bone wax, absorbable cellulose or collagens are also useful to minimize bleeding risk. Less invasive techniques are associated with less blood loss and should be always considered. Splitting surgical time, in bilateral surgery, can avoid excessive bleeding. During surgery, one of the best and safest way to prevent excessive bleeding, is hypotensive anesthesia (MAP to 50-65 mmHg) to reduce the extent of intraoperative blood loss [21]. One of the major treat during haemostasis in controlled hypotension, is the underestimation of bleeding. This could result in severe postoperative hemorrhage. It's mandatory to test the haemostasis once blood pressure is returned to normal. On the other hand, excessive hypotension and preoperative alteration in organ perfusion, can result in irreversible ischemic damage to kidneys, brain or myocardium [22]. To make blood lost during surgery with a low haemoglobin concentration, it's possible to perform acute normovolaemic haemodilution (ANH): the removal of whole blood from the patient before surgery, replacing it with fluids to keep adequate blood volume. As previously stated, the first physiological compensation to the acute blood loss is an increase in cardiac output, stroke volume, heart rate and, consequentially, oxygen extraction [23]. The removed blood is available for transfusion if needed. ANH is accepted by JW, only if it's kept in a closed circuit [24]. To transfuse back blood to the patient, it's possible to perform cell salvage collecting blood removed by suction and give back to the patient. Re-administering cell salvage blood with tumour cells could seem dangerous in oncologic surgery, but any oncologic patient has already a high rate of haematogenous dissemination of cancer cells without any correlation with survival [25]. To avoid any risk of iatrogenic metastasis, even if only theoretical, the use of leucocyte depletion filters removes tumor cells in a highly effective way and, in medical literature, no increase in metastasis or mortality has been reported using leukocyte depletion filter [26-30]. Reducing blood loss with early detection of possible postoperative bleeding, is mandatory. In case of refusal of blood transfusion, any hemorrhagic source should be fast surgically controlled with a damage control approach. To avoid blood loss due to postoperative laboratory tests, blood samples were collected in pediatric tubes [27]. To reduce need for blood samples, it's also possible to monitor hemoglobin with noninvasive devices: the use of Continuous Noninvasive Hemoglobin Monitoring (CNHM) is an accurate option to serial laboratory tests, reducing iatrogenic blood loss, saving blood volume. During postoperative monitoring, it's likewise fundamental to improve erythropoiesis if needed and the preoperative hemodynamic optimization should be continued until patient has low hemoglobin level [31-34].

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