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ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

Can bloodless surgery be applied to every patient undergoing major abdominal surgical intervention?

OBJECTIVE To evaluate the outcome of patients undergoing bloodless surgery compared with patients who did not refuse transfusions and to evaluate the possible extension of a relevant protocol to patients undergoing surgery to reduce the use of autologous blood transfusions. **METHOD** A retrospective study was performed with Jehovah's Witness patients undergoing major abdominal surgery between 2009 and 2013 at the Department of Surgical Sciences, "Sapienza" University of Rome, with no blood transfusions, compared with a homogeneous control group of patients undergoing similar major abdominal surgery performed by the same team in the same period. The type of surgery and the use of hemostatic agents for all the enrolled patients were recorded and analyzed. **RESULTS** The study group consisted of 55 Jehovah's Witness patients (33 males, 22 females; mean age 61.7 years, range 33–84 years) and 55 control patients (25 males, 30 females; mean age 74.1 years, range 48–90 years). There was no intraoperative or postoperative bleeding, and no cardiorespiratory complications were observed during or after surgery among the patients in the study group. This study showed that bloodless surgery is not associated with a greater number of complications. The postoperative recovery was comparable to that of transfused patients undergoing standard surgical procedures. **CONCLUSIONS** The present study demonstrates that bloodless surgery is feasible and safe when conducted according to a specific protocol by an experienced and dedicated multidisciplinary team. It is suggested that the protocol followed for bloodless surgery be further evaluated in prospective studies, involving traditional surgery in order to evaluate the benefits of minimization of blood loss.

Bloodless surgery is an approach that was introduced in the 1960s for simple avoidance of the use of allogenic blood transfusion. Bloodless surgery and medicine (BSM) is defined as "the timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis and minimize blood loss in an effort to improve patient outcome".¹

The practice was developed initially in response to the religious requirements of patients, especially Jehovah's Witnesses, who believe that blood transfusion is forbidden by God because a passage in the Bible (Acts 15: 19–21) states: "... Abstain from what is strangled and from blood". The need to treat these patients gave impetus to the development of intraoperative techniques that minimize blood loss and medical strategies to prepare the patient for bloodless surgery.

This kind of surgery also responds to other needs; limited blood supplies can be used more effectively, costs can be reduced and the safety and efficacy of blood transfusion can be improved. The aims of this study were to evaluate the outcome of patients undergoing bloodless surgery compared with that of patients who do not refuse transfusions, and to evaluate the possible extension of a bloodless surgery protocol to other patients undergoing surgical intervention, in order to reduce the use of autologous blood transfusion.

MATERIAL AND METHOD

A retrospective study was performed which enrolled Jehovah's Witness patients undergoing major abdominal surgery between

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Η χειρουργική επέμβαση χωρίς
μετάγγιση αίματος μπορεί να
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της κοιλιάς;

Περίληψη στο τέλος του άρθρου

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2009 and 2013 at the Department of Surgical Sciences, "Sapienza" University of Rome and compared them with a homogeneous control group of patients undergoing similar major abdominal surgery performed in the standard way by the same team over the same period.

The patients in the Jehovah's Witness group and the control group were prepared for surgery following a well-defined protocol described below. A multidisciplinary team of surgeons, anesthesiologists, nurses and a hematologist working in the transfusion center ensured the comprehensive approach required for a successful outcome. The protocol is divided into three integrated phases: pre-operative, intra-operative and post-operative.

Pre-operative phase

The patients were given information concerning the surgery and put on the waiting list. Pre-admission tests, including electrocardiogram, chest X-ray, spirometry and blood tests were performed in order to assign the patient an ASA score and define the surgical risk. Informed consent was secured for surgery and anesthesia, and the consent/refusal for blood transfusions and or the administration of other blood components was elicited. The possible increased risk associated with the refusal of blood transfusion was discussed with each patient in the study group, who then signed a specific form detailing the refusal of blood products.

According to the official authority, Jehovah's Witnesses refuse transfusion of allogenic whole blood, red blood cells (RBCs), white blood cells (WBCs), platelets (PLTs), plasma, and preoperative autologous blood. They may accept non blood volume expander, drugs to enhance hemostasis (tranexamic acid, aprotinin), hematopoietic growth factors and hematinics, including erythropoietin (EPO), folic acid or iron supplementation, recombinant products (coagulation factors) and hemostatic agents (collagen, gelatin-based hemostasis).

Article 11 of the Italian Ministerial Decree 3.3.2005 states that a person receiving or refusing a transfusion of blood and or blood products, must be previously informed and must express consent/dissent in writing. The only exception to this obligation to obtain written consent is in cases involving imminent danger to life, where the physician is authorized to transfuse blood without the patient's consent (8 D.M. 1.9.1995, article 4).

The study protocol included the avoidance of medications that increase bleeding (aspirin, NSAIDs, anticoagulants, antiplatelets), if allowed by the patient's condition. Programmed substitution therapy with low molecular weight heparin could be given, if necessary.

Disorders secondary to kidney disease, liver disease or platelet dysfunction were identified and corrected. Jehovah's Witnesses affected by anemia were treated with EPO, iron, vitamin B and folate. The use of EPO as a synthetic drug began in 1989; EPO was initially used in patients with anemia undergoing dialysis and its use was then extended to patients affected by chronic renal failure. The

drug used in the study, EPREX[®], contains epoetin alfa (40,000 IU/mL) and is produced by recombinant DNA technology in Chinese hamster ovarian cells. Iron deficiency must be excluded before starting treatment with EPREX[®]. In the case of iron deficiency, the treatment should be given orally (200/300 mg per day) in order to maintain efficient erythro-differentiation. During the study, this treatment achieved an increase in the hemoglobin level (Hb) of 1–3 g/dL.

The patients in the control group were not treated with EPO or iron supplementation. In the case of severe anemia the control patients were transfused pre-operatively.

Intra-operative phase

The patient was positioned so as to reduce venous pressure and maintained in normothermia. Acute hypervolemic hemodilution was achieved by giving plasma substitutes without the removal of autologous blood. Colloids (approximately 15–20% of hematocrit) were infused quickly (100 mL/min) before starting the intervention. To prevent the hemodynamic effects linked to the hypervolemic state, drugs that induce vasodilation were used; the hypervolemia decreases as the intervention progresses as a result of blood loss. Intra-operative blood salvage (IBS), which is also known as intraoperative autologous transfusion, intraoperative salvage or intraoperative autotransfusion, was organized. In this process, the surgeon aspirates blood from the surgical field through an aspirator connected to dual-channel tubing; in this way the blood is mixed with anticoagulant as it is being aspirated. The aspirated blood is collected in a reservoir and then pumped into a centrifuge bowl, where it is concentrated and then washed with an isotonic electrolyte solution. The processed red cell suspension is then pumped from the centrifuge bowl into an infusion bag. IBS allows the team to salvage about 50% of blood lost during surgery² from the surgical field. An adequate depth of anesthesia and muscle relaxation was set in order to avoid hypertension and hypercapnia. Meticulous surgical technique and careful hemostasis, using local hemostatic agents or an antifibrinolytic in selected cases, limited bleeding.

In the control group, intra-operative blood salvage was not scheduled. For the operation, two bags of blood were required, ready for transfusion, with two further bags of blood available. The patients were transfused if it was considered necessary. The rest of the surgery protocol was similar.

Post-operative phase

The post-operative bleeding and Hb were monitored in all patients. Certain initiatives, such as the prevention of hypertension and pain, administration of iron and vitamin B, folate and EPO to maximize blood production, and thromboembolic prophylaxis were considered basic to the protocol effectiveness for the Jehovah's Witnesses. The control group patients were transfused with blood when necessary and some were also treated with iron supplementation and folic acid.

RESULTS

The study group consisted of 55 Jehovah's Witnesses (33 males, 22 females; mean age 61.7 years, age range 33–84 years). Of the 55, 31 patients with Hb >13 g/dL were not treated with EPO, iron or folic acid but 19 patients with Hb between 10 and 13 g/dL were treated with 40,000 IU EPO (subcutaneous injection) weekly, and also with oral iron and folic acid, starting about 10 days before surgery.

There were 5 patients with Hb <10 g/dL, and these were treated with EPO 40,000 IU weekly (subcutaneous injection), plus oral iron and folic acid, starting about 21 days before surgery. In patients treated with EPO, the mean increase in Hb was approximately 1 g/dL. Preoperatively, the mean Hb was 11.88 g/dL. Seven days prior to surgery, 7 patients stopped their antiplatelet or anticoagulant therapy, which was substituted with enoxaparin sodium (Clexane® 4,000–6,000 IU).

No intraoperative or postoperative bleeding was recorded and no cardiorespiratory complications were observed either during or after surgery in the study patients. Antiplatelet therapy with enoxaparin sodium was started postoperatively in 31 patients. Therapy with EPO, iron and folic acid was continued in 15 patients for one week following surgery.

In the study patients, the mean Hb was 12.50 g/dL immediately after surgery, 11.91 g/dL the first day after surgery and 11.41 g/dL at discharge. On average, discharge took place on post-operative day 10.23.

A control group of 55 patients (25 males, 30 females, mean age 74.1 years, range 48–90 years) was enrolled. The mean preoperative Hb in the control patients was 10.34 g/dL and 47 patients were transfused during surgery and 11 after surgery. Of the 47 patients transfused during surgery, 6 were also treated postoperatively with iron and folic acid. The mean Hb of the control group was 11.36 g/dL immediately after surgery, 10.92 g/dL the first day after surgery and 10.29 g/dL at discharge.

Postoperative antiplatelet therapy with enoxaparin sodium was administered in 35 patients. There was no intraoperative or postoperative bleeding. One patient suffered severe respiratory failure during the first postoperative day, which was treated successfully with non-invasive ventilation (NIV). On average, discharge took place on post-operative day 11.

The surgical procedure and the use of hemostatics for the study and the control patients are shown in tables 1 and 2, respectively.

Table 1. Surgery distribution for patients enrolled in the study.

Surgical procedure	Jehovah's Witnesses n=55	Control group n=55
Transurethral bladder resection	4	2
Radical prostatectomy	3	1
Hysterectomy and ovariectomy	6	2
Transurethral prostatectomy	13	–
Nephrectomy	7	2
Appendicectomy	1	–
Omentectomy	1	1
Adrenalectomy	1	–
Exploratory laparotomy	2	2
Rectum resection	3	7
Total gastrectomy	3	3
Splenectomy	1	1
Ileostomy closure	2	1
Colostomy closure	1	2
Right colectomy	3	12
Subtotal gastrectomy	2	4
Colectomy	2	5
Ovariectomy	–	2
Left colectomy	–	3
Esophagectomy	–	1
Colostomy	–	1
Abdominoperineal resection of the rectum (Miles operation)	–	3

Table 2. Characteristics and dosage of hemostatics administered to minimize blood loss during abdominal surgery.

Hemostatics	Jehovah's Witnesses n=55	Control group n=55
Floseal 5 mL	18	3
Floseal 5 mL (2 units)	4	3
Floseal 5 mL (5 units)	1	–
Floseal 5 mL + Tisseel 4 mL	2	1
Floseal 5 mL + Quixil 1 mL	2	–
Floseal 5 mL + Surgiflo	1	–
Floseal 5 mL×2 + Evicel 5 mL	2	4
Tissucol 1 cc	1	–
Tisseel 4 mL	1	3
Evicel 5 mL	1	4
Evicel 2 mL + Tisseel 2 mL	1	–
Surgiflo	6	2

DISCUSSION

Bloodless surgery was developed initially to respond to the religious needs of certain patients, especially in the treatment of Jehovah's Witnesses. Nowadays, however, bloodless surgery also meets other needs, such as helping to deal with limited blood supplies, saving on costs, and enhancing the safety and efficacy of blood transfusions.

Concerning the limited blood supplies, in Italy the National Institute of Health reported an increase of 38% in donations from 2000 to 2012, and currently the country has achieved self-sufficiency for the approximately 2.4 million blood units needed each year in Italian hospitals. A large gap in sufficiency remains between North and South Italy, which can only be solved by the transfer of blood units from one region to another. In addition, there are months of the year when demand is greater and availability is lower. Moreover, even though blood donation is free, the costs of collection, preparation and distribution are high.

Regarding safety, many patients refuse a transfusion because they are afraid of contracting blood-borne diseases such as human immunodeficiency virus (HIV) and hepatitis. Currently, thanks to the use of more sensitive tests and more scrupulous donor recruitment procedures, the incidence of hepatitis C and HIV associated with transfusions has almost been eliminated in Western countries (<0.9%), although it remains high in developing nations. Finally, there remains the problem of adverse reactions to transfusions, described in certain studies that report an increase in morbidity in transfused patients.⁷

The present study showed that bloodless surgery need not be associated with a greater number of complications and that postoperative recovery is comparable to that of transfused patients. A multidisciplinary approach is essential to achieve these results. The aim is to achieve an increase in Hb preoperatively, to reduce intraoperative blood loss and to establish close postoperative monitoring for the early detection of possible bleeding.

In this study, there was no need for intraoperative blood salvage, which still remains an excellent tool in the event of major intraoperative blood loss. A larger amount of hemostatic agents was used in the Jehovah's Witnesses, but only as a preventive measure.

A preoperative increase in Hb can be achieved with the administration of EPO, along with iron and folic acid. In this study an increase in Hb of about 1–2 g/dL was obtained. It might be helpful to extend this multidisciplinary approach to carefully selected patients about to undergo major abdominal surgery as this would allow a reduction in blood transfusion.

Clinical trials have shown that preoperative treatment with EPO reduced the need for transfusion by up to 75% in patients operated on for total hip arthroplasty, whose preoperative Hb was 10–13 g/dL.⁴

Certain studies have shown that transfused patients were likely to suffer increased mortality, length of hospital stay and end organ dysfunction.^{7,5–10}

It is essential to stress that a multidisciplinary approach and very careful planning are required in order to achieve safe, effective bloodless surgery. Specifically, the success of bloodless surgery requires a dedicated team composed of surgeons, anesthesiologists, nurses and hematologists working in the transfusion center.

In conclusion, the present study demonstrates that a bloodless surgery is feasible and safe when applied according to a specific protocol, by an experienced and dedicated multidisciplinary team. Bloodless surgery, introduced to treat Jehovah's Witnesses, who refuse blood transfusions for religious reasons, nowadays also meets other needs such as the reduced availability and high cost of blood and the hazards of transfusion. According to the experience of the authors, bloodless surgery could and should be proposed to all patients undergoing major abdominal operations.

ΠΕΡΙΛΗΨΗ

Η χειρουργική επέμβαση χωρίς μετάγγιση αίματος μπορεί να εφαρμοστεί σε κάθε ασθενή που υποβάλλεται σε μείζονα επέμβαση της κοιλιάς;

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ΣΚΟΠΟΣ Αξιολόγηση της πορείας της χειρουργικής επέμβασης χωρίς μετάγγιση αίματος σε σύγκριση με ασθενείς που δεν αρνούνταν τις μεταγγίσεις και αξιολόγηση ενός πιθανού πρωτοκόλλου ασθενών οι οποίοι θα χειρουργη-

θούν, με στόχο τη μείωση χρήσης αυτόλογων μεταγγίσεων. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Διεξήχθη μια αναδρομική μελέτη σε Μάρτυρες του Ιεχωβά που υποβλήθηκαν σε μείζονες χειρουργικές επεμβάσεις στην κοιλιά κατά το χρονικό διάστημα 2009–2013 στο Department of Surgical Sciences, “Sapienza” University of Rome. Οι εν λόγω ασθενείς συγκρίθηκαν με μια ομοιογενή ομάδα ελέγχου που υποβλήθηκαν σε μείζονες χειρουργικές επεμβάσεις στην κοιλιά από την ίδια ομάδα στην ίδια χρονική περίοδο. Καταγράφηκαν και αναλύθηκαν η χειρουργική επέμβαση και η χρήση αιμοστατικών παραγόντων. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Αξιολογήθηκαν 55 ασθενείς, Μάρτυρες του Ιεχωβά (33 άνδρες και 22 γυναίκες, μέση ηλικία τα 61,7 έτη, διακύμανση 33–84 έτη), και 55 ασθενείς ελέγχου (25 άνδρες και 30 γυναίκες, μέση ηλικία τα 74,1 έτη, διακύμανση 48–90 έτη). Δεν παρουσιάστηκε αιμορραγία κατά τη διάρκεια της επέμβασης ή και μετά από αυτή, ούτε καρδιοπνευμονικές επιπλοκές κατά τη διάρκεια και μετά την επέμβαση. Φάνηκε ότι η επέμβαση χωρίς μετάγγιση αίματος δεν συνοδεύεται από μεγαλύτερο αριθμό επιπλοκών. Η αποκατάσταση μετά το χειρουργείο ήταν συγκρίσιμη με τους ασθενείς που έλαβαν μεταγγίσεις. **ΣΥΜΠΕΡΑΣΜΑΤΑ** Η εμπειρία μας δείχνει ότι η χειρουργική επέμβαση χωρίς μετάγγιση αίματος είναι δυνατή και ασφαλής, με την εφαρμογή ενός ειδικού πρωτοκόλλου από μια έμπειρη χειρουργική ομάδα. Το πρωτόκολλο αυτό θα πρέπει να αξιολογηθεί με επιπλέον προοπτικές μελέτες που αφορούν στην κλασική Χειρουργική, με στόχο τη μείωση των απωλειών αίματος.

Λέξεις ευρητηρίου: Επέμβαση στην κοιλιά, Ερυθροποιητίνη, Μάρτυρες του Ιεχωβά

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